Nutrición Hospitalaria

Nutr. Hosp. (2001) XVI (6) 239-256
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Use of Pro-, Pre- and Synbiotics in the ICU - Future options

S. Bengmark*, A. García de Lorenzo** y J. M. Culebras***

** Departamento de Cirugía, Universidad de Lund, Suecia. ** Servicio de Cuidados Intensivos, Hospital Universitario La Paz, Madrid. *** Servicio de Cirugía II, Hospital de León, León, España.*

Abstract

Although the word synbiotics was coined to describe the combined action of pre- and probiotics, the ability to, like antibiotics, control infection, the term is now increasingly used in a wider sense, as a name for all the substances released by microbial fermentation in the lower gut. One obvious reason is that most of the substances released seem to influence the immune defense, increase resistance to disease, and, most important, prevent complications to surgery such as infections and thrombosis. Protection layer of lactobacillus does not exist only on the GI tract mucosa, it is important at all exterior body surfaces including those of the eye, the nose, the mouth, the respiratory tract, the vagina, not to forget the skin. It is clearly reduced at all sites when the patient is in the settings of ICU.

Each human being has his/her own unique microbial collection, especially of strains of *Bifidobacterium* and *Lactobacillus,* and it should be possible to identify an individual on the basis of his/her personal intestinal microflora.

The flora seems always to be significantly reduced in the sick, especially in connection with severe disease, care in ICU, and in patients with little food intake or on parenteral nutrition. Supply of both pre- and probiotics can modify functions such as appetite, sleep, mood and circadian rhythm, and this most likely through metabolites produced by microbial fermentation in the gut. Supply of lactic acid bacteria (LAB) can also significantly reduce serum levels of a variety of toxins such as endotoxin.

An umbrella of supplemented probiotics could provide to the patients with liver cirrhosis a tool to reduce spetic manifestations and the incidence of bleeding. LAB are effective in controlling diarrhea of both bacterial and viral origin. A series of experimental studies and se-

Correspondencia: Abelardo García de Lorenzo.
Formación Médica Continuada.
Hospital Universitario La Paz.
P.º Castellana, 261
Madrid, España
fmc@hulp.insalud.es

Recibido: 5-V-2001.
Aceptado: 12-VIII-2001.

EL USO DE PRO, PRE Y SIMBIÓTICOS EN CUIDADOS INTENSIVOS: POSIBILIDADES FUTURAS

Resumen

Aunque la palabra simbióticos fue acuñada para describir la acción combinada de pre y probióticos de controlar la infección, como los antibióticos, el término se utiliza cada vez en sentido más amplio, incluyendo todas las sustancias que son liberadas en el intestino distal por fermentación bacteriana. Una razón obvia es que la mayor parte de esas sustancias parece tener influencia en los mecanismos de defensa, en la resistencia a la infección y, lo que es más importante, en la prevención de complicaciones quirúrgicas tales como infecciones y trombosis. La capa protectora de lactobacillus no está presente únicamente en el tracto gastrointestinal. Es importante también en las superficies externas del organismo, el ojo, la nariz, la boca y el tracto digestivo, la vagina y la piel. Se reduce claramente en todos estos lugares cuando el paciente se encuentra en la unidad de cuidados intensivos.

Cada ser humano tiene su colección única de microbios, con cepas específicas de bifidobacteria y lactobacilli, y sería posible identificar a los individuos a través de su microflora intestinal personal.

La flora parece reducirse siempre de manera significativa en los enfermos, especialmente en enfermedades graves, en cuidados intensivos, en pacientes con ingesta alimentaria reducida y en los sometidos a nutrición parenteral. El suplemento de pre y probióticos puede modificar el apetito, el sueño, el estado anímico y el ritmo circadiano, probablemente a través de metabolitos producidos por la fermentación microbiana en el intestino. La administración de bacterias del ácido láctico también reduce de manera significativa los niveles séricos de una variedad de toxinas, como la endotoxina.

Un paraguas de suplemento de probióticos podría facilitar a pacientes con cirrosis una herramienta para protegerse frente a manifestaciones sépticas y a hemorragia. Las bacterias del ácido láctico son efectivas en controlar la diarrea tanto de origen bacteriano como viral. Una serie de experimentos clínicos no controlados

veral uncontrolled clinical studies support the idea of using probiotics in patients with IBD. Ecoimmunonutrition with pre- pro- and synbiotics offer to be suitable tools in the new millenium.

(Nutr Hosp 2001, 16:239-256)

Key words: **Econutrition. Symbiotics. Critical Care. Prebiotics. Probiotics.**

sugieren que los probióticos podrían ser de utilidad en la enfermedad inflamatoria intestinal. La ecoinmunonutrición con pre-, pro y simbióticos parece ser un arma terapéutica adecuada en el futuro.

(Nutr Hosp 2001, 16:239-256)

Palabras clave: **Econutrición. Simbióticos. Paciente Crítico. Prebióticos. Probióticos.**

Introduction

The large intestine was not long ago regarded as an organ with almost only one function - to beabsorb water and electrolytes. It has not been realized for long, at least not among clinicians, that the coon is a highly active metabolic organ, in which numerous metabolic processes take place and almost uncountable nutrients are released and absorbed. Here bacterial enzymes of *probiotic* bacteria metabolize *prebiotics* (various fruit and vegetable fibers, but also gastrointestinal secretions and apoptotic cell) and countless numbers of products are released and absorbed - products increasingly referred to as synbiotics.

Today colon is known as a metabolic organ with eventually more and also more complex functions than the rest of the gastrointestinal tract, where chemical processes are promoted by enzymes produced by bacterial instead of eukaryotic cells. An indication of the complexity of the metabolic activities in the large intestine is the information that the colonic "microbial organ" contains about 300 000 genes, to be compared to the about 65 000 genes in the rest of the human body. Numerous substances, several hundred thousand if not millions, are produced, released and absorbed at the level of the lower small and the large intestine. Among these are various fatty acids, especially short chain fatty acdis (SCFA's), carbohydrates, amino acids, polyamides, vitamins, antioxidants, phytoestrogens, and coagulation and growth factors. Only of polyphenols such as flavonoids exist more than four thousand and of carotenoids about six hundred.

Although the word synbiotics was coined to describe the combined action of pre- and probiotics, the ability to like antibiotics control infection, the term is now increasingly used in a wide sense, as a name for all the substances released by microbial fermentation in the lower gut. One obvious reason is that most of the substances released seem to influence the inmune defense, increase resistance to disease, and, most important, prevent complications to surgery such as infections and thrombosis.

The food ingredients (fibers, complex proteins, etc.), which mainly unchanged reach the colon, are usually referred to as "colonic foods". It is recommended that at least ten per cent of the total calorie intake should be of this type, a goal difficult to meet in the very sick patients. As prebitic fibers are low-caloric, at leas one fourth of the vood eaten under healthy conditions is recommended be of the type "food destined for the colon", e.g. food ingredients that not are broken down by gastrointestinal juice enzymes and absorbed in the upper small intestine. In the past it was usually regarded as ore or less impossible to provide colonic foods to patients in the ICU, a view, which in recent years has been revised.

Fibers are prebiotics

Research regarding various probiotics have in recent years explosed and information about the various probiotic bacteria is fast increasing. Prebiotics are as importante, as availability and content of various fibers limits the production of symbiotic compounds produced.

Fibers are carbohydrates derived from plant cell walls, and dietary fibers are usually classified into three groups: *soluble fibers* such as pectins and various gums, *insoluble fibers* such as cellulose and *mixed type fibers* such as brans. The most important characteristic for them all is that they are resistant to hydrolysis by human alimentary tact enzymes, which make some of them ideal substrate for microbial fermentation in the lower GI tract. soluble fibers (prebiotics) constitute an important source for bacterial fermentation and microbial production of nutrients, antioxidants, vitamins, and growth and other important factors. This far, the main interest has focused on the production of various short chain fatty acids (SCFAs) and fermentation by-products such as hydrogen, methane and carbon dioxide. But the content of other nutrients; various bioactive amino acids, polyamins, antioxidants and various growth factors etc are equally important.[1-5]

Prebiotic fibers are slow carbohydrates, which have a strong influence glucose and fat metabolism, and cause decrease in postprandial glycemia, reduction in the concentration of free fatty acdis and in serum cholesterol levels.[6-7] An increase in proliferation

Table I
Probiotics-molecular effects

— Stimulates sIgA production.
— Inhibits IgE production.
— Modulates Th1/Th2 response.
— Modulates cytokine response.
— Stimulates NO production.
— Stimulates macrophage function.
— Stimulates NK cell activity.
— Activates the MALT system.
— Stimulates apoptosis.
— Promotes growth and regeneration.
— Controls PPMs.
— Reduces endotoxin production.
— Reduces mutagenicity.
— Produces antioxidants, nutrients (synbiotics) and various growth and clotting factors.

of mucosa epithelial cells will occur in the caecum and in the colon as a result of increased fiber consumption, associated with a significant decrease in intraluminal pH.[6] But fibers have also their own direct physiological effects. Common to soluble and viscous fibers is that they delay gastric emptying, increase intestinal transit time, and imporve glucose tolerance. Soluble dietary fibers do also sequestrable bile salts and significantly affect lipid absorption. Here follows a short introduction to some interesting bioactive fibers.

Pectin

We observed, when studying a pectin solution in water, that when pH is reduced to a level of 1.0. e.g. the pH seen in the stomach, a so called two-phase separation will occur,[8] with leading to formation of a gel phase and a watery phase. It is likely that, when this separation occurs in the stomach the gel phase will adhere to the mucosa layer and increase the protective capacity of the mucus. Banana, when green and immature, is rich in both pectin and phospholipids, both known to have strong protective effects against peptic ulcer.[9-10] The effects we observed when concentrations, greater than normally seen in the fruit, were tried did not differ much from what is obtained with established drugs such as H_2-blokers, proton inhibitors and surface-protecting agents.[11, 12] Another interesting feature of pectin is that it is a strong antioxidant, which offer mucosal protection against all three main types of oxidation damages: peroxy-, superoxide, and hydroxyl radical.[13] This could be the mechanism by which pectin stimulates the GALT system and prevents disruption of the intestinal microflora.[14] A disadvantage with pectin is, that it is difficult to use in tube-feeding, as it is has a tendency to clog the tube.

Betaglucans

Another most interesting group of fibers are the betaglucans, a group of unique water soluble fibers often extracted from oat, which contains as much as up to 17% of betaglucans.[15] This gum fiber compares favorably with other high viscosity polysaccharides such as substituted celluloses, guar gums and locust bean gums. The clinical effects of oat gums are yet not explored to the same extent as those os pectin, but are likely to be similar as describen for pectin. Most clinical studies have concentrated on oat's unique cholesterol-lowering effects[60], and its unique and strong antioxidant effects, extensively used in the past for food stabilizing purpose.

Resistant starch

Resistant starch is a type of starch, which resist digestion in the small intestine and reaches the colon, which all starches do not generally do. Resistant starch is one of the main sources of carbohydrate substrates for colonic microflora and is a good determinant of human large bowel function. It is know to release large quantitites of butyrate when fermented.

Fructooligosacharides

Fructooligosaccharides (FOS), composed of one molecule glucose and one to three molecules of fructose, have been shown to have unique abilities to effectively stimulate the intestinal fora.[17] Fructooligosaccharides exist naturally in many kinds of plants such as onions, asparagus roots, tubers of Jerusalem artichoke and wheat, but also in banana, beer, burdock, chinese chives, garlic, graminae (fodder grass), honey, oat, pine, rye, chicory, stone leak, and even bacteria and yeasts. The daily intake of inulin and oligofructose by the North American populations has in a recent survey been estimated to be 2-8 g.[18] It is important to recognize that only few lactic acid bacteria strains have the ability to ferment fructans such as phlein and inulin. When 712 LAB strains were tested, only 16 could utilize phleins and only eight inulins.[71] Of these *L plantarum*, followed by *L paracasei* were the most effective both to ferment the fibers and to reduce pH.[19] Beneficial effects of fructooligosacharides on serum cholesterol, triglyceride levels and blood pressure in elderly patients with hyperlipemia has been reported.[20]

Algal fibers

Algal polysaccharides are receiving a newborn and fast increasing interest. Most of these fibers are resistant to hydrolysis by human endogenous digestive enzymes[21-23] and should be suitable as dietary fibers. Their physiological effects have only recently begun to be investitaged.[24] Especially their fermentative de-

gradation by the colonic flora.[25] The soluble fibers in seaweed consist of *laminarans* (a sort of b-glucans associated with mannitol residues), *fucans* (sulphated polymers associated with xylose, galactose and glucoronic acid) and *alginates* (mannuronic and guluronic acid polymers), whereas the *isolubles algal fibers* are essentially cellulose. Fermentation of alginates results in a high acetate production (80%) and laminarans have a very high yield of butyrate. Seaweed with its high content of fermentable fibers, its documented ability to produce large quantities of SCFAs and its high content of omega-3 fatty acdis should be an interesting source of medical fibers, most likely soon to be explored.

Glucomannans

Glucomannan, a nonabsorbable polysaccharide (glucose/mannose polymer), derived from *Amorphophallus konjak* (english names: devil tongue, elephant yam, umbrella arum) is also receiving increasing attention for its potential health effects, most likely associated with to its unique hydroscopic ability. On contact with water it swells and becomes a viscous gel.[26] Like other soluble fibers it delays both the gastric emptying and intestinal transit time. It is also effective in decreasing the intake of digestible energy.[27] Glycomannans are frequently used in Japan in conditions such as hypercholesterolemia, hypertension and diabetes.[98, 99]

A complex flora

It has been calculated that the human body contain more than ten times as many bacterial cells (10^{14}) than eukaryotic (10^{13}). The large intestine is supposed to contain when on Western type diet about one kilogram of bacteria. However, individuals living under more rural circumstances, consuming larger amounts of gruits and vegetable fibers and live lactobacilli do often harbor in their large intestine about two kilogram of live bacterial flora. But it is not only the gut, which as a "protection layer" of probiotic bacteria", there is supposed to be 200 gram on our skin, about twenty gram in each of the mouth, the lung and the vagina, ten gram in the nose and about ne gram in the eyes. This "protection layer" is most often lost in the environment of ICU, and especially when treated with antibiotics and cytostatics.

About 400 bacterial species are normally found in the fecal/colonic microflora of a healthy individual, vut 30 to 40 species seem to constitute 99% of the collextion in any one human subject.[28] The bacterial genera, which are common components of the human intestinal microflora, are: *Bacteroides, Bifidobacterium, Clostridium, Enterococcus, Eubacterium, Fusobacterium, Peptostreptococcus, Ruminococcus, Lactobacillus* and *Escherichia.* It is suggested that each human being has his/her own unique microbial collection, especially of strains of *Bifidobacterium* and *Lactobacillus,* and that it should be possible to identify an individual on the basis of his/her personal intestinal microflora.[28] The most common LAB strains found on the rectal mucosa of healthy humans living a Western lifestyle are *Lacttobacillus plantarum, Lactobacillus rhamnosus* and *Lactobacillus paracasei* ssp *paracasei,* isolated in 52%, 26% and 17% of tested individuals respectively.[29] The colonization rate of commonly used milk-born probiotic bacteria such *Lactobacillus casei, Lactobacillus reuteri* and *Lactobacillus acidophilus* es in the same study only 2%, 2% and 0% respectively. *Lactobacillus plantarum* is likely to more often colonize vegetarians (appr 2/3 of that population) than omnivorous (appr 1/4 of that population).[30] Lactic acid bacteria (LAB) seem not tolerate well modern, so called Western, lifestyle. Swedish children have a different and less rich flora than Pakistani childrenz[31] or Estonian children.[32]

Commensal flora reduced early in disease

Cosmonauts are reported to on return from space flights have lost most of their commensal flora including *Lactobacillus* species such as *Lactobacillus plantarum* (lost to almost 100%), *Lacobacillus casei* (lost to almost 100%), *Lactobacillus fermentum* (reduced by 43%), *Lactobacillus acidophilus* (reduced by 27%), *Lactobacillus salivarius* (reduced by 22%) and *Lactobacillus brevis* (reduced by 12%).[33] These changes ae attributed to poor eating (dried food, no fresh fruits and vegetales) and much reduced supply of fiber and antioxidants, but also lack of excercise and mental and physical stress - conditions not very different from those of the patients in the ICU. The flora seems always to be significantly reduced in the sick, especially in connection with severe disease; care in ICU, and in patients with little food intake or on parenteral nutrition.

The reduction of the commensal flora occurs early in disease. It is observed in experimental pancreatitis

Table II
Probiotics-clinical effects

- Prevents or reduces duration of diarrhea (rotavirus).
- Reduces atopic dermatitis.
- Induces remission of IBD.
- Reduces symptoms in irritable colon.
- Delays onset of diabetes (animals).
- Reduces the rate of colonic cancer (animals).
- Prevents or reduces Helicobacter infections (animals).
- Reduces the incidence and severity of pancreatic sepsis in pancreatitis (animals).
- Reduces the incidence and severity of ICU sepsis.
- Reduces the incidence and severity of sepsis after major surgery.
- Reduces biofilm.

Table III

Lactic acid bacteria in the settings of icu - collected experience

Site of study	*Type of patients*	*TPN*	*SBD*	*LAB + FIBER*	*Inactivated LAB + FIBER*
Mortality:					
Hongkong[130]	Mixed ICU			26% (5/19)*	42% (8/19)
Rate of infections:					
Berlin[131]	Abdom. surg.	30% (9/30)	10% (3/30)**	10% (3/30)	
Berlin[132]	Gastr. + pancr.	50% (8/16)	7% (1/15)**	17% (3/17)	
Berlin[132]	Liver transpl.		48% (15/32)	13% (4/31)***	34% (11/32)
Györ[133]	Acut. pancreat.			4.5% (1/22)****	30% (7/23)

Abdom. TPN: total parenteral nutrition, SBD: selective bowel decontamination, Abdom. Surg.: abdominal surgery patients, Acut. pancreat.: acute pancreatitis, Gastr.: gastric surgery patients, Liver transpl.: liver transplant patients, Pancr.: pancreatic surgery patients, Mixed ICU: mixed group of various ICU patients.

* not statistically significant, ** $p < 0.0001$, *** $p = 0.017$, **** $p = < 0.05$.

that anaerobic bacteria and lactobacilli are significantly reduced both in the distal small bowel and in the colon already within 6-12 hours after induction of disease. The changes in pattern of probiotic flora are almost instantly followed by significant increase in numbers of potentially pathogenic microorganisms (PPMs) such as *Escherichia coli*, and dramatic increases in musocal barrier permeability (lumen to blood) and in endothelial permeability (blood to tissue),[34, 35] both associated with increased microbial translocation and microbial growth both of mesenteric lymph nodes and, in the case of pancreatitis, the pancreatic tissue.[36].

Postoperative morbidity still high - and unchanged?

The incidence following trauma and surgical treatment of major complications such as infections and venous thrombosis and of major sequelae such as formation of serosal adhesions has, seemingly in recent years not been reduced at all, or at least not as much as would have been expected. Almost every second patient subjected to transplantation, especially bone marrow, liver, pancreas and intestinal transplantation, every third patient subjected to major live and pancreas resection, and every fifth patient having extensive gastric and large intestinal surgery suffer episodes of infection.[37, 38] Also laryngopharyngeal, orthopedic and cardiac surgery do often report a double digit incidence of infections. Accumulating evidence suggest that the occurrence of septic complications in intimately associated with a reduced immunological protection of the patient, and a large proportion of the complications are seen in patients over the age of 65 and in immuno-compromized patients.

Venous thrombosis is a frequent complication even today. It is true that clinical manifestations of thrombosis can successfully be eliminated by prophylactic use of various anti-thrombotic agents, but 50 to 70 per cent of the patients will, if phlebography is performed, show signs of venous thrombosis. High incidence of thrombosis seems particularly to be associated with parenteral nutrition (PN), and especially total parenteral nutrition (TPN). Thrombosis and infection seem to be inter-related, and it has recently been suggested that *"one common complication may facilitate the occurrence of another common complication by synergistic stimulation of the coagulation system"*.[39] Also the incidence of serosal adhesions in cavities such as the peritoneum, pleura and pericardium and around tendons remains high following surgery, making reoperations more difficult and sometimes impossible, but also leading to other sever health problems such as intestinal obstruction and to infertility.

A life-style associated predisposition?

There is accumulating evidence that Western lifestyle, especially Western food habits, predisposes to super-inflammation and to subsequent clinical complications. It is rather old observation that men eating large amounts of fiber are protected from postoperative venous thrombosis.[40, 41] It has also been reported that men living in rural areas and consuming large quantities of cellulose and vegetable fibers + live lactobacilli (fermented milk) have a significantly longer mean clotting time, and soft jelly-like clots compared to those living in urban areas.[42] Reduced plasma levels of fibrinogen and factor X has been observed in baboons on Western diet, when supplemented with a fiber such as konjak-glucomannan.[43] Decreased levels of plasma viscosity and fibrinogen are found diabetic children supplemented with another fiber, guar-gum.[44]

Serosal adhesions are associated with an increased endotoxin production, and with overespression of TGFβ,[45] and germ-free animals do not develop serosal

adhesions,[46] both observations supporting an assumption that peritoneal adhesions produced in connection with trauma are associated with alterations in the intestinal environment and in the immune defense.

Increased coagulation is associated with dyslipidemia, glucose intolerance and intravascular coagulation and thrombosis. Diabetic and obese rats with insulin deficiency show raised levels of circulating free acids (FFA).[47] Raised levels of circulating saturated FFAs stimulates fibrinogen synthesis.[48] Insulin resistance is suggested to promote increased levels of FFA and increased fibrinogen synthesis,[49] which can be preventd by increased intake of prebiotics; dietary fibers such as cellulose, pectin, hemicellulose, or some starches, all substrates for production in the large intestine of short chain fatty acids (SCFA), which improves insulin sensitivity.[50]

Diet-induced superinflammation

Consumption of saturated fatty acids, as well as trans fatty acids, induces significant alterations in the immune response;[51] inhibits the macrophage functions,[52] and stimulates Th2 response relative to the Th1 response. A recent study in mice observed higher IgM and IgG antibody levels, worsened proteinuria and shortened life span in mice fed a high fat diet (200 g fat/kg food) compared to those fed a low fat diet (50 g fat/kg food). In vitro LPS stimulation of peritoneal macrophages from the two groups showed significantly higher release of IL-6 (134 vs 59 ng/10^6 cells, p = 0.02), TNF-α (311 vs 95 pg/10^6 cells, p = 0.001) and PGE_2 (906 vs 449 pg/10^6 cells, p = 0.01) in the group fed a high fat diet.[53]

The response of splanchnic cytokines to a challenge with endotoxin is significantly enhanced in the absence of adequate oral/enteral mutrition supply as in bowel rest of TPN. Lack of luminal nutrition is postulated to predispose to amplification on injury-induced metabolic and immunological responses. Accumulating evidence suggests that particularly IL-6 is a key mediator to a suerinflammation during the acute phase response (APR). It is well known that an exaggerated IL-6 response (e.g. prolonged and/or extreme elevations of circulating IL-6) is associated with adverse clinical events such as acute respiratory distress (ARDS) and multiple organ failure (MOF) in patients suffering from conditions such as infection, burns of trauma.[54] Among the effects associated with an exagerated IL-6 response are augmented endothelial adhesion of polymorphonuclear (PMN) cells, increased production of intracellular adhesion molecule-1 (ICAM-1), and priming of the PMNs for an oxidative burst, release of pro-inflammatory platelt activating factor (PAF), and associated with this, a delay in PMN apoptosis.[54] Observations made in live trasplant patients are of special interest. It was observed that patients, who show a six-fold or more increase in cytokines such as TNFα and IL-6 as elarly as during the later phase of the operation with great certainty will develop sepsis in the subsequent postoperative days.[55]

Table IV
Possible candiates for treatment with pre- pro- and symbiotics

Prematures.
Infants.
As alternative to antibiotics.
"Astronatus" e those with insufficient intake of fresh fruits and vegetables.
When treated with antibiotics or chemoterapeutics.
When irradiated or treated with cytostatics.
When treated with renal or peritoneal dialysis.
Biliary obstruction.
Liver cirrhosis, portal hypertension.
Cancer.
When allergy.
When immunodepressed.
Hematological malignancies.
HIV/Aids.
Inflammatory bowel disease.
Irritable bowel disease.
Rheumatoid arthritis.
Hepatitis.
Pancreatitis.
Stomatitis.
Diarrhea.
When infected.
After trauma.
In major surgery, especially transplantation.
In Intensive Care.

The majority of immune system in the gut

About 80% of the total immunoglobulin-producing cells of the body are localized in lamina propria of the gut,[56] and large quantitites especially of IgA are each day released to the gut lumen. The synthesis of IgA is highly dependent on T-cells and several cytokines produced bi activated lymphocytes influence different steps in the IgA differentiation pathway.[57] Transforming growth factor-β (TGF-β) has, at least in the mice, been found to be a crucial "switch" factor, but also cytokines such as IL-2, IL-5 and IL-10 are known to be involved - see further.[58] Changes in nutrition, physical activity, sleep, mood, age, gender, circadian rhythm, body temperature, consumption of drugs, and illness are known to influence lymphocyte function and the production of immunoglobulins and hereby resistance to disease. Care in the ICU settings is most often associated, not only with dramatic changes in nutrition provided, but also in physical activity, body temperature, sleep, mood, circadian rhythm and other innate functions as well as with increased consumption of drugs, which all will have profound influence on the immune response of the patients. It is suggested in the

literature that supply of both pre- and probiotics can modify functions such as appetite, sleep, mood and circadian rhythm, and this most likely through metabolites produced by microbial fermentation in the gut.[59-62] Supply of LAB can also significantly reduce serum levels of a variety of toxins such as endotoxin.

Neuroendocrine regulation of the acute phase response

Functions such a resistance to disese and size and extent of the acute phase response are unquestionably regulated from the gut, but also by the liver and to a large extent by neuroendocrine mechanisms. Knowledge has during the last decade rapidly increased about the complex adaptative mechanisms that regulate psychobiological states (mood, sleep, appetite, libido, etc.) in response both psychological and physical stressors such as noxious antigenic toxins and invasive microbiological organisms. Evidence is mounting that nervous, endocrine, immune and inflammatory systems are both anatomically and functionally interconnected. Stressors influence the immune functions and the inflammatory response to a large extent via the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis.[64]

Excessive cytorime production (IL-1, TNFα, but also IL-6) is normally down-regulated by corticosteroids. Various defects in the interaction of these systems will undoubtedly lead to increased morbidity in acute conditions such as SIRS, MODS and MOF and in chronic conditions such as autoimmune diseases. Elimination of neuroendocrine by adrenalectomy and subsequent "unrestricted" production of inflammatory cytokines increases lethality on challenge with LPS 500-fold.[65] Whereas acute stressor in general seem to stimulate immunity, chronic stress (environmental, social, physiological or nutritional) is generally considered to down-regulate the immune system.[66]

Enteral nutrition is today regarded as more important as a tool to control APR and immune response than as a tool to provide calories and nutrients to the very sick patient. Recent studies in surgical patients supports such an assumption. In a recent study comparing parenteral hyperalimentation (PN) and early enteral feeding (EN) after major liver resection no differences were found between the groups when studying nutritional parameters, but significant differences observed when studying immunological parameters such as natural killer cell activity, lymphocyte numbers, response to phytohemagglutinin (PHA) and natural killer cell activity. Most important the incidence of ifectious complications was 8% in the EN group compared to 31% in the PN group.[67] Similar results have been reported in patients with severe acute pancreatitis. The changes in C-reactive protein (CRP) and disease severity severity scores (APACHE II) were significantly improved with EN compared to PN.[68] The IgM anticore endotoxin antiboides (EndoCab) and total antioxidant potential (TAC) were both significantly better in the EN group compared to PN. But most important systemic inflammatory response (SIRS), sepsis, organ failure and stay in intensive care were globally improved in the EN fed patients.[68]

Immuno-enchancing nutrition solutions controversial

The knowledge that some nutritional components such as some amino acids, polyunsaturated fatty acids, vitamins and antioxidants have all strong immuno-modulatory effects lead to commercial production of special immune-enhancing nutrition solutions, based on a mixture of these various nutritional components. The experience so far has not been what was originally expected.[69-71] Despite the fact that some compelling data have been presented in the literature, there is much to support the view of these reviewers and others that at present *"routine use of these formulas can not be recommended"*. There seems to be several reasons why the success has not been as expected, but the most important is probably that the need of supply the various immuno-stimulatory to the colon has been neglected, as these formulas do not contain substrate (fibers) for microbial fermentation and supply of immuno-stimulatory nutrients from microbial fermentation at the level of the colonic mucosa . It is reasonable to assume that adding fibers (prebiotics) and lactic acid bacteria (probiotics) can significantly improve the efficacy of these nutrition solutions.

In addition, EN is also often instituted too late in order to have an ability to significantly affect APR. It is also often combined with nutrition solutions rich in fat, which at least in theory should inhibit immune functions and counteract the purpose. Furthermore, EN is often combined with treatment with antibiotics, which reduces or even eliminates the important commensal flora.

Lactic acid bacteria initiates immunoglobulin production

It has been suggested that LAB during fermentation may release components that possess immuno-modulatory activities. The ability of bifidobacteria to induce production of more significant quantities of IgA by Peyer's patches has been studied in vitro. It is interesting to note that only three of tested 120 strains, all isolated from human feces, had such an ability.[72] Two of them were identified as *Bifidobacterium breve* and one as *B. longum.* As far as I am aware no similar study has compared the ability of various *Lactobacillus* to initiate production of IgA. There are, however, studies, which show that at least some LAB do possess the ability to induce production of IgA. *Lactobacillus* GG is reported to significantly increase the IgA immune response in Crohn's disease,[73] and to enhance the IgA response to rotavirus.[74] Human intake of *Lactobacillus acidophilus*

is also known to results in a > 4 fold increase in IgA response, when challenged by *S typhy.*[75] Supplementation of both *Lact. reuteri* (R2LC) and *Lact. plantarum* (199 V, DSM 9843) to animals with methotrexate-induced colitis does, in addition to elevating the numbers of both CD4 and CD8 T-cells, significantly increase small as well as large bowel IgA secretion, both the soluble and insoluble fractions.[76]

Lactic acid bacteria restores macrophage function

The ability of special cells to engulf, kill and eliminate invading microorganisms and/or defective cells but also to eliminate toxins, mutagens, and other poisonous substances is important to health and to outcome in ICU patients. That enteral and/or parenteral supply of fat, as mentioned above, has a profound effect on APR and inhibits immune functions is supported by several clinical observations. It is also observed that intravenous infusion of 20% of fat emulsions (Intralipid) significantly potentiates endotoxin-induced coagulation activation.[77] But, also a diet too rich in polyunsaturated fatty acdis can be negative. Studies in mice with standardized thermal injuries showed a significantly increased mortality on challenge with *Pseudomonas aeruginosa* when as much as 40 per cent of total calories were supplied as fish oil.[78]

Modern man is richly exposed to chemicals, especially pharmaceuticals. Many of these inhibit the macrophage functions, the bactericidal function as well as the production and secretion of cytokines κ effects, which has not been studied to the extent they should be. Antibiotics are no exception. Supply of antibiotics (150 mg/kg body weight of Mezlocillin, Bayer) did result suppression of the various macrophage functions as demonstrated by studies of chemiluminescence response, chemotactic motility, bactericidal and cytostatic ability and of lymphocyte proliferation.[79] Subsequent work[80] has demonstrated that the reduction in peritoneal macrophage function and in mymphocyte proliferation after microbial decontamination of the digestive tract is significantly restituted by supply of low molecular weight peptides obtained from indibenous gastroingestinal tact microflora species such as *Bacteroides sp., Clostridium sp, Propionebacterium sp.* and from *Lactobacillus sp.*[80–1] Other studies demonstrate that supply of live or nonviable bacteria or bacterial wall components such as peptidoglucan stimulates macrophage recruitment and function[81] and cell-free extacts of both *Bifidobacterium longum* and *Lactobacillus acidophilus* have been shown to significantly enhance phagocytosis both of inert particles and viable *Salmonella.*[82] However, not all LAB are capable of activating macrophages. As an example, an increased macrophage activation (increased expression of Ia antigen on the surface) was observed in mice after intraperitoneal administration of *Lactobacillus casei* or *Corynobacterium parvum,* but not after administration of *Lactobacillus fermentum.*[83]

Lactic acid bacteria, and fiber, stimulate apoptosis

Programmed cell death is one of the important mechanisms by which the body controls both infections, especially those of viral origin, but also neoplastic transformation. Diary products, rich in saturated fat and various growth factors[84, 85] including insulin growth factor 1 and various cow oestrogens and sometimes xenoestrogens (from presticides) have been suggested to inhibit or delay apoptosis and to promote malignant cell proliferation. These changes are associated with increased luminal concentratins of bile acdis[86] and also modifications in composition of bowel microflora. There are several reports, which demonstrate that increased consumption of prebiotics; plant fibers such as pectin, oat, whreat, rye, or chicory fibers (inulin)[87] significantly increases the rate of apoptosis. Also cells infected with a virus are supposed to undergo apoptosis in order to prevent spreading of the viral infection.[88] Also these various processes seem to be enhanced by supply of both fiber and LAB (symbiotics) most likely through production of SCFAs, known to enhance the process of apoptosis.[80, 90] As examples, it has been observed in experimental animals that feeding beans increase the SCFA production seven-fold.[91]

Lactic acid bacteria modulate lymphocyte functions

Lymphocyte proliferation studies are commonly used to evalute the efficacy of immunosuppressive or immuno-enhancing therapies, to test chemicals for their potential immuno-toxicity and to monitor congenital immunological effects. Four probiotic lactic acid bacteria were recently testd in an animal model. Intrestingly, *Lactobacillus acidophilus* ATCC 4356 did enhance basal proliferation by 43%, while *Lactobacillus casei* (Yakult), *Lactobacillus gasseri* ATCC 33323 and *Lactobacillus thamnosus* DSM 7061 instead inhibited both basal (by 14-51%) and mitogen-stimulated proliferation by the mitogen concanavalin A (by 43-68%) and by LPS (by 23-63%), and particulraly at supra-optimal concentrations.[92] As appears from this study various LAB have different immune effects and experience cannot be extrapolated from one *Lactobacillus* to another *Lactobacillus* strain or species, even if they are closely related.

It is suggested that a balance between Th1 limphocytes, primarily associated with cellular immunity, and TH2 lymphocytes, mainly associated with humoral immunity is essential for maintenance of health. Most of the studies on this balance have been done in atopic persons, a group of individuals, who also suffer an aberrant inflammation. I am not aware of any specific studies of this balance in ICU patients, but implications for the ICU patient should be obvious and future studies warranted.

Reduced microbial stimulation during early infancy and childhood, especially in developed countries, has been associated with the considerably increased prevalence of atopic diseases in children and young adults.[93] Reduced microbial stimulation is associated with slower postnatal maturation of the immune system, a delayed development and lack of balance between Th1 and Th2 immunity.[94] Swedis infants have as already mentioned a significantly different gut flora than both Pakistani[31] and Estonian children.[32] Children prone to develop allergies are also more sensitive to infections, also when in the ICU.

The super-inflammation seen in atopic diseases is thought to be caused by inapproprieta generation and activation of Th2 cells, a process inhibitied by IFN-γ, but also by IL-12. It is of special interest to know that some *Lactobacillus* species, eventually only a few, have the ability to stimulate both IFN-γ and IL-12 production and to promote of Th1-type responde, inhbiit Th2-type immune response, and restore the Th-1/Th-2 balance.[96] It was observed that stimulation of human peripheral blood mononuclear cells (PBMC) using *Lactobacillus thamnosus* or *Lactobacillus bulgaricus* strains lead to induction of Th1 type cytokines IL-12, Il-18, and IFN-γ.[97] It was also observed that supply of *Lactobacillus casei*[98] and *Lactobacillus plantarum*[96] totally inhibited antigen-induced IgE secrtion in ovalalbumin- and casein-primed mice, an effect not obtained with *Lactobacillus johnsonii.* Furthermore, IL-12 production by peritoneal macrophages was enhanced, and Il-4 production of concanavalin A-stimulated spleen cells suppressed in animals treated with *Lactobacillus plantarum.*[96]

Lactic acid bacteria modulate cytokine release

Oral administration of LAB seem to determine the direction and efficacy of the humoral responde, a responde is differently modulated by different LAB. Most of the attention has so far been given the cytokine production by monocytic cells such as macrophages, but also mononuclear eukaryotic cells are important sources of cytokines. It has thus become increasingly clear that tissues such as intestinal epithelial cells[99, 100] and prokaryotic cells such as commensal flora and/or supplemented probiotic bacteria[101, 102] when challenged will secrete a spectrum of chemo-attractants and cytokines or cytokine-like molecules (sometimes called bacteriokines). As an example, it has been demonstrated in cell cultures that intestinal epithelial cells on challenge with LPS and PGE_2 produce significant amounts of IL-6, a process, which can be blunted by supply of indomethacin[103] and inhibited by nitric oxide.[104]

Supplementation with some LAB seems to significantly influence the expression of cytokines, but the response varies with strain of LAB supplied. The activity in blood mononuclear cells in healthy subjects of 2'-5' synthetase, an expression of interferon-gamma (IFN-γ), is significantly increased (appr. 250%= 24 hours after a LAB-containing meal.[75] Significant increases in cytokine activity compared to controls are also observed when human mononuclear cells are incubated in the presence of the yogurt bacteria; *Lb bulgaricus (BUL),* and *S. thermophilus (Ther),* alone or in combination (Yog); *INF-γ: Bul* 775%, *Ther* 2100%, Yog 570%, *TNF-α: Bul* 1020%, *Ther* 3180% Yog 970%, and in Il-1β: *Bul* 2120%, *Ther* 1540%, Yog 1920%, all indicating a significant immuno-activiation after supply of these LAB. Another recent study compared both in a macrophage model and in a T-helper-cell model the in vitro ability to induce cytokine production by some LAB used by the dairy industry for yogurt production.[105] Although there eas a considerable variation in response between various *S. thermophilus* strains this LAB seemed to stimulate macrophage and T-cell cytokine production to a somewhat greater extent than did *Lactobacillus bulgaricus, Bifidobacterium adolescentis* and *Bifidobacterium bifidum.*[105] Also heat-killet *Lactobacillus acidophilus* (LA 1) has been shown in vitro to increase the mouse macrophage production of IL1-α (appr 300%) and TNF-α (appr 1000%) to a considerably greater extent than other *Lactobacillus* and *Bifidobacteria* tried.[106]

It is mainly effects of mil-born LAB that has been studied, which is understandable, as in more recent years it has been mainly or only the diary industry, which has maintained an interest in producing and supplying food products containing live LAB. One can expect, as interest in LAB with specific ability to ferment plant fibers gains popularity, that studies also with LAB such as *Lactobacillus plantarum, Lactobacillus paracasei,* various *Lactococcus* and *Pentococcus* strains and other related LAB, known for there special ability to metabolize fibers, will be undertaken.

Lactic acid bacteria increases mucin production

Numerous studies hver demonstrated that supplied nonpathogenic bacteria of various kinds including LAB haver the ability to prevent and/or improve various infections. Several mechanisms have suggested such as release of avrious bakteriokines (cytokine-like molecules), nitric oxide, free radicals and lowering pH. Two other mechanisms have recently been suggested, blocking of receptors and inhbition of attachment to epitheial cells by intestinal mucins.

While the adherence of most LAB are via protease-sensitive mechanisms or via lipid (lactosylceramide) receptor, *Lactobacillus plantarum* seem to adhere via carbohydrate (mannose) adhesion mechanisms, e.g. the same receptors as Gram-negative bacteria such as *E. coli, Enterobacter, Klebsiella, Salmonella, Shigella, Pseudomonas* and *Vidrio cholerae.*[107] This know-

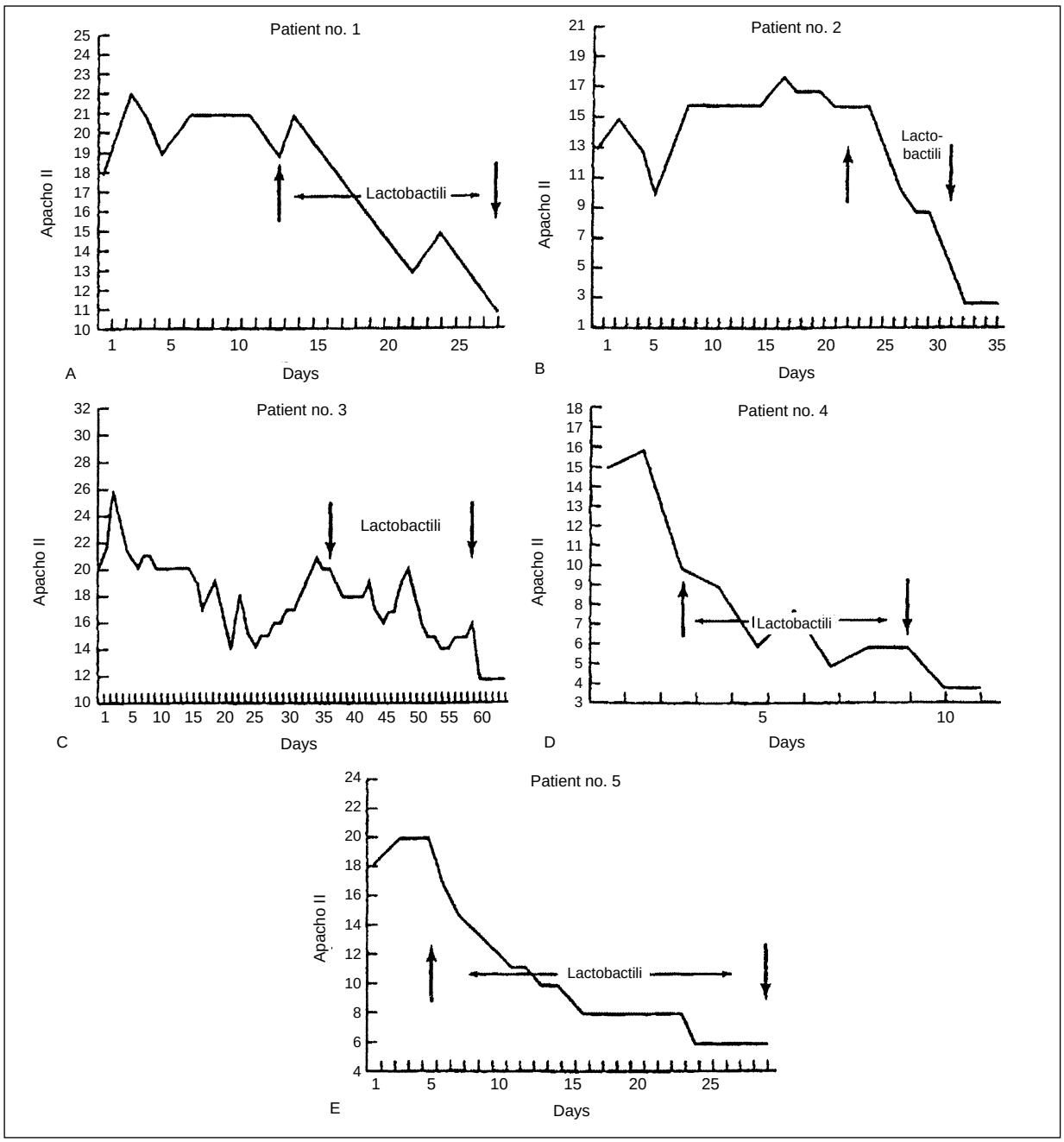


Fig. 1.—Changes in Apache-II scores in five patients with multiorgan dysfunction and treated with pre- and probiotics.

ledge offer unique possibilites to prevent infections and to reduce endotoxemia.

Binding of pathogens to mucosal epithelial cell mucins is an importante defense mechanism for the host.[108] The density of Goblet cells and the intestinal mucus production seem to increase with distance from the mouth. Several human genes are involved in mucin production, but MUC2 and MUC3 are the predominant ileo-colonic mucins. Both mucins show expression in Goblet cells in the large and small intestine, but MUC2 is suggested to be the major secreted mucin component of the colon.[109] Increased MUC2 and MUC3 mRNA expression and inhibition of adherence of pathogenic *Escherichia coli* to HT29 intstinal cells, but not to non-intestinal cells, has recently been demonstrated in vitro, when the cells were incubated with *Lactobacillus plantarum 299v*,110 suggesting that the ability of probiotic agents such as *L. plantarum* to inhibit adhrence of attaching and effacing organisms to intestinal epithelial cells is also mediated through their ability to increase expression of MUC2 and MUC3 intestinal mucins.

Lactic acid bacteria eliminate toxins and mutagens

Several studies show strong effects of various lactobacilli to significantly reduce and sometimes eliminate various toxins and mutagens. Several *lactobacillus*[111] and *bifidobacteria*[112] strains have proven to non-covalently bind and sequestrate very potent endotoxins such as aflatoxin B, both in vitro and in vivo. Also other bacterial toxins such a *E coli* endotoxin are effectively reduced by probiotic bacteria. This is important as translocation of endotoxin and pathogenic bacteria occur in high frequency in critical conditions such as burns, hemorrhagic shock, severe pancreatitis and after larger operations such as transplantation.

Infections and endotoxemia are regarded as critical factors, responsible for the hemodynamic alterations and leading to increased risk of bleeding in subjects with liver cirrhosis, esophageal varices and portal hypertension,[113] which was the reason why it is suggested that antibiotics treatment, might prevent bleeding. Supplementing *Lactobacillus* has been shown to reduce endotoxemia and severity of experimental lcoholic liver disease.[114] Strong effects of supplied *Lactobacillus* is for example observed in galactosamine-induced chemical hepatitis. Supplemented *Lactobacilus rhammnosus* DSM 6594 (= strain 271), *Lactobacillus plantarum* DSM 9843 (= strain 299v), *Lactobacillus fermentum* DSM 8704:3 (strain 245) and *Lactobacillus reuteri* (= strain 108), did significantly reduce the extent of liver injury but also reduce bacterial translocation. Again, the most pronounced effect was seen when supplementing *Lactobacillus plantarum*, especially if combined with arginine. Significant reduction in release of liver enzymes, extent of hepatocellular necrosis, inflammatory cell infiltration and bacterial translocation were observed parallel with a significant reduction in number of *Enterobacteriaceae*, both in caecum and colon.[115] A subsequent study could demonstrate that the extent of liver injury and bacterial translocation is increased after supply of *Bact. fragilis* and *E. coli*, but again significantly inhibited by *Lact. plantarum.*[116] A recent study, undertaken in one patient, is against this background of particular interest. Supply of a cocktail of seven probiotic bacteria, LAB most likely chosen at random, and without any deeper knowledge about the immunological and other cellular effects of each of the bacteria seemed to result in a greatly increased blood velocity and flow when studied one month after the initiation of treatment.[117] If this proves to be reproducible an umbrella of supplemented probiotic could provide to the patients with liver cirrhosis a tool to reduce septic manifestations, but also the incidence of bleeding.

Lactic acid bacteria stimulate mucosal growth

Reduced epithelial cell proliferation and mucosal atrophy are associated with increased invasion of various pathogens to peritoneal lymph nodes and to interior organs, which produces a risky situation in critically ill patients, especially those on parenteral nutrition or on elemental diet.[118, 119] Local degrading in the gut by microbial fermentation of fibers and proteinous material constitute the mechanisms by which SCFAs, but also lactic acid, succinic acid and ammonia are made available throughout the lower gastrointestinal tract. SCFAs do in addition to providing fuel for the enterocytes also promote sodium and water absorption and suppress colonic propulsive motility and hereby reduce diarrhea (mainly propionic and buturic acid). SCFAs derive mainly from carbohydrate degradation and ammonia and isovaleric acid from degradation of proteinous material. It seems reasonable to assume that in the absence of supply of fibers for SCFA production the remaining bacteria will ferment proteinous material, which always is available (gastrointestinal secretions, apoptotic cells), and more ammonia be produced, which is highly unwanted in the cirrhotic patient, especially when treated in the ICU for liver failure.

A recently published study[120] suggest that probiotic bacteria, even in absence of supply of prebiotics is capable of stimulating growth of the mucosa in the lower gastroingestinal tract. Three groups of animals, all kept on elemental diet without any supply of fibers, were studied. One group served as contro, the other two sere treated with two different LAB. The cell crypt production rate (CCRP) was about 25-40% higher in the jejunum and ileum, 70% higher in the caecum and more than 200% higher in the distal colon in LAB supplied than in control rats. The effect was more pronounced in jejunum when treated with *Lactobacillus casei* and in the colon when supplied *Clostridium bytyricum,*[120] again suggesting that a combination of a few LAB could be advantageous.

Lactic acid bacteria prevents/reduces diarrhea

There seem to be no conditions is which LAB (and fibers) have been as extensively tried as in diarrhea of various kinds, varying from rather simple tourist diarrhea to severe and life-threatening conditions such as antibiotic-associated and radiotherapey-induced diarreha. It clear from al these studies that LAB provides a simple, inexpensive and effective tool, with no ducmented side effects, to be used both in prevention and treatment of all forms of diarrhea.[121] It is obvious that LAB are effective in controlling diarrhea of both bacterial and viral origin, but seem to be slightly more effective in virus-induced diarrhea. This is promising, as an increasing number of infections today both in connection with extensive surgery such as transplantation and severe chronic disease such as HIV are of viral origin.

A larger European multi-center trial in children one month to three years of age was recently reported. One group consisting in 140 children were randomly

allocated to oral rehidration + placebo, the other group of 147 children to oral rehydation + supply of 10^{10} cfu of Lactobacillus GG. The duration of diarrhea was 58.3 ± 27.6 hours in the LAB-treated group v. 71.9 ± 35.8 hours ($p = 0.03$). In rotavirus-positive children did in the LAB-treated group the diarrhea last 56.2 ± 1.9 hours vs 76.6 ± 41.6 in the control group ($p = 0.008$).[122]

Lactic acid bacteria prevents/reduces severity of colitis

Experimental studies as well as clinical observations suggest that the contents of the intestinal luminal enviroment are responsible for the initiation and/or perpetuation of inflammatory bowel disease. It has been convincingly demonstrated the concentrations of endogenous *Lactobacillus* and *Bifidobacteria* are significantly reduced in patients with active Crohn's disease, ulcerative colitis, pouchitis and experimental colitis.[123-126] These observations has stimulated interest in trying various probiotic bacteria in inflammatory bowel disease (IBD).

A series of experimental studies[124] and several uncontrolled clinical studies support the idea of using probiotics in patients with IBD, but so far few controlled studies have been reported.

A cocktail called VSL#3 consisting in four lactobacillus strains, three bifidobacteria strains plus *Streptococcus salivarius* ssp *thermophilus* (5×10^{11} cells/g), and most probably chosen at random without any further documentation of the molecular/immonological effects of each of the LAB was recently tried in an uncontrolled study in patients with ulcerative colitis.[127] The patients were given 3 gram a day during one year and 15/20 patients remained in remission, one was lost to follow up and 4/20 had signs of relapse. The same LAB cocktail was also tried in a small controlled study in patients with pouchitis.[128] Twenty patients served as controls, all showed remission within 9 months. In sharp contrast to this did only 3/20 patients develop remission during the same time period, when supplied with VSL#3 probiotic cocktail.[128] It is reasonable to assume that if a cocktail of LAB was provided, where each bacteria would be chosen based on well documented metabolic and immunological effects, one should be able to expect even better results.

A recently published Columbian study[129] compared the outcome of 1237 newborns (inpatients and transfer patients), who all received daily 250 million live *Lactobacillus acidophilus* and 250 million live *Bifidobacterium infantis* until they were discharged, usually after about one week. As controls served similar children treated during the year before. The incidence of necrotizing enterocolitis was with probiotic prophylaxis reduced to one third (18 vs 47, $p < 0.0005$) in the inpatients group, and by half (19 vs 38, $p < 0.03$) in the patients transferred from other hospitals (which most likely came under treatment late).[129] It is most importante to observe that no complications could be attributed to the use of probiotic preparations even in these very sick newborn children, weighing in average 2600 gr (range < 1000 to > 4000 g), and which in as much as one third of the babies suffered from severe conditions such as sepsis, pneumonia or meningitis. It was incidentally observed that the LAB-treated children suffered significantly less diaper dermatitis.

Lactic acid bacteria in intensive care patients

Few studies have been performed in a mixed ICU patient population. A small study was performed by a nurse in Hongkong as a thesis for B Sc Degree in Health Studies.[130] 19 patients received daily from within 12 hrs of arrival to the ICU 10^{10} of *Lactobacillus plantarum* 299, another 19 patients heat-killed *Lactobacillus plantarum* 299 (controls). 5/19 (26%) died in the treated group vs 8/19 (42%) in the control group, the difference did not reach statistical significance. However, it stimulated the physicians at the unit to undertake a larger study, which is under way. A somewhat larger prospective, randomized placebo controlled study was undertaken in a mixed abdominal surgery patient at the University of Berlin.[131] Thirty patients were treated with *Lactobacillus plantarum* 299 in a daily dosis of 10^{10} and compared to 30 patients receiving inactivated heat-killed *Lactobacillus plantarum* 299. Another thirty received parenteral nutrition (PN). The rate of complications were for the various groups: PN 30%, heat-inactivated lactobacilli 17% and active lactobacilli 13%. Infections developed in 3/30 (10%) patients in each of the two treated groups vs 9/30 (30%) in the PN group ($p = 0.001$). Furthermore, significantly more antibiotics were administerd to the PN group. The difference was even larger when the subgroup of patients having more extensive surgery (gastric and pancreatic surgery, mainly resections) were separately analysed. One of fifteen patients (7%) developed infections in the in the group receiving *Lactobacillus plantarum* vs 3/17 (17%) in the group receiving heat-inactivated *Lactobacillus plantarum* and 8/16 (50%) in the group on parenteral nutrition. Another and separate study was undertaken by the same group at Virchow Clinic, Charité University Hospital in patients undergoing liver transplantation.[132] Treatment with active as well as heat-killed *Lactobacillus plantarum* 299 and inulin fiber added was compared to selective bowel decontamination (SBD), which during several years was the golden standard of the clinic. Four of 31 patients (13%) in the group receiving active *Lactobacillus plantarum*, 11/32 (34%) in the group receiving inactivated *Lactobacillus plantarum* and 15/32 (48%) in the group treated by SBD developed infection within 30 days ($p = 0.017$).

A randomized study was just concluded in Györ, Hungary in material of patients with severe pancreatitits.[133] The rate of septic complications was significantly reduced in the group supplied live *Lactobaci-*

llus plantarum 299 compared to the group supplied heat-inactivated *Lactobacillus plantarum* 299; 4.5% (1/22) vs 30.4% (7/23), $p < 0.05$. Similarly the rate of reoperation was significantly reduced; 4.5% (1/22) vs 26.1% (6/23), $p < 0.05$.

General comments: Table III summarizes the present limited experience in ICU patients. All studies have been performed with a single, but well documented bioactive LAB, *Lactobacillus plantarum* 299. some of the studies discussed above were not large enough to allow satistical significance, but the trend is the same in all studies, the lowest mortality or the lowest infection rate always obtained in the group receiving supply of LAB and fiber. But the differences observed are impressive: in extensive gastric and pancreatic surgery 7% infection with and 50% without supply of pro- and prebiotics ($p < 0.05$, in liver transplant 13% with and 48% ($p = 0.017$) without supply of pro- and prebiotics, and acute pancreatitis 4.5% vs 30.4% ($p < 0.05$).

It has been calculated, based on the present Berlin experience, that groups of appr 30 patients are needed to reach statistical significance in mixed patient materials. Several such studies are on the way. However, when used in very sich patients, statistical significance seem to occur also with smaller groups; gastric and pancreatic surgery and severe pancreatitis resp.; appr 20 in each group. It is important to stress at this stage, that the limited documentation of clinical efficacy of treatment with *Lactobacillus* in very sick patient is further supported by extensive studies in experimental animals, using a variety of models.[1-5]

It has this far been necessary to accept that treatment of patients with *Lactobacillus* is done in parallel to treatment with strong antibiotics, which most likely will reduce the efficacy of LAB treatment. Although the doses of *Lactobacillus* supplied in the above studies were large compared to what has been given in other probiotic treatments, and even larger dose could eventually further improve the outcome. The treatment was also often instituted late and the supply of substrate (fibers) was never optimal. The supply of fibers could be both larger and more diverse, e.g. contain several different bioactive fibers.

Lactic acid bacteria to patients with fulminant MOF

Lactobacillus was supplied as a desperate action to five consecutive patients suffering from severe MOF after gastrointestinal surgery (fig. 1). The mean Apache II score fell from as a mean 18 before institution of treatmet to 12 and 9, after respectively 5 and 10 days of treatmente. All patients left the ICU unit in improved condition. A short description of each of the patients follows:

Patient 1 (fig. 1A) 74 year old man with Parkinson disease, who suffered severe upper GI bleedings. No source of bleeding could be found at emergency laparotomy. After the laparotomy did severe gastric wall necrosis, wound dehiscence and peritonitis develop. An emergency gastric resection was performed and a feeding jejunostomy applied. The patient was referred to the University hospital with severe sepsis and signs of pulmonary and renal insufficiencies. *Lactobacillus* and oat fiber was administered via a jejunal feeding tube. Dramatic recovery was observed and the patient could be weaned off the ventilator after 10 days and leave the ICU.

Patient 2 (fig. 1B) 65 year old man initically operated for perforated duodenal ulcer and diffuse peritonitis. He developed postoperatively severe sspsis with pulmonary inssuficiency. Repeated scans showed no signs of abscesses, and exploratory laparotomy was performed on two occasions. His general condition deteriorated with increasing leukocytosis and increasing plasma creatiine levels. Daily enteral supply of *Lactobacillus* and oat fiber was instituted from the 22nd day and a slow recovery began. He could leave the ICU after about 2 weeks of treatment.

Patient 3 (fig. 1 C) 52 year old man was operated at a local hospital with an emergency partial gastrectomy and later referred to the University hospital with a leaking duodenal stump. He was reoperated, gastrostomy performed and drainage of the retroduodenal stump and PTC applied. Despite these measures did the conditions quickly deteriorate and the patient developed high fever, leucocytosis, and signs of pulmonary, renal and hepatic insufficiencies. Treatment with *Lactobacillus* and oat was instituted from the 45th day. An inmmediate but slow recovery began and continued over the following three weeks. The function of the organs did steadily improve, he could be weaned off the ventilator and leave the ICU.

Patient 4 (fig. 1D) 43 year old man, who had an emergency sigmoid resection for a perforated diverticulitis. He developed postoperative anastomotic dehiscence with faecal peritonitis, and was reoperated with a Hartmann procedure. He continued to deteriorate and developed high fever and signs of ventilatory insufficiency and was referred to the Univesity hospital for care in the ICU. Probiotic treatment was instituted and he could leave the ICU after about one week on *Lactobacillus* and oat.

Patient 5 (fig. 1 E) 63 year old lady suffering from diabetes and operated on with an emergency colectomy and ileostomy due to a colonic ischemia with colonic wall necrosis. She developed postoperatively abdominal abscesses, wound dehiscence and semall bowel fistulas, and increasing signs of circulatory, ventilatory and renal insufficiencies. Treatment with Lactobacillus and oat was instituted. The patient recovered slowly during the following weeks and was able to leave the ICU after 24 days on pro- and prebiotics.

General Comments: None of the patient had positive blood cultures before or during the treatment. They developed all clinical signs of sepsis and organ dysfunction despite treatment with broad-spectrum anti-

biotics, which continued inparallel to the *Lactobacillus* and fiber treatment. All patients had received TPN before the institution of enteral nutrition with *Lactobacillus* and oat. Also TPN was often continued in parallel with the enteral nutrition. A dramatic improvement in general condition and Apache II scores ocurred from the day *Lactobacillus* and oat treatment was instituted in all cases. Especially encouraging is, that recovery was obtained even when the treatment was instituted late in the disease process (22 days in case 2 and 45 days in case 3).

Conclusions and final remarks

The molecular effects of pre-, pro- and synbiotics are well documented in the literature. The documentation of clinical effects is presently thin for all indications except diarrheal diseases. It is encouraging that the treatment seems to be even more effective in preventing viral diseases. This is important, as especially in transplantation viral complications are increasingly common. It also offers hope that the treatment can be of benefit in viral diseases such as HIV and positive experience has also been reported in this disease.[134]

As mentioned above the protection layer of lactobacillus does not exist only on the GI tract mucosa, it is imortant at all exterior body surfaces including those of the eye, the nose, the mouth, the respiratory tract, the vagina, not to forget the skin. It is clearly reduced at all sites when the patient is in the settings of ICU with its special hygienic conditions and supply of antibiotics and other drugs. Some observations support that an overflow of probiotic bacteria continuously occurs under normal hygienic conditions from the GI tract to all the other sites mentioned, but this is more unlikely to occur in the ICU, with all its vigorous hygienic conditions. Of that reason might in the future be indicated that the gastrointestinal supply is complemented use of LAB-containing gels on sensitive body surfaces and of LAB-containing aerosols for the respiratory tract, where this protection layer is much needed. The incidental observation that LAB supplementation reduces the incidence of diaper dermatitis is in this connection of interest. It is also interesting that two recent reports suggest that consumption of LAB-containing drinks prevents formation of biofilm and removes both yeast and bacteria from prothesis, in this case silicon rubber voice prostheses,[135, 136] suggesting that LAB could be effective also in the prevention of catheter infections.

As the problems with anbitiotic-associated microbial resistance increase, the medical world is increasingly looking for a tool to replace antibiotics, also for the sensitive and very artificial microbial world of ICu. Such a tool exists in combined use of pre- and probiotics. It is necessary to also remember that all fibers are not identical, they are each precursors for their special nutrients. It seems therefore important to provide several types of fibers and, if in any way possible, always fresh fruits and vegetables. Nor are all lactic acid bacteria similar in effects. It is salid the genetic differences between two LAB can be greater than those between a fish and a human being. In addition many of ingested LAB do not survive the acidity of the stomach, the bile acids of the small intestine, nor do they adhere to the intestinal mucosa Each LAB has its own marrow metabolic spectrum, which is why the LAB are more effective in consortia. This suuports the idea, that a composition of several LAB could have stronger effects than what can be obtained from administration of a single strain.

LAB cocktails for medical purpose must only be composed of bacteria with scientifically well documented bioactivities and demonstrated abilities such as a strong mucus adhesivity, great ability to ferment also semiresistant fibers such as inulin, strong antioxidant capacity and strong ability to modulate the immune response. Such LAB are normally not found in milk products, which LAB in general tend to have comparatively weak bioactivities. Instead they are found in fiber ferments such as saurkraut, sourdoughs, exotic dishes of fermented fruits and vegetables. An attempt to construct such a scientifically based composition of fibers and LAB, chosen on the basis of documented bioactivities, in which I am involved, is Synbiotic 2000. It consist in four bioactive LAB (containing 10^{10} of each of four LAB *Lactobacillus plantaru, Lactobacilus paracasei* subsp *paracasei, Pediacoccus pentoceus* and *Lactococcus raffinolactis*) and is combined with 10 gram of bioactive fibers (2.5 grams of each of betaglucan, inulin, pectin and resistant starch). It is presently the object of extensive studies on various indications around the world.

It is likely that the settings and premises of ICU, as we move further into the new millennium, wil be made less artifical and more to look natural. The physical and psychological environment will most likely be dramatically improved. Strong attempts will also be made to reduce the amount of pharmaceuticals, and to try to feed much more of natural food. The goal will be to reduce the stay in ICU and to use the home of the patient as much as possible. Patients, who not long ago where treated for long periods of time in the ICU, such as bone marrow transplant patients, are increasingly treated in an ecologically much more friendly place, their own home. Ecoimmunonutrition with pre-pro- and symbiotics offer to be suitable tools in a continuously changing process.

References

1. Bengmark S: Ecological control of the gastrointestinal tract. The role of probiotic bacteria. *Gut*, 1998, 42:2-7.

2. Bengmark S: Immunonutrition: Role of biosurfactans, fiber and probiotic bacteria. *Nutrition*, 1998, 14:585-594.
3. Bengmark S: Gut and the immune system: Enteral nutrition and immunonutrients. In SIRS, MODS and MOF —sysemic inflammatory response syndrome, multiple organ dysfunction syndrome, multiple organ failiure— pathophysiology, prevention and therapy. En: Baue AE, Faist E, Fry D (eds.). New York: Springer, 2000: 408-424.
4. Bengmark S: Refunctionalization of the gut. En: SIRS, MODS and MOF —systemic infllamatory response syndrome, multiple organ dysfunction syndrome, multiple organ failure— pathophysiology, prevention and therapy. En Baue AE, Faist E, Frey D (eds.): New York: SApringer, 2000: 435-446.
5. Bengmark S: Prospect for a new and rediscovered form of therapy: Probiotic and phage. En: Andrew PW, Oystron P, Smith GI Stewart-Tull DE (eds.): Fighting Infection in the 21st century. *Blackwells*, 2000: 97-132.
6. Macfarlane GT y Cummings JH: The colonic flora, fermentation and large bowel digestive function. En: Phillips SF, Pemberton JH, Shorter RG (eds.): The large intestine: physiology, pathophysiology and disease. Raven Press, New York, 1991: 51-92.
7. Roberfroid M: Dietary fiber, inulin and oligofructose: a review comparing their physiological effects. *Crit Rev Food Sci Nutri*, 1993, 33:103-148.
8. Bengmark S, Larsson K: to be published.
9. Best R, Lewis DA y Nasser N: The anti-ulcerogenic activity of the unripe banana (Musa species). *Br J Pharmacol*, 1984, 82: 107-116.
10. Hills BA y Kirwood CA: Surfactant approach to the gastric mucosal barrier: protection of rats by banana even when acidified. *Gastroenterology*, 1989, 97:294-303.
11. Dunjic BS, Svensson I, Axelsson J y cols.: Is resistance to phospholipase important to gastric musocal protective capacity of exogenous phosphatidylcholine? *Eur J Gastroenterol Hepatol*, 1994, 6:593-598.
12. Dunjic BS, Svensson I, Axelsson J y cols.: Green banana protection of gastric musoca against experimentally induced injuries in rats - a multicomponent mechanism? *Scand J Gastroenterol*, 1993, 28:894-898.
13. Kohn CL y Keithly JK: Enterla nutrition: Potential complications and patient montoring. *Nurs Clin Norte Am*, 1989, 24:339-353.
14. Zaporozhets TS, Besednova NN, Liamkin GP y cols.: I Antibacterial and therapeutic effectiveness of a pectin from sea grass zostera. II Immunomodulating properties of pectin from seawater grass zostera. *Antibiot Khimother*, 1991, 36:24-26 and 31-34.
15. Hohner GA y Hyldon DJ: Oat groat fractionation process. *US Patent*, 4,028, 468.
16. Beer MU, Arrigino E y Amado R: Effects of oat gum on blood cholesterol levels in healthy young men. *Eur J Clin Nutri*, 1995, 49:517-522.
17. Wang X y Gibson GR: Effects of the in vitro fermentation of oligofructose and inulin by growing bacteria in the human large intestine. *J Appl Bacteriol*, 1993, 75:373-380.
18. Egan SK y Petersen BJ: Estimated consumption of inulin and oligofructose by the US population. Technical Assessment Systems Inc Washington DC, USA, 1992.
19. Müller M y Lier D: Fermentation of fructans by epiphytic lactic acid bacteria. *J Appl Bacteriol*, 1994, 76:406-411.
20. Fiordaliso M, Kok N, Desager JP, Goethals F, Deboyser D, Roberforid M y Delzenne N: Dietary oligofructorse lowers triglycerides, phospholipids and cholesterol in serum and very low density lipoproteins of rats. *Lipids*, 1995, 30:163-167.
21. Southgate DAT: The definition and analysis of dietary fibre. *Nutr Rev*, 1977, 35:31-37.
22. Salyers AA, Palmer JK y Wilkins TD: Degradation of polysaccharides by intestinal bacterial enzymes. *Am J Clin Nutr*, 1978, 31 (suppl):S128.S130.
23. Anderson DMW, Brydon WG, Eastwood MA y Sedgwick DM: Dietary effects of sodium alginate in humans. *Food Add Contam*, 1991, 8:225-236.
24. Torsdottir I, Alpsten M, Holm G y cols.: A small dose of soluble alginate-fiber affects postprandial glycemia and gasric emptying in humans with diabetes. *J Nutr*, 1991, 121:795-799.
25. Gibson GR, Macfarlane S y Cummings JH: The fermentability of polysaccharides by mixed human faecal bacteria in relation to their suitability as bulk-forming laxatives. *Lett App Microbiol*, 1990, 11: 251-254.
26. García MJ, Charlez M, Fauli C y cols.: Physicochemical comparison of the dietary fibres glucomannan, galactomannan, carboxymethil cellulose, pectin and wheat bran. *Curr Ther Rres*, 1988, 43:1010-1013.
27. Biancardi G, Palmiero L y Ghirardi PE: Glucommannan in the treatment of overweight patients with osteoarthrithosis. *Curr Ther Res*, 1989, 46:908-912.
28. Tannock GW: Probiotic properties of lactic-acid bacteria: plenty of scope for fundamental R&D. *Trends in Biotechnology (BIBTECH)*, 1997, 15:270-274.
29. Ahrné S, Nobaek S, Jeppsson B y cols.: The normal *Lactobacillus* flora in healthy human rectal and oral mucosa. *J Appl Microbiol*, 1998, 85:88-94.
30. Finegold SM, Sutter VL y Mathisen GE: Normal indigenous intestinal flora. En: Hentges DJ (ed.): Human ingestinal microflora in health and disease. London: Academic Press, 1983: 3-31.
31. Adlerberth I, Carlsson B, de Mann P y cols.: Intestinal colonization with *Enterobacteriaceae* in Parkistani and Swedish hospital-delivered infants. *Acta Pediatrica Scandinavica*, 1991, 80:602-610.
32. Sepp E, Julge K, Vasur M y cols.: Intestinal microflora of Estonian and Swedish infant. *Acta Pediatrica*, 1997, 86:956-961.
33. Lencner AA, Lencner CP, Mikelsaar ME y cols.: Die quantitative Zusammensetzung der Lactoflora des Verdauungstrakts vor und nach kosmischen Flügen unterschiedlicher Dauer. *Die Nahrung*, 1984, 28:607-613.
34. Andersson R, Wang X y Ihse I: The influence of abdominal sespis on acute pancreatitis in rats: A study on moartality, permeability, arterial blood pressure and intestinal blood flow. *Pancreas*, 1995, 11:365-373.
35. Leveau P, Wang X, Soltesz V y cols.: Alterations in intestinal permeability and microflora in experimental acute pancreatitis. *In J Pancreatology*, 1996, 20:119-125.
36. De Souza LJ, Sampietre SN, Figueiredo S y cols.: Bacterial translocation during acute pancreatitis in rats. (In Portuguese, with English summary). *Rev Hosp Clin Fac Med S. Paolo*, 1996, 51:116-120.
37. Schwartz MN: Hospital-acquired infections; diseases with increasingly limited therapies. *Prox Natl Acad Sci USA*, 1994, 91:2420-2427.
38. Hasse J; Blue LS, Crippin JS y cols.: The effect of nutritional status on length os stay and clinical outcomes following liver transplantation. Abstract. *J Am Diet Assoc*, 1994, 88:143-145.
39. van der Poll T, Levi M, Braxton CC y cols.: Parenteral nutrition facilitates activation of coagulation but nor fibrinolysis during human endotoxemia. *The Journal of Infectious Diseases*, 1998, 177:793-795.
40. Frohn MJN: Letter to the Editor. *Lancet*, 1976, 11:1019-10-20.
41. Latto C: Postoperative Deep-vein thrombosis, pulmonary Embolism, and High-Fibre Diet. *The Lancet*, 1976, 11:1197.
42. Malhotra SL: Studies in blood coagulation, diet and ischemic heart disease in two population groups in India. *British Heart Journal*, 1968, 30:303-308.
43. Vorster HH, Kruger HS, Fryllinck S y cols.: Physiological effects of the dietary fiber component konjac glucomannan in rats and baboons. *J Plant Food*, 1985, 6:263-274.
44. Koepp O y Hegewisch S: Effects of guar on plasma viscosity and related parameters. *Europ J Pediatr*, 1981, 137:31-33.
45. Chegini N: The role of growth factors in peritoneal healing: transforming growth factor beta (TGF-betaq). *Eur J Surg*, 1997, (supp):17-23.
46. Bothin C, Okada M, Midtvedt T y Perbeck L: The intestinal

flora influences adhesion formation aqround surgical aqnastomoses. *Br J Surg,* 2001, 1:143-145.
47. Antoniades HN y Westmoreland N: Metabolic influences in experimental thrombosis. *Ann N Y Acad Sci,* 1976, 275:28-46.
48. Pilgeram LO y Pickart RL: Control of fibrinogen biosynthesis: the role of free fatt acid. *J Atheroscler Res,* 1968, 8:155-166.
49. Venter CS y Vorster HH: Possible Metabolic Consequences of Fermentation n the Colon for Humans. *Medical Hypothesis,* 1892, 29:161-166.
50. Randle PJ, Hales CN, Garland BP y Newsholme EA: The glucose fatty-acid cicyle. Its role in insulin sensitivity and the meatbolic disturbances of diabetes mellitus. *The Lancet,* 1963, 1:785-789.
51. Wang H, Storlien LH y Huang XF: Influence of dietary fats on c-Fos-like immunoreactivity in mouse hypothalamus. *Brain Research,* 1999, 843:184-192.
52. Watanabe S, Onozaki K, Yamamoto S y Okuyama H: Regulation by dietary essential fatty acid balance of tumor necrosis factor production in mouse macrophages. *J Leukoc Biol,* 1993, 53:151-156.
53. Lin BF, Huang CC, Chiang BL y Jeng SJ: Dietary fat influences Ia antigen expression, citokines and prostaglandin E_2 production in immune cells in autoimmune-prone NZBxNZW F1 mice. *British Journal of Nutrition,* 1996, 75:711-722.
54. Biffl WL, Moore EE, Moore FA y Barnett CC: Interleukin-6 delays neutrophil apoptosis via a mechanism involving platelet-activating factor. The Journal of Trauma, Injury. *Infection and Critical Care,* 1996, 40:575-579.
55. Sautner T, Függer R, Götzinger P y cols.: Tumour necrosis factdor-α and interleukin-6: Early indicators of bacterial infection after human orthotopic liver transplantation. *Eur J Surg,* 1995, 161:97-101.
56. Brandtzaeg P, Halstensen TS, Kett K y cols.: Immunobiology and immunopathology of human gut mucosa: humoral immunity and intraepithelial lymphocytes. *Gastroenterology,* 1989, 97:1562-1584.
57. Kiyono H y McGhee JR: T helper cells for mucosal immune responses. En: Ogra PL, Mestecky J, Lamm ME y cols. (eds.): Handboo, of mucosal immunology. Adademic Press, Orlanda, Florida, 1994: 263-274.
58. Brandzaeg P: Molecular and cellular aspects of the secretory immunoglobulin system. *APMIS,* 1995, 103:1-9.
59. Bermann JF, Chassany O, Perit A y cols.: Correlation between echographic gastric emptying and appetite: influence of psyllium. *Gut,* 1992, 33:1041-1043.
60. Rhee YH y Kim HI: The correlation between sleeping-time and numerial change of intestinal normal flora in psychiatric insomnia patients. *Bull Nat Sci Chungbuc Natl Univ,* 1987, 1:159-172.
61. Brown R, Price RJ, King MG y cols.: Are Antibiotic Effects on Sleep Behavior in the Rat Due to Modulation of Gut Bacteria? Physiol Behav, 1990, 48:561-565.
62. Meiselman HL, Lieberman HR: En GOldberg I (ed.): Mood and Performance Foods. Chapter 7 in FUnctional Foods. Designer Foods, Pharmafoods, Nutraceuticals. *Chapman and Hall,* 1994: 126-150.
63. Del Águila LF, Claffey KP y Kirwan JP: TNF-alfa impairs insulin signaling and insulin stimulation of glucose uptake in C2C12 muscle cells. *Am J Physiol,* 1999, 39: E849-855.
64. Bertini R, Bianci M y Ghezzi P: Adrenalectomy sensitizes mice to the lethal effects of interleukin-1 and tumor-necrosis factor. *J Exp Med,* 1988, 167:1702-1712.
65. Ramachandra RN, Sehon AH y Berczi I: Neuro-hormonal host defence in endotoxin shock. *Brain Beahv Immun,* 1992, 6:157-169.
66. Olff M: Stress. Depression and immunity: the role of defense and copying styles. *Phychiatry Res,* 1999, 85:7-15.
67. Shirabe K, Matsumata T, Shimada M y cols.: A comparison of parenteral hyperalimentation and early enteral feeding regarding systemic immunity after major hepatic resection - the results of a randomized prospective study. *Hepato-Gastroenterology,* 1997, 44:205-209.
68. Windsor ACJ, Kanwar S, Li AGK y cols.: Compared with parenteral nutrition, enteral feeding attenuates the acute phase response, and improves disease severity in acute pancreatitios. *Gut,* 1998, 42:431-435.
69. Barton RC: Immune-enchancing enteral formulas: are they benificial in critically ill patients? *Nutrition in Clinical Practica,* 1997, 12:51-62.
70. Dickerson RN: Immune-enhancing enteral formulas in critically ill patients. *Nutrition in Clinical Practice,* 1997, 12:49-50.
71. Bengmark S: Gut microenvironment and immune function. Current Opinion in Clinical Nutrition and Metabolic Care, 1999, 2:83-85.
72. Yasui H, Nagaoka N, Mike A y cols.: Detection of *Bifidobacterium* strains that induce large quantities of IgA. *Microb Ecol Health Dis,* 1992, 5:155-162.
73. Malin M, Suomalainen H, Saxelin M y Isolauri E: Promotion of IgA immune response in patients with Crohn's disease by oral bacteriotherapy with *Lactobacillus* GG. *Annals of Nutrition and Metabolism,* 1996, 40:137-145.
74. Kaila M, Isolauri E, Soppi E y cols. Enhancement of the circulating antibody secreting cell responde in human diarrhea by a human *lactobacillus* strain. *Pediatric Research,* 1992, 32:141-144.
75. Solis-Pereyra B, Aattouri N y Lemonnier D: Role of food in the stimulation of citykine production. *Am J Clin Nutri,* 1997, 66:521S-525S.
76. Mao Y, Nobaek S, Kasravi B y cols.: The effects of *lactobacillus* strains and oat fiber on methotrexate-induced enterocolitis in rats. *Gastroenterology,* 1996, 111:334-344.
77. Van der Poll T, Coyle SM, Levi M y cols.: Fat emulsion infusion potentiates coagulation activation during human entotoxemia. *Thrombosis and Heamostasis,* 1996, 75:83-86.
78. Peck MD, Alexander JW, Ogla CK y Babcock GF: The effect of dietary fatty acids in responde to *Pseudomonas* infection in burned mice. *J Trauma,* 1990, 30:445-452.
79. Roskowski K, Ko KL, Beuth J y cols.: Intestinal microflora of BALB/c-mice and function of local immune cells. *Zeitschr Baketeriol Hygien,* 1988, 270:270-279.
80. Pulverer G, Ko HL, Roszkowski W y cols.: Digestive Digestive tract microflora liberates low molecular weight peptides with immunotriggering activity. *Zentralbl Bakteriol,* 1990, 272:318-327.
81. Kilkullen JK, Ly OP, Chang TH y cols.: Nonviable *Staphylococcus aureus* and its peptidoglucan stimulate macrophage recruitment angiogenesis, fibroplasia and collagen accumulation in wounded rats. *Wound, Reapir and Regeneration,* 1998, 6:149-156.
82. Hatcher GE y Lamprech RS: Augmenmtation of macrophage phagocytic activity by cell-free extracts of selected lactic acid-producing bacteria. *J Diary Scien,* 1993, 76:2485-2492.
83. Kato I, Yokokura T y Mutai M: Correlation between increase in Ia-bearing macrophages and induction of T-cell-dependent antitumor activity by *Lactobacillus casei* in mice Cancer, Immunology and Immunotherapy, 1988, 26:215-221.
84. Outwater JL, Nicholson A y Barnard N: Dairy products and breast cancer: The IGE-1, estrogen and bGH hypothesis. *Medical Hypotheses,* 1997, 48:453-461.
85. Westin JB y Richter E: The Israeli Breast-Cancer anomaly. *Ann NY Acad Scien,* 1990, 609:269-279.
86. Hague A, Manning AM, Hanlon KA y cols.: Sodium butyrate induces apoptosis in human colonic tumour cell lines in a p53-independent pathway: implications for the possible role of dietary fiber in the prevention of large-bowell cancer. *Int J Cancer,* 1993, 55:498-505.
87. Hong MY, Chang WC, Chapkin RS y Lupton JR: Relationship among colonocyte proliferation, differentiation, and apoptosos as a function of diet and carcinogen. *Nutrition and Cancer,* 1997, 28:20-29.
88. Solary E, Dubrez L y Eymin B: The role of apoptosis in the apthogenesis and treatment of diseases. *Eur Resp J,* 1996, 9:1293-1305.
89. Heerdt BG, Houston MA y Augenlicht LH: Potentiation by

specific short-chain fatty acdis of differentiation and apoptosis in human colonic carcinoma cell lines. *Cancer Research,* 1994, 54:3288-3294.
90. Marchetti MC, Graziella Migliorati, Rosalba Moraca y cols.: Possible mechanism involved in apoptosis of colon tumor cell lines induced by deoxycholic acid, short-chain fatty acdis, and their mixtures. *Nutrition and Cancer,* 1997, 28(1):74-80.
91. Key FB y Mathers JC: Digestive adaptations of rats given white bread and cooked haricot beans (Phaseolus vulgaris): large bowel fermentation and digestion of complexes carbohydrates. *Brit J Nutr,* 1995, 74:93-406.
92. Kirjavainen PV, El-Nezami HS, Salminen SJ y cols.: The effect of orally administered viable probiotic and dairy lactobacilli on mouse lymphocyte proliferation. *FEMS Immun and Med Microbiol,* 1999, 26:131-135.
93. Björksten B: Risk factors in early childhood for the development of atopic diseases. *Allergy,* 1994, 49:400-407.
94. Lucey DR, Clerici M, Shearer GM: Type 1 and type 2 cytokine dysregulation in human infections, neoplastic and inflammatory diseases. *Clin Microbil Rev,* 1996, 9:532-562.
95. Björksten B: Allergy priming early in life. *Lancet,* 1999, 353:167-168.
96. Murosaki S, Yamamoto Y, Ito K y cols.: Heat-killed *Lactobacillus plantarum* L-137 suppresses naturally fed antigen-specific IgE production by stimulation of IL-12 production in mice. *J Allerg Clin Immunol* 1998, 102:57-64.
97. Miettinen M, Matikainen S, Vuopio-Varkila J, Pirhonen J y cols.: Lactobacilli and Streptococci induce Interleukin-12 (IL-12), IL-18, and gamma interferon production in human peripheral blood mononuclear cells. Infect Immun, 1998, 66:6058-6060.
98. Shida K, Makino K, Takamizawa K y cols.: *Lactobacillus casei* inhibits antigen-induced IgE secretion through regulation of cytokine production in murine splenocyte cultres. *Internat Arch Allerg Immunol,* 1998, 115:278-287.
99. Eckmann L, Kagnoff MF y Fierer J: Intestinal epithelial cells as watchdogs for the natural immune system. *Trends Microbil,* 1995, 3:118-120.
100. Ogle CK, Guo X, Hasselgren PO y cols.: The gut as a source of inflammatory cytokines after stimulation with endotoxin. *Europ J Surg,* 1997, 163:45-51.
101. Henderson B, Poole S y Wilson M: Microbial/host interactions in health and disease: Who controls the cytokine network? *Immunopharmacol,* 1996, 35:1-21.
102. Henderson B, Wilson M y Wren B: Are bacterial exotoxins cytokine network regulators? *Trends in Microbiology,* 1998, 5:454-458.
103. Meyer TA, Noguchi Y, Ogle CK y cols.: Endotoxin stimulates interleukin-6 production in intestinal epithelial cells. A synergistic effect with prostaglandin E_2. *Arch Surg,* 1994, 129:1294-1295.
104. Meyer TA, Tiao GM, James JH y cols.: Nitric oxide inhibits LPS-induced IL-6 production in enterocytes. *J Surg Res,* 1995, 58:570-575.
105. Marin ML, Tejada-Simon MV, Lee JH y cols.: Stimulation of citykine production in clonal macrophage and T-cell models by *Streptococcus thermophilus:* comparison with *Bifidobacterium* sp. and *Lactobacillus bulgaricus. J Food Protect,* 1998, 61:859-864.
106. Rangavajhyala N, Shahani KM, Sridevi G y Srikumaran S: Nonlipopolysaccharide compoent(s) of *Lactobacillus acidophilus* stimulate(s) the production of interleukin 1α and tumor necrosis factor-α by murine macrophages. *Nutr Cancer,* 1997, 28:130-134.
107. Adlerberth I, Ahrné S, Johansson ML y cols.: A mannose-specific adhesion mechanism in *Lactobacillus plantarum* conferring binding to the human colonic cell line HT-29. *Appl Environ Microbiol,* 1996, 62:2244-2251.
108. Forstner JF y Forstner GG: Gastrointestinal mcuus. En: Johnson LG (ed.): Physiology of the Gastrointestinal Tract (3rd ad). New York: Raven, 1994: 1255-1283.
109. Van Klinken BJ, tytgat KMAJ, Buller HA y cols.: Biosynthesis of intestinal mucins: MUC1, MUC2, MUC3 and more. *Biochen Soc Trans,* 1995, 23:814-818.
110. Mack DR, Michail S, Wei S y cols.: Probiotic inhibit enteropathogenic *E. coli* adherence in vitro by inducing intestinal mucin gene expression. *Am J Physiol,* 1999, 276 (Gastrointest. Liver Physiol 39: G941-G950.
111. Haskard C, Binnion C y Ahokas J: Factors affecting the squestration of aflatoxin by *Lactobacillus thamnosus* strain GG. 2Chemico-Biological Interactions, 2000, 128:39-49.
112. Oatley JT, Rarick MD, Ji GE y Linz JE: Binding of Aflatoxin to Bividobacteria in vitro. *J Food Protect,* 2000, 63:1133-1136.
113. Goulis J, Patch D y Burroughs AK: Bacerial infection in the pathogenesis of variceal bleeding. *Lancet,* 1999, 353:139-142.
114. Nanji AA, Khetty U y Sadrzadeh SMH: *Lactobacillus* feeding reduces endotoxemia and severity of experimental alcoholic liver disease. *Proc Soc Exp Med Biol,* 1994, 205:243-247.
115. Adawi D, Kasravi FB, Molin G y Jepp·on B: Effect of *Lactobacillus* supplementation with and without arginine on liver damage and bacterial translocation in an acute liver injury model in the rat. *Hepatol,* 1997, 25:642-647.
116. Adawi D, Molin G, Ahrné S y cols.: Modulation of the colonic bacterial flora affects differently bacterial translocation and liver injury in acute 117. De Santis A, Famularo G y De Simone C: Probiotics for the hemodynamic alterations in patients with liver cirrhosis. Letter to the editor. *AJG,* 2000, 95:323-324.
118. Alverdy J, Aoys E y Moss G: Effects of commercially available defined liquid diets on the intestinal microflora and bacterial translocation from the gut. *JPEN J Parenter Enteral Nutr,* 1990, 14:1-6.
119. Deich E, Xu Du, Naruhn M y cols.: Elemental diet and IV-TPN-induced bacterial translocation in associated with loss of intestinal barrier function against bacteria. *Ann Surg,* 1995, 22:299-307.
120. Ichikawa H, Kuroiwa T, Inagaki A y cols.: Probiotic bacteria stimulate epithelial cell proliferation in rat. *Dig Dis & Scien,* 1999, 44:2119-2123.
121. Heyman M: Effect of Lactic Acid Bacteria on diarrheal diseases. *J Am Coll Nutr,* 2000, 19:S137-S146.
122. Guandalini S, Pensabene L, Zikri MA y cols. *Lactobacillus* GG administered in oral rehydration solution to children with acute diarrhea: a multicenter European study. *J Pediatr Gastr Nutr,* 2000, 30:54-60.
123. Fabia R, Ar'Rajab A, Johansson ML y cols.: Impairment of bacterial flora in human ulcerative colitis and in experimental colitis in ther at. *Digestion,* 1993, 54:248-255.
124. Fabia R, Ar'Rajab A, Johansson ML y cols.: The effect of exogenous administration of *Lactobacillus reuteri* R2LC and oat fibre on acetic acid-induced colitis in the rat. *Scand J Gastroenterol,* 1993, 28:155-162.
125. Favir C, Neut C, Mizon C y cols.: Fecal β-D-galactosidase and bifidobacteria are decreased in Crohn's disease. *Dig Dis Sci,* 1997, 42:817-822.
126. Sartor RB: Microbiol factors in the pathogenesis of Crohn's disease, ulcerative colitis and experimental intestinal inflammation. En: Kirsner JG (ed.): Inflammatory bowel diseases. 5 ed., Philadelphia, Saunders, 1999: 153-178.
127. Venturi A, Gionchetti P, Rizzello F y cols.: Impact on the composition of the faecal flora by a new probiotic prepartion: preliminary data on maintenance treatment of patients with ulcerative colitis. *Aliment Pharmacol Ther,* 199, 13:1103-1108.
128. Gionchetti P, Rizello F, Venturi A y cols.: Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis: a double-blind, placebo-controlled trial. *Gastroenterology,* 2000, 119:305-309.
129. Hoyos AB: Reduced incidence of necrotizing enterocolitis associated with enteral administration of *Lactobacillus acidophilus* and *Bifidobacterium Infantis* to neonates in an intensive care unit. *In J Infect Dis,* 1999, 3:197-202.
130. Gomersall Carolyn M: Does the administration of lactobacillus to critically ill patients decrease the severity of multi-organ dysfunction or failure. Thesis for B Sc degree in Health

Studies at University of Surrey, Roehampton Institute, School of Life Sciences, London, 1998.
131. Rayes N, Hansen S, Boucsein K y cols.: Comparison of parenteral and early enteral nutrition with fibre and lactobacilli after major abdominal surgery - a prospective randomized trial. In manuscript.
132. Rayes N, hansen S, Boucsein K y cols.: Early enteral supply of *Lactobacillus* and fibre ve selective bowel decontamination (SBD) - a controlled trial in liver transplant recipients. In manuscript. 2001.
133. Oláh, Attila y cols. To be published.
134. Cunningham-Rundles S, Ahrne S, Bengmark S y cols.: Probiotics and immune response. *Am J Gastroenterol*, 2000, 95(1 suppl):S22-25.
135. Buscher HJ, Free RH, Van Weissenbruch R y cols.: Preliminary observations on influende of diary products on biofilm removal from silicon rubber voice prosthesis in vitro. *J Dairy Science*, 1999, 83:641-647.
136. van der Mei HC, Free RH, Elving GJ y cols.: Effect of probiotic bacteria on prevalence of yeast in oropharingeal biofilmson silicone rubber voice prostheses in vitro. *J Med Microbiol*, 2000, 49:713-718.

Nutrición Hospitalaria

Nutr. Hosp. (2001) XVI (6) 257-261
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Situación actual de la nutrición enteral domiciliaria en Galicia. Estudio multicéntrico

L. F. Pérez Méndez*, R. V. García-Mayor** y Grupo de Trabajo de la Sociedad Gallega de Nutrición y Dietética***

* *Sección Nutrición.* ** *Servicio de Endocrinología. Hospital Xeral-Cíes de Vigo.* *** *Ver lista de colaboradores en pág. 261.*
Este trabajo fue subvencionado por la Sociedad Gallega de Nutrición y Dietética.

Resumen

Objetivo: **Ante la falta de datos sobre la prevalencia de pacientes en nutrición enteral domiciliaria (NED) nosotros diseñamos el presente estudio cuyo objetivo es conocer la prevalencia de NED en nuestra comunidad.**

Diseño: **Estudio transversal.**

Pacientes: **Pacientes, mayores de 14 años, edad media de 56 ± 2,29 años (rango 14-96) atendidos entre enero de 1998 y diciembre de 1999, en las unidades de nutrición de hospitales de la Comunidad Autónoma Gallega y sometidos a NED. Total pacientes: 2.784; población de referencia: 1.789.983.**

Método: **Los datos se obtuvieron a partir de un cuestionario previamente diseñado.**

Resultados: **La prevalencia de nutrición enteral domiciliaria global fue del 10,34 casos/10.000 habitantes, por provincias fue de 18,8 para La Coruña, 1,3 para Lugo, 0,4 para Ourense y del 20,85 para Pontevedra. Los servicios que demandan con más frecuencia soporte nutricional son las especialidades médicas (48,3%), seguidas de las especialidades quirúrgicas (20,2%) y los centros de Atencion Primaria (19,2%). Las enfermedades que con más frecuencia necesitaron soporte nutricional fueron en orden de importancia: 1) anomalías neurológicas (43,6%); 2) neoplasias (30,7%); 3) enfermedad inflamatoria intestinal (10,5%). La vía de administración de la NED, más frecuentemente utilizada fue la vía oral (58,3%) seguida de la nutrición enteral por sonda nasogástrica (28,46%), la PEG (9,87%), gastrostomía (6,5%) y yeyunostomía (0,65%). El índice de complicaciones fue de 0,18 pacientes-año, las complicaciones gastrointestinales fueron las más frecuentes (0,12 paciente-año) seguidas de las mecánicas (0,09 paciente-año). El índice de**

Correspondencia: Luisa Fernanda Pérez Méndez.
Sección de Nutrición.
Hospital Xeral-Cies de Vigo.
Pizarro, 22.
36204 Vigo.
Correo electrónico: lpm@unicies.cesga.es

Recibido: 6-II-2001.
Aceptado: 3-V-2001.

HOME ENTERAL NUTRITION IN GALICIA. MULTICENTRIC STUDY

Abstract

Aim: **To determinate the prevalence of patients with Home Enteral Nutrition (HEN) in Galicia.**

Design: **Transversal study.**

Subjects: **Patients aged ≥ 14 years, treated with HEN in our community since January 1998 to December 1999. Population of reference was 1.789.983.**

Method: **Questionnaire previously designed.**

Main results: **During the study period were treated 2,784 patients which represent a prevalence of 10.34 cases/10,000 inhabitants, being 18.8 for La Coruña, 1.3 for Lugo, 0.4 for Ourense and of the 20.85 for Pontevedra. The mean age of the patients was of 56 ± 2.29 years (range 14-96). The Clinics units that required more frequently HEN were the Medical Units (48.3%), followed of the Surgery Units (20.2%) and the Primary Care Units (19.2%). Neurological abnormalities (43.6%), Neoplasias (30.7%) and Intestinal Inflammatory Disease (10.5%) were patients more frequently required HEN. Regarding to administration route 58.3%, 28.46%, 9.87%, 0.5% and 0.65% used oral, nasogastric tube, PEG, gastrostomy and yeyunostomy respectively. The Index of complications was 0.18 of patient-year, due to gastrointestinal anomalies 0.12 patient-year, mechanical 0.09 patient-year. The index of hospitalizations in relation to the nutritional treatment was 0.026 patient-year.**

Conclusions: **The prevalence of HEN in our community is of 10.34 cases/10,000 inhabitants. This kind of treatment is more frequently in the areas with high-density population. The frequency of complications was low.**

hospitalizaciones/paciente-año relacionados con la terapia nutricional fue del 0,026.

Conclusiones: **La prevalencia de la NED en nuestra comunidad es de 10,34 casos/10.000 habitantes. La NED se lleva a cabo en todas las áreas sanitarias de nuestra comunidad con mayor predominio en las áreas más pobladas. La ruta de administración más frecuente fue la vía oral y destaca el bajo número de complicaciones. Estos datos pueden servir para comparar con otras localidades.**

(Nutr Hosp 2001, 16:257-261)

Palabras clave: Nutrición enteral domiciliaria. Prevalencia.

This data may be useful to compare with date from other areas and countries.

(Nutr Hosp 2001, 16:257-261)

Key words: Home Enteral Nutrition. Prevalence.

Introducción

En las últimas décadas ha aumentado de forma importante la prevalencia de enfermedades de origen nutricional y de las enfermedades que requieren soporte nutricional ya sea de forma coadyuvante o paliativa[1].

La nutrición artificial (NA) que puede ser: parenteral (NP) y enteral (NE), esta última por su menor coste[2] y por ser más fisiológica[3], se está convirtiendo en la mejor alternativa para una adecuada nutrición de los pacientes subsidiarios de NA.

En España, la NE ha supuesto una contribución importante en el manejo del paciente extrahospitalario que precisa de soporte nutricional, el Real Decreto 63/1995 y la Orden Ministerial del 2 de junio de 1998, ha regularizado las prestaciones y permitido la creación de unidades de nutrición, imprescindibles para el adecuado manejo y control de este tipo de enfermos, mejorando tanto su calidad de vida como disminuyendo las complicaciones derivadas de estados de malnutrición crónicos. Influyendo igualmente de forma positiva en los costes sanitarios que generan este tipo de enfermos.

Ante la falta de datos sobre la prevalencia de pacientes en nutrición enteral domiciliaría (NED) nosotros diseñamos el presente estudio cuyo objetivo es conocer la prevalencia de NED en nuestra comunidad.

Sujetos y métodos

Sujetos y métodos Pacientes, mayores de 14 años, atendidos en las unidades de nutrición existentes en los siguientes hospitales de la Comunidad Autónoma Gallega: C. H. Juan Canalejo, C. H. Universitario de Santiago, C. H. Arquitecto Marcide, Hospital Naval de la provincia de La Coruña; C.H. Xeral-Calde, H. C. de Burela de la provincia de Lugo; C. H. de Ourense y C. H. Xeral-Cíes de Vigo, H. Provincial de Pontevedra y Clínica Povisa de la provincia de Pontevedra, población de referencia: 1.789.983 habitantes[4] (población protegida por el SERGAS, mayor de 14 años, año 1999). Período de estudio: enero de 1998 a diciembre de 1999.

Diseño: Estudio transversal.

Metodología: Se elaboró un formulario para la recogida de datos, en el que figuraban los siguientes ítems: motivo de consulta, servicio de procedencia, enfermedad de base, hábitat, edad, sexo, vía de administración, pauta de infusión, fórmulas utilizadas, número de hospitalizaciones, complicaciones relacionadas con la nutrición, evolución del soporte nutricional, tiempo de soporte nutricional. Los datos se obtuvieron de la historia nutricional del paciente. Tanto los índices de complicaciones como de hospitalizaciones se calcularon dividiendo número de las mismas por el número de pacientes tratados en el año 1999.

Análisis de los resultados: Los datos obtenidos se introdujeron en una base de datos que permita la gestión de los mismos y su exportación a otras aplicaciones informáticas. Para el estudio estadístico se empleó el paquete estadístico SPSS 10.0.

Resultados

En el período de estudio fueron tratados 2.784 pacientes, que representa una prevalencia de nutrición enteral domiciliaria del 10,34 casos/10.000 habitantes. Por provincias fue de 18,8 para La Coruña, 1,3 para Lugo, 0,4 para Ourense y del 20,85 para Pontevedra (tabla I) (fig. 1).

Datos demográficos: La media de edad de los pacientes fue de 56 ± 2,29 años (rango 14-96). Observamos un discreto predominio del paciente procedente del medio urbano sobre el de procedencia rural (La Coruña 63,5/36,5%, en Ourense 70/30%, Pontevedra 61,15/38,85%, siendo Lugo similares ambas poblaciones al 50%. En cuanto al sexo, el predominio de uno u otro fue diferente dependiendo de las provincias (tabla II).

Unidades que demandan NED: De forma general los servicios que demandan con más frecuencia soporte nutricional son las especialidades médicas (48,3%), seguidas de las especialidades quirúrgicas (20,2%) y los centros de atención primaria (19,2%), las características del centro hace que predominen uno u otras unidades de procedencia (tabla III).

Tipo de paciente que con más frecuencia demanda NED: 1) pacientes neurológicos (43,6%); 2) pacientes

Tabla I
Población y pacientes sometidos a NED

Provincia	*Centro*	*Población protegida*	*Pacientes tratados*	*Prevalencia (casos/10.000 habitantes)*
La Coruña	C. H. Juan Canalejo	349.825	475	13,5
	C. H. U. S.	272.344	864	31,7
	C.H.A. Marcide	168.131	150	8,9
	H. Naval de Ferrol	–	16	
	Subtotal	790.300	1.489	18,8
Lugo	C. H. Xeral-Calde	194.696	8	0,4
	H. Costa de Burela	57.887	25	4,3
	Subtotal	252.583	33	1,3
Ourense	C. H. Ourense	225.957	10	0,4
Pontevedra	C. H. Xeral-Cies. Vigo	133.314	408	30
	H. Meixoeiro	140.914	198	16
	H. Provincial	139.801	372	13,4
	C. Povisa	107.114	258	24
	Subtotal	521.143	1.236	20,85`
	Global	1.789.983	2.784	10,34

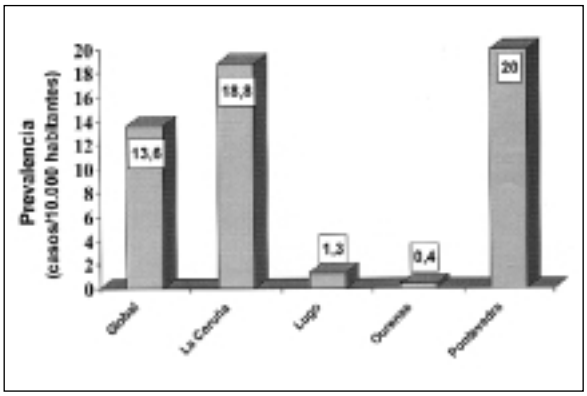


Figura 1.—Prevalencia de nutrición enteral domiciliaria.

neoplásicos (30,7%); 3) pacientes con enfermedad inflamatoria intestinal (EII) (10,5%), seguido en orden de importancia por pacientes con diferentes tipos de desnutrición causados por SIDA, anorexia nerviosa, etc. (tabla IV).

Vía de administración: La vía de administración de la NED más frecuentemente utilizada fue la vía oral (58,3%) seguida de la nutrición enteral por sonda nasogastrica (28,46%), la PEG (9,87%), gastrostomía (6,5%), y yeyunostomía (0,65%) (tabla V).

Tiempo de soporte nutricional: El tiempo medio de soporte nutricional fue de 1,5 años ± 0,88 (rango 0,4-3). Las causas de retirada de la NED fueron exitus relacionado con la enfermedad de base (58,49%), exitus debido a otras causas (0,94%), paso a dieta oral (40,57%).

Fórmulas utilizadas: La dieta polimérica fue la más utilizada en el 97,5% de los casos, y dentro de las poliméricas las dietas que se prescriben con más frecuencia fueron: 1) estándar sin fibra (46%); 2) estándar con fibra (25%); 3) específicas (13%); 3) hipercalórica (8%); 4) hiperproteica (8%). Dentro de las fórmulas específicas, las más utilizadas fueron la diabética (5%) y la específica para enfermos renales (2,4%).

Complicaciones: El número de complicaciones fue de 103, en 531 pacientes, el registro corresponde únicamente a dos centros hospitalarios, C. Hospitalario Universidad de Santiago (CHUS) y H. Xeral-Cíes de Vigo, lo que da un índice de complicaciones de 0,18 paciente-año, en orden de frecuencia las complicaciones gastrointestinales fueron las más frecuentes (0,12 paciente-año) seguidas de las mecánicas (0,09 paciente-año). Entre las complicaciones gastrointestinales destacan la diarrea y el estreñimiento y entre las mecánicas la broncoaspiración, una peritonitis química tras una gastrostomía y un caso de úlcera por decúbito de la sonda. No se valoró como complicación el cambio de sonda. El índice de hospitalizaciones/paciente-año relacionados con la terapia nutricional fue del 0,026.

Discusión

El objetivo del estudio fue determinar la prevalencia de la NED en nuestra comunidad, para ello se realizó el presente trabajo multicéntrico con la participación de todas la unidades de nutrición de la comunidad siendo patrocinado por la Sociedad Gallega de Nutrición y Dietética. Este tipo de soporte nutricional comenzó a emplearse en 1996 en nuestra comunidad. Se lleva a cabo en todas las provincias y dependen de un centro de referencia hospitalaria de acuerdo con la organización sanitaria del SERGAS,

Tabla II
Datos demográficos

	Global	*La Coruña*	*Lugo*	*Ourense*	*Pontevedra*
Edad (años)	55,98 ± 2,2*	56 ± 1,2*	–	–	55,97 ± 3,39*
Sexo (%)					
Mujer	42,4	54,5	25	40	50
Varón	57,6	45,5	75	60	50
Hábitat (%)					
Rural	31,5	36,5	50	30	38,85
Urbano	68,5	63,5	50	70	61,5

Media ± SEM.

Tabla III
Unidades que demandan NED

	Global	*La Coruña*	*Lugo*	*Ourense*	*Pontevedra*
Especialidades médicas (%)	48,3	43,9	50	–	51
Cirugía (%)	20,2	19	25	–	16,6
Atención primaria (%)	12,8	18	–	–	20,4
Otras (%)	18,7	19,1	25	–	12

Tabla IV
Tipo de paciente que necesita NED

	Global	*La Coruña*	*Lugo*	*Ourense*	*Pontevedra*
Alteraciones neurológicas (%)	43,6	40,9	29	70	34,8
Neoplasias (%)	23,05	23,4	45	–	23,8
EEII (%)	7,87	9,8	13	–	8,7
Otras (%)	25,4	25,9	13	30	32,7

Tabla V
Vías de administración del soporte nutricional

	Global	*La Coruña*	*Lugo*	*Ourense*	*Pontevedra*
Oral (%)	58,4	52,7	66	50	64,5
SNG (%)	28,45	30	28	30	25,85
PEG (%)	9,8	5	6	20	8,5
Gastrostomía (%)	3	12	–	–	1
Yeyunostomía (%)	0,325	0,3	–	–	1

en otras comunidades autónomas no existe un criterio uniforme acerca de quien controla este tipo de tratamiento lo que hace más difícil conocer el estado real de la NED en una comunidad[5].

La prevalencia global de la NED en nuestra comunidad fue de 10,34 pacientes/10.000 habitantes, siendo más frecuente su utilización en las provincias con mayor densidad de población, aunque las características de los pacientes que reciben soporte nutricional ambulatorio son similares. La media de edad y el sexo son similares a los observados en otros estudios[6, 8].

Las unidades sanitarias que demandan NED en nuestra comunidad dependen del grado de especialización de las mismas, así las especialidades médicas (digestivo, oncología, neurología, medicina interna) demandan con más frecuencia este tipo de soporte nutricional que las unidades de cirugía o atención primaria. El tipo de pacientes que con más frecuencia demanda NED fueron los aquejados de anomalías neurológicas, este dato es distinto al observado en otros lugares de España y Europa[6, 7], donde predominan los pacientes oncológicos; en nuestra comunidad

únicamente en La Coruña predominan este tipo de pacientes debido a la existencia de un centro oncológico regional. El tipo de especialización puede condicionar el tipo de pacientes que demandan NED. En el presente estudio la vía de administración más frecuente de NED fue la oral (58,4%) de acuerdo con el estudio NADYA (48%)[6], pero diferente de lo observado en Cataluña donde la vía más empleada fue la SNG (61%)[8].

En cuanto a la duración del tratamiento, en nuestra comunidad el 54% de los pacientes precisaron soporte nutricional por un espacio de tiempo superior a 6 meses, estos datos son similares a los del estudio NADYA (58%) y a los del H. Vall D'Hebrón.

Tanto el índice de complicaciones como el de ingresos relacionados con el tratamiento son inferiores a las observadas en el estudio de NADYA[6]. Esto podría ser explicado por el año de estudio, y que conforme pasa el tiempo y se tiene más experiencia con NED los resultados serán mejores.

El presente trabajo es fruto de la actividad científica y de coordinación de la Sociedad Gallega de Nutrición y Dietética. La nutrición artificial domiciliaria ha representado un avance en el manejo de pacientes crónicos que antes requerían largas estancias hospitalarias con la consiguiente repercusión económica. Esto se ha visto favorecido por la creación de las diferentes unidades de nutrición en las distintas áreas sanitarias de la comunidad y la experiencia ha demostrado que es una forma de tratamiento viable en cualquier medio y que no necesita un equipamiento demasiado refinado para llevarlo a cabo. En nuestra comunidad se utiliza con más frecuencia en las provincias más pobladas, pero es probable que en un futuro su utilización sea similar en toda la comunidad. Es conveniente la realización de este tipo de estudios cada cierto tiempo con el fin de analizar las tendencias en este tipo de terapia así como un registro del número, tipo y evolución de las nutriciones con el fin de conocer la situación y dar las soluciones a los problemas que van surgiendo así como las novedades que en la terapia enteral puedan llegar al medio extrahospitalario.

Referencias

1. Gómez Candela C y Cos Blanco Al (ed.): ¿Cuál es el marco de la nutrición clínica? *Nutri Hosp*, 1999, XIV (suppl 2): 1s-3s.
2. Howard L: Home parenteral and enteral nutrition in cancer patients. *Cancer*, 1993; 73 (suppl 11), 3531 DK, CooK DJ, 3451.
3. Hayland DK, Cook DJ y Guyatt GH: Enteral nutrition in the critically ill patient: a critical review of the evidence. *Crit Care Med*, 1993; 19:435-442.
4. Referencias poboacionais para hospitalización xeral dos habitantes protexidos polo SERGAS, ano 1999, División de Asistencia Sanitaria, Subdirección Xeral de Coordinación e Avaliación Asistencial, novembro 1998.
5. Riba Sicart M, Rivero i Urgell M y Serra Majen L: Análisis de la nutrición artificial en Cataluña en el período 1989-1993. *Nutr Hosp*, 1999, 16(1): 44-50.
6. Artificial nutrition in the home. Annual information 1996. Group NADYA-SENPE. *Nutr Hosp*, 1999, 14:145-52.
7. Gaggiottii G, Ambrosi L, Spazzafumo L et al. Two year outcome data from the Italian Home Enteral Nutrition in the community. 1994 In Elian M, ed. Maidenhead, Berks. England: BAPEN.
8. Planas M, Castella M, Pérez-Portabella C, González T, Romero C y Rosello J: Nutrición enteral domiciliaria: análisis descriptivo. *Nutr Clin*, 1999, 19(4):25-29.

*** Grupo de trabajo de la Sociedad Gallega de Nutrición y Dietética:
Dr. Germán Adrio Díaz. C. H. A. Marcide. Ferrol.
Dra. Victoria Alonso de Castro. C. Povisa. Vigo.
Dra. Ana Ayúcar Ruiz de Galarreta. C. H. J. Canalejo. La Coruña.
Dr. Diego Bellido Guerrero. H. Naval. Ferrol.
Dr. Manuel Botana. C. H. Xeral-Calde. Lugo.
Dra. Emma Camarero González. C. H. U. S. Santiago.
Dra. J. A. Fernández Fernández. H. Costa. Burela.
Dr. Fernando Ferrón Vidán. C. H. U. S. Santiago.
Dra. M.ª Teresa Inaraja Bobo. H. Meixoeiro. Vigo.
Dra. M.ª José Martínez Vázquez. H. Meixoeiro. Vigo.
Dra. Concepción Padrón Gil. C. H. Ourense. Ourense.
Dra. Guadalupe Piñeiro Corrales. H. Provincial. Pontevedra.
Dra. Luisa Fernanda Pérez Méndez. C. H. Xeral-Cíes. Vigo.

Nutr. Hosp. (2001) XVI (6) 262-267
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Nutrición Hospitalaria

Original

Intolerancia enteral gástrica en pacientes con lesión cerebral de origen traumático, ventilados mecánicamente

J. A. Acosta Escribano, R. Carrasco Moreno, M. Fernández Vivas, J. Noé Navarro Polo*, P. Más Serrano*, J. Sánchez Payá, Isabel, J. Caturla Such

Servicio de Medicina Intensiva. Servicio de Farmacia. Hospital General Universitario de Alicante. Alicante. España.*

Resumen

Objetivos: **Pacientes con trauma craneal grave (TCS), a los que se analiza la incidencia y relación entre la aparición de intolerancia gástrica (IG), el retraso en el vaciado gástrico (RVG) medido por el test del paracetamol (AUC_{60}) y la hipertensión intracraneal (HIC), así como su asociación con las variables de gravedad al ingreso y evolutivas y con las dosis de sedación y analgesia. También se avaluó la ventajas de la alimentación transpilórica.**

Ámbito: **Estudio prospectivo, clínico y observacional. Realizado en una unidad de medicina intensiva polivalente.**

Población: **Veinticinco pacientes con traumatismo craneal grave (TCS) Glasgow Coma Score (GCS < 9), con soporte nutricional gástrico, en los primeros diez días de ingreso y que precisaron sedación, ventilación mecánica y monitorización intracraneal.**

Resultados: **El 44% de los pacientes presentaron IG, los valores de AUC_{60} demostraron la existencia de RVG. La medicación sedante se relacionó con la IG ($p < 0,005$), con la HIC ($p < 0,01$) y el AUC_{60} ($p < 0,01$). En cuanto a los índices de gravedad el GCS se relacionó con el AUC_{60} ($p < 0,01$); la escala de Marshall con la HIC ($p < 0,005$) y el AUC_{60} ($p < 0,01$). De las variables cuantitativas se observaron correlación entre la HIC y la IG ($p < 0,001$), la HIC y la aparición de neumonía ($p < 0,01$), la IG y la neumonía ($p < 0,001$) y el AUC_{60} ($p < 0,001$) y finalmente el AUC_{60} con la neumonía ($p < 0,05$).**

Conclusiones: **La intoleracia gástrica en pacientes con TCS se debe a la existencia de RVG, cuya intensidad es proporcional a la gravedad del trauma y su repercusión sistémica. La relación entre la HIC, IG y la neumonía**

Correspondencia: José A. Acosta Escribano.
Ur. Suiza Melva, 6, 1.º
03540 Playa San Juan. Alicante.

Recibido: 9-IV-2001.
Aceptado: 20-V-2001.

GASTRIC ENTERAL INTOLERANCE IN MECHANICALLY VENTILATED PATIENTS WITH TRAUMATIC HEAD INJURY

Abstract

Objective: **To check the correlation between gastric intolerance and hipertension intracranial pressure and their association with the clinical parameters and severity indexes in patients with severe head injury (HI); to evaluate the advantages of transpyloric feeding.**

Design: **Prospective and observational clinical study.**

Setting: **Intensive Care Unit (ICM) of a General University Hospital.**

Patients and participants: **25 brain injured patients requiring sedation, mechanical ventilation and hipertensión intracranial monitoring.**

Interventions: **Analysis of the incidence of delayed gastric emptying (area under the curve (AUC_{60})) and of gastrointestinal intolerance; study of their correlation with hipertension intracranial, severity indexes and sedative medication administered; evaluation of the alternative effectiveness of transpyloric feeding.**

Measurements and results: **44% of the patients showed GI, which was measured by means of the paracetamol test (AUC_{60}). The sedative medication was related to IG ($p < 0,005$), HIC ($p < 0,01$) and AUC_{60} ($p < 0,01$). Of the severity indexes, there was a correlation between Glasgow Coma Score and AUC_{60} ($p < 0,01$); the Marshall score HIC ($p < 0,005$) and AUC_{80} ($p < 0,01$). Of the quantitative variables, we found a correlation between HIC and IG ($p < 0,001$), HIC and pneumonia ($p < 0,01$), IG as well pneumonia ($p < 0,001$), and AUC_{60} ($p < 0,001$) and AUC_{60} and pneumonia ($p < 0,05$).**

Conclusions: **Enteral intolerance in patients with HI is due to delayed gastric emptying (DGE) which is proportional to the severity of the head injury and to the intensity of the systemic response. The high incidence of GI makes transpyloric feeding advisable in order to at-**

apoya a la alimentación transpilórica en orden a satisfacer los objetivos nutricionales y reducir el riesgo de neumonía nosocomial de aspiración.

(Nutr Hosp 2001, 16:262-267)

Palabras clave: Hipertensión intracraneal (HlC). Intoleracia gastrointestinal (IG). Retraso en el vaciado gástrico (RVG). Trauma craneal grave (TCS). Ventilación mecánica (VM).

tain the nutritional objective and to reduce the risk of aspirative nosocomial pneumonia.

(Nutr Hosp 2001, 16:262-267)

Key words: Delayed gastric emptying. Gastric intolerance. Hipertension intracranial pressure. Severe head injury. Area under the curve. Mechanical ventilation.

Introducción

Los pacientes con lesión cerebral grave de origen traumático (TCS), presentan un estado hipercatabólico[1, 2] e hipermetabólico[3] y una elevada incidencia de intolerancia gástrica (IG), relacionada con factores mecánicos o gastrointestinales[4].

Durante su estabilización, precisan de ventilación mecánica y reciben medicación que también favorece la aparición de IG[5].

El conjunto de estos factores condiciona episodios de aumento en el residuo gástrico y regurgitación que son atribuidos al retraso en el vaciado gástrico (RVG) y que favorecen la reducción del volumen nutricional eficaz, la malnutrición y la aparición sepsis y neumonía[6].

Los objetivos del estudio fueron: comprobar la incidencia y relación entre la IG, el RVG y HIC, en pacientes con TCS. Definir el grado de asociación entre estas variables y los parámetros clínicos, analíticos e índices de gravedad, analizando finalmente las ventajas que ofrece como alternativa la alimentación transpilórica.

Método

Estudio clínico, prospectivo y observacional. Los pacientes fueron incluidos en el estudio de forma consecutiva y durante los diez primeros dias de ingreso en una unidad polivalente de medicina intensivos, para control y tratamiento del TCS.

El protocolo de estudio se aprobó por el Comité de Ética. En todos los casos, se solicitó consentimiento informado a los familiares.

Los criterios de inclusión fueron: enfermos con lesión cerebral de origen traumático, sin lesiones graves asociadas (ISS < 15), con una puntuación en la escala de Glasgow (GCS) entre 4 y 9 puntos y con soporte ventilatorio artificial al ingreso.

Al inicio del estudio, todos los pacientes se encontraban sedados con midazolam, analgesiados con morfina y en algunos casos relajados con besilato de atracurium.

Los criterios de exclusión fueron: edad comprendida entre 18 y 75 años, cirugía gástrica previa, Apache II mayor de 25, fracaso renal (creatinina plasmática ≥3,4 mg/dl) o hepático (bilirrubina < 5 mg/dl), muerte encefálica, enfermedad metabólica o endocrina, contraindicación de nutrición enteral y una esperanza de vida menor a tres días.

Al ingreso fueron recogidos los parámetros antropométricos: talla, peso, edad y Harris-Benedit (HB), así como diversos índices de gravedad: Apache II[8], GCS, puntuación en la escala de Marshall[9] y grado de lesión cerebral según la clasificación del Traumatic Coma Data Bank[10].

En las primeras veinticuatro horas y al noveno día de estudio se determinaron en plasma los siguientes parámetros analíticos: glucosa, prealbúmina, albúmina, ferritina, colesterol y proteína C.

Previo al inicio del estudio, se comprobó por control radiográfico que el extremo distal de la sonda estuviese alojado en estómago y tras un período de estabilización hemodinámica de 18,5 ± 13,6 horas, se inició el estudio.

Se administraron 1.500 mg de parecetamol por sonda gástrica. A continuación, se obtuvieron 2 cc de sangre venosa a los 10, 20, 30, 60, 90, 120, 150 y 180 minutos que fueron recogidas en un Neotube®. Las muestras se centrifugaron y conservaron para ulterior determinación de los niveles plasmáticos de paracetamol[11].

El análisis de las muestras se realizó mediante inmunoensayo de polarización fluorescente (FPIA), utilizando una curva de calibración de seis puntos. Su rango de concentración osciló entre 1 mg/l (sensibilidad del ensayo) y 200 mg/dl[12, 13].

La técnica fue comparada con el método HPLC, con un coeficiente de correlación de 0,997.

Se calculó el área bajo la curva a los 60 y 120 minutos (AUC_{60} y AUC_{120}), según la fórmula de los trapezoides. Se definió como RVG a un valor del AUC_{60}[14] inferior a 600 mg min/l.

Tras la realización del test de paracetamol, se inició el soporte nutricional. Las necesidades calóricas se calcularon a partir del HB[15], utilizando un factor de estrés fijo de 1,2. La dieta administrada contenía un 23,1% de aporte proteico, un 15,4% de lípidos, 58,6% de hidratos de carbono y un 12,9% de fibra soluble (Precitene Hiperproteico® más Precitene GI Control®). Se administró en régimen de infusión continua mediante bomba peristáltica. El objetivo nutricional fue conseguir el 50% de las necesidades calóricas el primer día, aumentando progresivamente hasta completar los requerimientos a las 48 horas.

Para la definición y manejo de las complicaciones gastrointestinales, se siguieron los criterios del estudio COMGINE[16]. Se definió como IG a la existencia de dos interrupciones consecutivas de la dieta por aspirado gástrico superior a 200 cc, o regurgitación re-

petida, que condujo a la suspensión del soporte nutricional durante más de doce horas.

En caso de suspensión definitiva del SG, se procedió a la colocación de una sonda nasoduodenal (Stay-Put®, Novartis Consumer Health, Spain) con control radioscópico, dejando su extremo distal en posición transpilórica.

Diariamente, se recogieron el volumen programado y administrado, obteniéndose el volumen eficaz resultante.

A los pacientes incluidos en el estudio, se les monitorizó la presión intracraneal desde el ingreso. Los episodios de HIC fueron definidos como un aumento mantenido de la presión intracraneal por encima de 20 mmHg[17].

Asimismo, se anotaron la aparición de neumonía[18], consignando día y germen. Los tiempos de ventilación mecánica (TVM), número de días de estancia en UCI (EU), estancia hospitalaria (EH), así como el exitus y la secuela neurológica grave[19] (SEC), al alta.

Estadística

Se calculó la media, desviación típica a las variables cuantitativas, utilizando la *t* de Student para su análisis comparativo entre grupos. Para estudiar la asociación entre las variables cualitativas se utilizó el test de la ji cuadrado. Y el análisis de comparación entre las variables cuantitativas, se realizó mediante el coeficiente de correlación de Pearson. El nivel de significación estadístico utilizado fue de $p < 0,05$.

Resultados

Se incluyeron 29 pacientes (26 hombres/3 mujeres), cuatro de ellos fueron excluidos, tres por presentar al ingreso signos de muerte encefálica y uno por traumatismo abdominal grave asociado.

Los veinticinco restantes, cumplieron los criterios del protocolo. Tres fallecieron tras la finalización del estudio. Dos pacientes fueron dados de alta por mejoría, el séptimo y noveno día respectivamente.

Tabla I

Medias y desviación típica de los parámetros antropométricos, índices de gravedad y área bajo la curva

Variables (n: 25)	*Media (DT)*
Edad	38 ± 19,5
Peso (kg)	67 ± 13,7
HB	1.566 ± 238
GCS	7 ± 1,3
Apache II	15,76 ± 5,1
Marshall	4,24 ± 1,85
TVM (días)	7,17 ± 6,26
EU (días)	15,9 ± 16
EH (días)	35,9 ± 23,9
AUC_{60} mg/dl/min	348 ± 246
AUC_{120} mg/dl/min	730,4 ± 582

En las tablas I y II se muestran los valores medios y sus correspondientes desviaciones típicas de los parámetros antropométricos, índices de gravedad, dosis de medicación sedante, relajante y analgésica administradas a lo largo del estudio, así como los valores analíticos al ingreso y al noveno día.

En la tabla III, se reseñan los porcentajes de las diferentes variables cualitativas del estudio.

Se midieron la significacion estadística de las tres variables de análisis: IG, HIC y AUC_{60}, con los parámetros antropométricos, índices de gravedad (edad, Apache II, puntuación de Marshall, SCG y tipo de lesión cerebral TVM, EU, EH, neumonía, SEC y exitus), las dosis medias de fármacos sedantes, relajantes y analgésicos, administradas a lo largo del estudio y los valores analíticos al ingreso y al noveno día de estudio (tabla IV). El resto de las variables analizadas no fueron significativas.

La IG estuvo presente en 11 pacientes (44%). La IG se correlacionó con el aumento en la dosis de sedación, la puntuación Marshall.

Tabla II

Media y desviación típica de las dosis de sedantes, relajantes, analgésicos y parámetros analíticos al ingreso y noveno día

Medicación	*Media (DT)*	*Duración/días*	*Pacientes*
Midazolam mg/kg/h	0,23 ± 0,06	5,6 ± 3,6	25
B atracurium mg/kg/h	0,62 ± 0,34	5,37 ± 3,6	19
Cl. mórfico mg/kg/h	0,112 ± 0,16	6,6 ± 3,49	25
P. analíticos	*Ingreso*	*9 días*	
Albúmina mg/dl	2,34 ± 0,43	2,06 ± 0,5	25/23
Prealbúmina mg/dl	13,16 ± 5,24	12,25 ± 4,6	25/23
Glucosa mg/dl	124,4 ± 34	139 ± 56	25/23
PCR mg/dl	16,9 ± 8,3	19,3 ± 17	25/23
Ferritina ng/ml	365 ± 237	669 ± 381	25/23
Colesterol m/dl	104 ± 40	125 ± 51,5	25/23

Tabla III
Porcentajes de las diferentes variables de estudio

Variables	*Porcentajes*	
	Sí	*No*
H. intracraneal	11 (44%)	14 (56%)
I. gástrica	11 (44%)	14 (56%)
Sec. neurológica	9 (41%)	13 (52%)
Exitus	3 (12%)	22 (88%)
Neumonía	13 (52%)	12 (48%)
N. transpilórica	11 (44%)	14 (56%)

En once pacientes se colocó una sonda transpilórica (6,6 ± 1,2 días), en siete por aumento en el residuo gástrico y en cuatro por regurgitación. En un paciente la alimentación transpilórica fue suspendida al noveno día por la aparición de una hemorragia digestiva por ulcus gástrico.

Once pacientes (44%) presentaron episodios de HIC, su duración fue de 3,73 ± 1,4 días. La HIC se relacionó con el aumento en la dosis de sedación y la puntuación del Marshall.

El valor global del AUC_{60} fue 348 g/min/l y el AUC_{120} de 730 mg/min/l. La disminución del AUC_{60} se relacionó con ei aumento de la puntuación del Marshall, las dosis de sedación y analgesia ($p < 0,02$) y la disminución del GCS al ingreso. El AUC_{120} no se correlacionó con ninguna de las variables.

La SEC se verificó en 9 pacientes y sólo se relacionó con la puntuación del Marshall ($p < 0,01$).

De los valores analíticos estudiados al ingreso y al noveno día, tan solo la prealbúmina al ingreso se asoció con la aparición de HIC, el aumento en la puntuación de Marshall ($p < 0,001$), y la existencia de SEC y exitus ($p < 0,005$).

La comparación entre las variables de estudio demostró una relación significativa entre la HIC, la IG y la aparición de neumonía. La IG también se relacionó con la aparición de neumonía (tabla V).

La neumonía fue demostrada en 13 pacientes (52%), su día de aparición fue 4 ± 1,5 y en los cultivos se aislaron ocho estafilococos de diferentes cepas, tres enterobacterias y en dos los gérmenes no fueron filiados.

En la tabla Vl se muestran el porcentaje calórico y gramos de nitrógeno eficaces administrados por vía gástrica y transpilórica. Nunca se alcanzaron los volúmenes nutricionales programados y los aportes proteicos se mantuvieron por debajo de 0,20 g/nitrógeno/kg/día (tabla VI).

Ninguno de los pacientes con alimentación transpilórica presentó intolerancia, alcanzándose volúmenes eficaces próximos al 92%, tras su colocación, a pesar de la persistencia de abundante residuo gástrico.

Discusión

La mayoría de los pacientes graves son nutridos por vía enteral gástrica. En la actualidad se dispone de evidencia[20] que apoya que la nutrición enteral se asocia a una menor estimulación hormonal y respuesta catabólica, produce menos complicaciones, preserva mejor la barrera inmune intestinal, disminuyendo el riesgo de colostasis y sepsis[21].

La IG es una complicación que afecta en el TCS a más del 50% de los pacientes y que es atribuida a la existencia de RVG.

Diferentes autores[22, 23, 24] han evaluado el RVG en TCS. Garrick[25] analiza de forma experimental la relación entre HIC y la motilidad gástrica, observando que el aumento de la presión intracraneal produce una inhibición neuronal por mecanismo vagal[26] y una reducción en la amplitud y motilidad gástrica, que desaparece tras su normalización. La estimulación adrenal secundaria al traumatismo también reduce la contracción gástrica.

McArthur[27], Ott[28] y Power[29] relacionaron el RVG con la HIC y el SCG, siendo sus resultados poco concluyentes.

Heiland[30] en pacientes ventilados mecánicamente demuestra un RVG, que atribuye a la ausencia de la fase cefálica, y asociado con el aumento de edad y la administracion de derivados mórficos.

El AUC60 se relacionó con las variables del estudio, su valor global estuvo por debajo de los 600 mg-

Tabla IV
Valores medios y relación entre las variables de estudio y los índices de gravedad y medicación sedante

V. numéricas	*Glasglow C*	*E. Marshall*	*Sedación*	*Estancia U.*
H. intracraneal	**NS**	**P < 0,005**	**P < 0,01**	**NS**
Sí	6,09 ± 1,3	5,18 ± 2,2	0,25 ± 0,07	16,36 ± 6,1
No	6,79 ± 1,25	3,5 ± 1,1	0,21 ± 0,03	15,57 ± 9
A. bajo curva$_{60}$	**p > 0,008**	**p < 0,009**	**p < 0,006**	**NS**
< 600 mg min/l	6,28 ± 1,5	4,72 ± 2	0,231 ± 0,07	19,5 ± 8,7
> 600 mg min/l	7,0 ± 0,6	3,0 ± 0,1	0,22 ± 0,01	8 ± 8,1
I. gástrica	**NS**	**p < 0,06**	**p < 0,002**	**NS**
Sí	5,91 ± 1,3	5,18 ± 2,2	0,24 ± 0,08	19,1 ± 8,7
No	6,94 ± 1,4	3,5 ± 1	0,22 ± 0,02	8 ± 4,1

Tabla V
Significación entre las variables de estudio y su relación con la aparición de neumonía

	AUC_{60}	*I. gástrica*	*Neumonía*
Sí	98/11 (72,7%)	9/11 (82%)	9/11 (88,8%)
H. intracraneal	**NS**	**p < 0,001**	**p < 0,008**
No	9/14 (57,1%)	2/14 (14,2%)	4/14 (28,5%)
< 600 mg min/dl		9/18 (50%)	12/18 (66,5%)
AUC_{60}	–	p < 0,001	p < 0,032
> 600 mg min/dl		1/7 (33,3%)	3/9 (33,3%)
Sí			11/11 (10%)
I. gástrica	–	–	p < 0,001
No			2/14 (14,28%)

incidentes de IG y permitiendo mantener un volumen eficaz próximo al programado. Las maniobras en su colocación, aun en pacientes con inestabilidad cerebral, no supusieron modificaciones en la presión de perfusión cerebral.

De los parámetros analíticos, tan sólo la prealbúmina se relacionó con las variables que midieron la gravedad del daño cerebral como el GCS, la HIC, la puntuación de Marshall y la SG.

A pesar del inicio precoz del soporte nutricional, del moderado grado de desnutrición, la incidencia de neumonía fue elevada, trece pacientes (52%), con un período de aparición tardío (4 ± 1,5 días). Diferentes autores se han referido a la aspiración gástrica como mecanismo desencadenante de la neumonía en pacientes ventilados mecánicamente [31, 32]. En nuestra serie, los gérmenes aislados, indican la aspiración precoz como mecanismo desencadenante, aunque esta hipótesis no fue contemplada.

Tabla VI
Porcentaje del aporte calórico y nitrogenado eficaz: total y administrado por vía transpilórica

Días de nutrición	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*Σ/días*
% kcal/totales	95	74,3	71,1	71,4	76,4	76,7	68,8	71,5	74,7	82,4	76,2
g/n/totales	0,20	0,11	0,17	0,18	0,20	0,19	0,18	0,19	0,19	0,21	0,18
% kcal/transpilóricas	–	80	97,7	95,1	89,3	92,4	91,4	95,8	87,2	94,8	91,5
g/n/transpilóricas	–	0,20	0,24	0,24	0,22	0,23	0,23	0,24	0,22	0,24	0,22

min/dl, lo que indica, que en las fases iniciales existe RVG, que se mantuvieron y que fueron potenciados por la acción posterior de los sedantes.

La realización precoz del test del paracetamol, excluye el efecto de los sedantes y analgésicos en la aparición del RVG, que estaría asociado a la propia lesión cerebral. Sin embargo, una mayor gravedad se acompañaría con el aumento en las dosis de medicación sedante y analgésica, que contribuiría a favorecer secundariamente el RVG.

En nuestro estudio, observamos una relación entre la IG y la aparición de episodios de HIC, que asociados a una AUC60, revelan que los pacientes con HIC, presentan un RVG, asociado a la gravedad del trauma y potenciado por la acción de la medicación sedante. También, encontramos suficientes datos de RVG: una disminución en el AUC60 y un porcentaje elevado de IG (44%), relacionados con la severidad del TCS, (número de episodios de HIC y disminución del nivel GCS al ingreso, así como al grado de afectación sistémica medido por la escala de Mashall). Estos valores, se normalizaron tardíamente como demuestra el análisis del AUC120.

El RVG, también fue evaluado. Mediante el volumen eficaz de dieta administrado diariamente, demostró que gran número de pacientes tuvieron episodios recortados de intolerancia (aspiración y aumento del residuo), que conllevó la suspensión temporal de la dieta y la reducción de forma significativa del volumen nutricional eficaz. En once pacientes (44%), una sonda transpilórica de doble luz fue colocada, reduciéndose de forma sustancial los

En resumen: Los pacientes con TCS, presentan una elevada incidencia de IG atribuida a la existencia de un RVG. Existe una relación entre la gravedad de la lesión neurológica y la aparición de episodios de IG.

Los episodios de IG conducen a una reducción del volumen eficaz programado, que mejoró tras el inicio de la alimentación traspilórica.

El precoz inicio de un soporte nutricional transpilórico, en pacientes con TCS con HIC, mediante sondas o catéteres de yenunostomía, son alternativas eficaces, para el mantenimiento del soporte nutricional enteral, para conseguir el objetivo nutricional y minimizar el riesgo de neumonía aspirativa.

* Nuestro agradecimiento al equipo de ATS/DUE de la unidad de polivalentes del servicio de medicina intensiva, por su colaboración desinteresada en el estudio.

Referencias

1. Deutsman CS, Konstantinides FN, Raup S y cols.: Physiological and metabolic response to isolated closed-head injury: Part 1: Basal metabolic state: correlations of metabolic and physiological parameters with fasting and stressed controls. *J Neurosurg,* 1986, 64(1):89-98.
2. Phillips R, Young DB, Twyman y cols.: The favorable effect early parenteral feeding on survival in head -injured patients. *J Neurosurg,* 1983, 58(6):906-912.

3. Young AB, Ott LG, Beard D, Demprey RJ, Tibbs PA y cols.: The acute-phase response of the brain-injured patient. *J Neurosurgery,* 1988, 69:375-380.
4. Minami H, Mccallum RW: The physiology and pathophysiology of gastric emptying in humans. *Gastroenterology,* 1984, 86:1592-1610.
5. Murphy DB, Sutton A, Prescott LF, Murphy MB: A comparison of the effects of tramadol and morphine on gastric emptying in man. *Anaesthesia,* 1997, 52:1212-1229.
6. Yanagawa T, Bunn F, Roberts I, Wentz R, Pierro A: Nutritional support for head-injured patients. *Cochrane Database Syst Rev,* 2000, (2):CD 001530.
7. Vincent JL y cols.: The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intensive Care Med*, 1997, 22:707-10.
8. Knaus WA: The Apache II prognotic system: risk prediction of hospital mortality for critically ill hospitalised adults. *Chest,* 1991, 100:1619-1636.
9. Marshall JC, Cook DJ, Christou NV y cols.: Multiple organ dysfunction score: A reliable descriptor of a complex clinical outcome. *Crit Care Med,* 1995, 23:1638-1653.
10. Marshall LS, Gautille T, Klauber MR, Glark MVB, Eisenberg HM, Jane JA y cols.: Report on the traumatic coma data bank: the outcome of severe closed head injury. *J Neurosurg,* 1991, 75 (suppl):28-36.
11. Acosta JA, Cortés J, Carrasco R, Navarro JN: Análisis del vaciado gástrico en enfermos postoperados de cirugía cardíaca. *Nutr Hosp,* 1999, 5:191-196.
12. Healing RC, Nimmo J, Prescott LF y Tothill P: The dependence of paracetamol absorption on the rate of gastric emptying. *Br J Pharmacol,* 1993, 47:415-421.
13. TDX®TDXFLX™: Ensayos del sistema. Ensayos de drogas de abuso y toxicología: Paracetamol. Lab. Abbott.
14. Tarling MM, Toner CC, Withington PS, Baxter MK, Whelpton R y Goldiddhill DR: A model of gastric emptying using paracetamol absorption in intensive care patients. *Intensive Care Med,* 1997, 23:256-260.
15. Weekees E y Elia M: Observations on the patterns of 24-hour energy expenditure changes in body composition and gastric emptying in head-injured patients receiving nasogastric tube feeding. *JPEN,* 1996, 20:31-37.
16. Montejo JC and the Nutricional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units. Enteral nutrition-related gastrointestinal complications in critically patients. A multicenter study. *Crit Care Med,* 1999, 27:1447-1453.
17. Rosner MJ, Rosner SD y Johnson AH: Cerebral perfusion pressure: manegement protocol and clinical results. *J Neurosurg,* 1995, 83:949-962.
18. Johanson WG, Seidenfeld JJ, Gómez P y cols.: Bacteriologic diagnosis of nosocomial pneumonia following prolonged mechanical ventilation. *Am Rev Respir Dis,* 1988, 137:259-264.
19. Jennett B, Snoek J, Bond MR y Brooks N: Disability after severe head injury: Observations on the use of the Glasgow Outcome Scale. *J Neurol Neurosurg Psychiatry,* 1981, 44:285-293.
20. Zaloga GP: Early enteral nutritional support improves autcome: Hypothesis o fact? *Crit Care Med,* 1999, 27:259-261.
21. Heyland DK, Cook DJ y Guyatt GH: Enteral nutrition in the critically ill patient: a critical review of the evidence. *Intensive Care Med,* 1993, 19:435-442.
22. Norton J, Ott LG, McClain C, Adams L, Dempsey J, Haack D y cols.: Intolerance to enteral feeding in the brain-injured patient. *J Neurosurg,* 1988, 68:62-66.
23. Kao CH, Changla SP, Chieng PU y Yen TC: Gastric emptying in head-injured patients. *Am J Gastroenterol,* 1998, 93:1108-1112.
24. Díaz M, Coves FJ, Acosta JA, Pérez M y González J: Alternativas al soporte nutricional gástrico en pacientes con lesión cerebral grave en fase aguda. *Nutr Hosp,* 1999, 14 (suppl 1): 40.
25. Garrick T, Mulvihill S, Buack S, Maeda-Hagiwara M y Tache Y: Intracerebroventricular pressure inhibits gastric antral and duodenal contractility but not acid secretion in conscious rabbits. *Gastroenterology,* 1988, 95:26-31.
26. Haig AJ, Ho Kc y Ludwig G: Clinical, physiologic and pathologic evidence for vagus dysfunction in a case of traumatic brarn injury. *J Trauma,* 1996, 40:441-444.
27. McArthur CJ, Gin T, McLaren IM, Critchley JA y Oh TE: Gastric emptying following brain injury: effects of choice of sedation and intracranial pressure. *Intensive Care Med,* 1995, 21:573-576.
28. Ott L, Young B, Phillips R, McCrain C, Adans L, Dempsey R, Tibbs P y Ryo UY: Altered gastric emptying in the head-injured patient: relationship to feeding intolerance. *J Neurosurg,* 1991, 74:738-742.
29. Power I, Easton JC, Todd JG y WS Nimmo: Gastric emptying after head injury. *Anaesthesia,* 1989, 44:563-566.
30. Heyland DK, Tougas G, King D y Cook DJ: Impaired gastric emptying in mechanically ventilated, critically patients. *Intensive Care Med,* 1996, 22:1339-1344.
31. Huxley E, Viroslav J, Gray W y Pierce A: Pharingeal aspiration in normal patients with depressed consciousness. *Am J Med,* 1978, 64:564-567.
32. DuMoulin GC, Hedley-Whyte J, Paterson DG y Lisbon A: Aspiration of gastric bacteria in antiacid-treated patients: a frecuent cause of postoperative colonization of the airway. *Lancet,* 1982, 1:242-245.

Nutr. Hosp. (2001) XVI (6) 280-283
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Nutrición Hospitalaria

Original

Ingesta oral de 24 horas de pacientes con tumores de vía aerodigestiva alta

D. de Luis Román*, **, O. Izaola*, ** y R. Aller**

* *Sección de Endocrinología y Nutrición Clínica. Hospital del Río Hortega. Valladolid.* ** *Instituto de Endocrinología y Nutrición Clínica (IEN). Facultad de Medicina de Valladolid. España.*

Resumen

Fundamento: **Son varios los trabajos que han demostrado una modificación en el patrón de ingesta, con alteración en la ingesta de macro y micronutrientes, en los pacientes con tumores de vía aerodigestiva alta. El objetivo de nuestro estudio fue comparar la ingesta de macro y micronutrientes en un grupo de pacientes con tumores de vía aerodigestiva frente a un grupo control.**

Métodos: **Se estudiaron un total de 35 pacientes con tumores de vía aerodigestiva alta (8 de cavidad orofaríngea y 27 de laringe). Como grupo control se estudiaron 35 pacientes no tumorales remitidos a la consulta de nutrición. A todos los pacientes se les tomaron los siguientes datos epidemiológicos: edad, sexo, hábito enólico y tabáquico, tipo de tumor y se realizó una encuesta dietética de 24 h.**

Resultados: **La valoración de la ingesta de macronutrientes mostró una ingesta de calorías superior en el grupo de pacientes tumorales (1.545,3 ± 359 cal/día frente a 1.264,4 ± 240 cal/día; p < 0,05). La ingesta de hidratos de carbono también fue superior en el grupo de pacientes tumorales (177,9 ± 57,9 g/día frente a 135,9 ± 38,5 g/día; p < 0,05), así como la ingesta de grasas totales (58,2 ± 18,4 g/día frentte a 45,9 ± 15,4 g/día; p < 0,05) sobre todo a expensas de las grasas saturadas (19,4 ± 7,7 g/día frente a 11,9 ± 6,1 g/día; p < 0,05). Se detectaron diferencias en la ingesta de vitaminas, así los pacientes tumorales ingieren menos vitamina C (59,4 ± 18,5 mg/día tumorales frente a 141,5 ± 83 mg/día controles; p < 0,05), ácido fólico (116,5 ± 56,3 mg/día frente a 180,5 ± 78,5 mg/día; p < 0,05), y vitamina B_2 (1,53 ± 0,5 mg/día frente a 23,9 ± 6,5 g/día; p < 0,05). En la ingesta de minerales los pacientes tumorales ingieren menos calcio (702,9 ± 363 mg/día frente a 942,4 ± 327 mg/día; p < 0,05), no se detectaron diferencias estadísticamente significativas en el resto de minerales.**

Conclusión: **Los pacientes con tumores de vía aerodigestiva alta consumen una mayor cantidad de calorías, grasas saturadas y carbohidratos, así como una menor cantidad de vitamina C, fólico, vitamina B_{12} y calcio.**

(Nutr Hosp 2001, 16:280-283)

Palabras clave: Ingesta oral. Tumores vía aerodigestiva alta.

Correspondencia: Daniel de Luis Román.
Prof. Asoc. Endocrinología y Nutrición.
Director Ejecutivo IEN.
Caamaño, 51bis, 3.º C.
47013 Valladolid
Correo electrónico: ddlr@pulso.com

Recibido: 28-II-2001.
Aceptado: 6-III-2001.

TWENTY-FOUR HOURS ORAL INTAKE IN PATIENTS WITH UPPER AERODIGESTIVE TUMORS

Abstract

Background: **A lot of works have shown alterations in oral intake of micro and macronutrients, in patients with upper aerodigestive tumors. The main aim of our work was to compare the daily intake in a group of patients with upper aerodigestive tumors versus a control group.**

Methods: **A group pf 35 patients with upper aerodigestive tumors were studied (8 oral cavity and 27 larynx). A group of 35 subjects were use as control group. In all patients the next parameters were taken; age, sex, smoking and alcohol consumption, type of tumors and a 24 hours oral intake questonnaire.**

Results: **Patients with upper aerodigestive tumors showed a high increase of calories intake (1545.3 ± 359 cal/day vs 1264.4 ± 240 cal/day; p < 0.05), carbohidrates intake (177.9 ± 57.9 g/day vs 135.9 ± 38.5 g/day; p < 0.05), total fats (58.2 ± 18.4 g/day vs 45.9 ± 15.4 g/day; p < 0.05) and saturated fats intake (19.4 ± 7.7 g/day vs 11.9 ± 6.1 g/day; p < 0.05). In micronutrients intake differences were detected, a low intake in tumoral patients of vitamin C (59.4 ± 18.5 mg/day vs 141.5 ± 83 mg/día; p < 0.05), folic acid (116.5 ± 56.3 mg/day vs 180.5 ± 78.5 mg/day; p < 0.05), and vitamin B_2 (1.53 ± 0.5 mg/day vs 23.9 ± 6.5 g/day; p < 0.05). In minerals intake we detected a low intake in tumoral patients of calcium (702.9 ± 363 mg/day vs 942.4 ± 327 mg/day; p < O.05).**

Conclusions: **Patients with upper aerodigestive tumors take a high amount of calories, saturated fats and carbohidrates, and a low intake of vitamin C, folic, vitmain B_{12} and calcium.**

(Nutr Hosp 2001, 16:280-283)

Palabras clave: Oral intake. Upper aerodigestive tumors.

Introducción

Los tumores del tracto aerodigestivo alto, son un grupo de tumores muy frecuentes en determinados grupos epidemiológicos como son varones, con hábi-

to tabáquico y consumo de alcohol. Son múltiples los estudios que han demostrado la grave desnutrición que presentan estos pacientes[1].

Las alteraciones antropométricas en este grupo de sujetos muestran una clara desnutrición proteica, con disminución de la masa muscular[2]. Aunque estos estudios muestran el gran problema nutricional que presentan estos pacientes, las causas son múltiples y en algunos casos poco estudiadas. Son varios los trabajos que han demostrado una modificación en el patrón de ingesta, con alteración en la ingesta de macro y micronutrientes[3].

El objetivo de nuestro estudio fue comparar la ingesta de macro y micronutrientes en un grupo de pacientes con tumores de vía aerodigestiva, con un grupo de pacientes sanos.

Material y métodos

Pacientes

Se estudiaron un total de 35 pacientes con tumores de vía aerodigestiva alta (8 de cavidad orofaríngea y 27 de laringe) que acudieron al Hospital Universitario del Río Hortega (Valladolid), desde enero a diciembre de 2000 (muestreo no probabilístico, consecutivo), para ser sometidos a cirugía resectiva. Estos pacientes procedían de un área rural y urbana de Valladolid. El diagnóstico del tumor se realizó mediante anatomía patológica con biopsia preoperatoria. Como grupo control se estudiaron 35 pacientes no tumorales remitidos a la consulta de nutrición.

A todos los pacientes se les tomaron los siguientes datos epidemiológicos: edad, sexo, hábito enólico y tabáquico, tipo de tumor y se realizó una encuesta dietética de 24 h.

Valoración y encuesta nutricional

A todos los pacientes se les peso en una báscula calibrada (100 gramos), se les midió con un tallímetro estándar calibrado (1 mm) y se calculó el índice de masa corporal (IMC) con la fórmula (peso/talla^2) (kg/m^2).

Se realizó una encuesta nutricional de 24 horas. Este método consiste en recoger la ingesta de nutrientes en las 24 horas precedentes, todas las encuestas fueron realizadas por la misma dietista. Para realizar esta encuesta se pregunta sobre el consumo de alimentos y bebidas, modo de preparación, nombre comercial, ingredientes de la receta y cantidad. Estas encuestas fueron calibradas posteriormente con un programa informático propio de la unidad utilizando las tablas de composición de alimentos nacionales[4].

Análisis estadístico

Con los datos obtenidos se abrió una base de datos con el paquete estadístico (SPSS: INC: IL., EE.UU.). Se realizó un análisis descriptivo de las variables cuantitativas, expresadas como (media ± desviación estándar). Las variables cualitativas se expresan en frecuencias absolutas y relativas. Las variables continuas fueron analizadas con el test de Kolmogorv-Smirvov, para estudiar la normalidad de las variables. Para comparar las variables cuantitativas paramétricas se utilizó el test de la *t* de studend no pareado con dos colas, las variables no paramétricas fueron analizadas mediante el test U-Mann. Se consideraron diferencias significativas $p < 0,05$.

Resultados

Se estudiaron un total de 35 pacientes con tumores de vía aerodigestiva alta (27 carcinomas de laringe y 8 carcinomas de cavidad orofaríngea), la distribución por sexos fue 30 varones y 5 mujeres, la edad media fue 62,9 ± 9,7 años, el peso 71,4 ± 15,6 kg y el índice de masa corporal 25,5 ± 5,3. Un 80% de los pacientes fumaban y un 51,4% ingerían más de 30 g de alcohol al día. Los controles sanos presentaban una distribución por sexos (26 varones y 9 mujeres), la edad media fue de 64,8 ± 9,9 años, el peso 77,9 ± 12,5 kg y el índice de masa corporal 30,9 ± 5,4. Un 77% de los pacientes fumaban y un 45,7% ingerían más de 30 g de alcohol al día. Existieron diferencias significativas en el peso e IMC ($p < 0,05$).

Tabla I
Comparación de la ingesta de macronutrientes en pacientes tumorales y no tumorales

Macronutriente ingesta diaria	*Tumorales*	*No tumorales*	*P*
Calorías totales (cal)	1.545,3 ± 359	1.264,4 ± 240	< 0,05
Hidratos de carbono (g)	177,9 ± 57,9	135,9 ± 38	< 0,05
Proteínas (g)	80 ± 20,8	80 ± 18,2	NS
Grasas totales (g)	58,2 ± 18,4	45,9 ± 15,4	< 0,05
Grasas saturadas (g)	19,4 ± 7,7	11,9 ± 6,1	< 0,05
Grasas monoinsaturadas	27 ± 9,6	22,6 ± 9,2	NS
Grasas poliinsaturadas (g)	5,4 ± 2,6	4,8 ± 1,5	NS
Colesterol (mg)	408,9 ± 201	270,7 ± 128	< 0,05
Fibra (g)	12,2 ± 5,4	11,1 ± 10	NS

Tabla II
Comparación de la ingesta de micronutrientes en pacientes tumorales y no tumorales

Ingesta diaria Micronutriente	*Tumorales*	*No tumorales*	*P*
Vit. A	439,1 ± 272 mg/día	583,7 ± 782 mg/día	NS
Vit. C	59,4 ± 48,6 mg/día	141,5 ± 83,9 mg/día	< 0,05
Vit. B_1	0,88 ± 0,3 mg/día	1,2 ± 1,3 mg/día	NS
Vit. B_2	1,5 ± 0,5 mg/día	23 ± 6,5 mg/día	< 0,05
Vit. B_{12}	5,1 ± 1,6 µg/día	6,2 ± 5 mg/día	NS
Ácido fólico	116,5 ± 56,3 mg/día	180,5 ± 78 mg/día	< 0,05
Niacina	26,9 ± 6,2 mg/día	28,4 ± 6,4 mg/día	NS
Zinc	10,8 ± 3,4 mg/día	9,3 ± 3,5 mg/día	NS
Hierro	10,4 ± 2,7 mg/día	9,7 ± 4,5 mg/día	NS
Calcio	702,9 ± 363 mg/día	942,4 ± 327 mg/día	< 0,05
Yodo	333,9 ± 236 µg/día	420,6 ± 233 µ/día	NS
Sodio	1.298 ± 597 mg/día	1.088 ± 490 mg/día	NS
Potasio	2.416 ± 643 mg/día	2.681 ± 696 mg/día	NS

La valoración de la ingesta de macronutrientes (tabla I) mostró una ingesta de calorías superior en el grupo de pacientes tumorales (1.545,3 ± 359 cal/día frente a 1.264,4 ± 240 cal/día; $p < 0,05$). La ingesta de hidratos de carbono también fue superior en el grupo de pacientes tumorales (177,9 ± 57,9 g/día frente a 135,9 ± 38,5 g/día; $p < 0,05$), así como la ingesta de grasas totales (58,2 ± 18,4 g/día frente a 45,9 ± 15,4 g/día; $p < 0,05$) sobre todo a expensas de las grasas saturadas (19,4 ± 7,7 g/día frente a 11,9 ± 6,1 g/día; $p < 0,05$). Los pacientes tumorales mostraron también un consumo significativamente superior de colesterol. No se detectaron diferencias en el resto de macronutrientes. No existieron diferencias en la distribución del valor calórico total de los diferentes nutrientes, carbohidratos (tumorales 45,8% VCT frente a 42,8% VCT controles; n.s), proteínas (tumorales 34% VCT frente a 31,8% VCT controles; n.s), y grasas totales (tumorales 20,2% VCT vs 25,4, 8% VCT controles; n.s). La ingesta de proteínas corregida por peso fue similar en ambos grupos (1,12 ± 0,8 g/kg/día tumorales frente a 1,02 ± 0,6 g/kg/día controles; n.s).

En la tabla II se muestran los resultados de la ingesta de micronutrientes. Se detectaron diferencias en la ingesta de vitaminas, así los pacientes tumorales ingieren menos vitamina C (59,4 ± 18,5 mg/día tumorales frente a 141,5 ± 83 mg/día controles; $p < 0,05$), ácido fólico (116,5 ± 56,3 mg/día frente a 180,5 ± 78,5 mg/día; $p < 0,05$), y vitamina B_2 (1,53 ± 0,5 mg/día frente a 23,9 ± 6,5 g/día; $p < 0,05$). En la ingesta de minerales los pacientes tumorales ingieren menos calcio (702,9 ± 363 mg/día frente a 942,4 ± 327 mg/día; $p < 0,05$), no se detectaron diferencias estadísticamente significativas en el resto de minerales.

Discusión

Nuestro estudio muestra cómo los pacientes tumorales presentan un aumento en la ingesta calórica, a expensas de un aumento de la ingesta de hidratos de carbono y grasas. Además existe una disminución en la ingesta de determinados micronutrientes como la vitamina C, B_2, ácido fólico y calcio.

Las alteraciones en la ingesta de macronutrientes ya han sido descritas en otros estudios. De Stefani y cols.[5] detectaron un aumento de la ingesta de calorías en los pacientes tumorales, con una ingesta superior frente a los controles de 380 cal/día un dato muy similar al encontrado en nuestro trabajo (280 cal/día). En este trabajo[5] se encontraron también mayores ingestas en las cantidades de grasas totales, pero a la inversa que en nuestros datos la ingesta de hidratos de carbono fue inferior en el grupo de tumorales. Otra de las diferencias encontradas con respecto a nuestros datos es la mayor ingesta de grasas polinsaturadas en pacientes tumorales, en nuestro grupo la diferencia en la ingesta de grasas fue a expensas de las grasas saturadas a favor de los pacientes tumorales. En el trabajo de De Stefani y cols.[5] la ingesta de proteínas fue también superior en los pacientes tumorales, en nuestro grupo la ingesta fue similar incluso corregida por peso del paciente. La ingesta de colesterol también fue superior en los pacientes tumorales como en el estudio previamente citado.

En otros trabajos ya se había detectado previamente esta relación entre la ingesta de grasas y el cáncer de vía aerodigestiva[6-7], sobre todo con la ingesta de grasas saturadas. No parece tan clara la relación con la ingesta de proteínas, existen estudios que han demostrado la relación entre este tipo de tumores y la baja ingesta de proteínas[8], otros que no consiguen demostrar ninguna relación[9], mientras otros encuentran una relación positiva[7]. La relación con la ingesta de otros macronutrientes no se han encontrado, en estos momentos los estudios se centran en la ingesta de grasas, sobre todo en la proporción de grasas saturadas y polinsaturadas. En estos últimos años se ha detectado cómo la ingesta de grasas polinsaturadas derivadas de

pescado disminuye el riesgo de cáncer de vía aerodigestiva alta, mostrándose riesgos relativos de 1,98 en las personas que toman menos de una vez pescado a la semana[10], al ajustar posteriormente los resultados se detectó cómo se convertía en un mejor predictor la proporción grasas polinsaturadas/grasas saturadas que la propia frecuencia semanal de ingesta de pescado.

En la literatura los datos son más claros en lo que respecta a micronutrientes sobre todo al grupo de vitaminas antioxidantes, siendo múltiples las revisiones sobre el tema[11, 12]. En el estudio de De Stefani[5] se mostró una mayor ingesta de vitamina C en los controles (diferencia de 30 mg/día), en nuestro estudio la ingesta fue también superior en el grupo de controles pero en una mayor cuantía (diferencia de 80 mg/día). Esta relación con la vitamina C está en consonancia con los estudios que muestran una disminución del riesgo en personas con alto consumo de frutas y vegetales, esta relación se ha constatado en diferentes áreas geográficas como Italia, China, Uruguay, Polonia e India. En algunos de estos estudios se ha demostrado que la relación es mayor con el consumo de determinados productos, de este modo en el estudio realizado en China[13] la mayor disminución del riesgo se asoció con el consumo de naranjas. No obstante, no solo se relaciona la disminución del riesgo con el aumento del consumo de frutas del grupo de los cítricos, sino también con el aumento del consumo de vegetales. De nuevo el estudio realizado en China[13], demostró cómo esta disminución del riesgo se relacionaba con determinados vegetales como son aquellos de hoja verde oscura y también el ajo.

De todas las vitaminas antioxidantes parece que la vitamina que con más claridad se ha relacionado su bajo consumo con el aumento del riesgo de cáncer de vía aerodigestiva alta es la vitamina C, con un aumento del riesgo en los dos cuartiles más bajos de ingesta[14]. La relación de la baja ingesta de antioxidantes con los tumores de vía aerodigestiva es plausible biológicamente, ya que estas sustancias podrían prevenir la oxidación generada en la mucosa por el tabaco y alcohol que consumen estos pacientes. En nuestro trabajo los pacientes tumorales mostraron una menor ingesta de fólico y vitamina B_2, no encontrándose este dato en ningún otro trabajo realizado previamente.

Los trabajos sobre ingesta de minerales no ha aportado ningún dato relevante, en algunos estudios la ingesta de zinc y hierro mostraron una relación inversa con el riesgo de cáncer[15], sin poder explicar esta relación con ninguna hipótesis biológica. En nuestro estudio los controles mostraron una mayor ingesta de calcio.

En conclusión, los pacientes con tumores de vía aereodigestiva alta consumen una mayor cantidad de calorías, grasas saturadas y carbohidratos, así como una menor cantidad de vitamina C, fólico, vitamina B_{12} y calcio.

Referencias

1. Luis DA, Aller R, Cabezas G, Terroba C y Cuellar L: Estado nutricional en pacientes con tumores de cuello. *Nutrición Clínica y Dietética*, 2000, 2:21-26.
2. Luis DA, Cabezas G, Terroba C y Cuellar L: Valoración antropométrica nutricional utilizando dos tablas de referencia en pacientes con tumores de cabeza y cuello. *Nutrición Hospitalaria*, 2000, 3:114-118.
3. Esteve J, Riboli E, Pequignot G, Terracini B, Merletti F, Crosignani P, Ascunce N, Zubiri L, Blanchet F y Raymond L: Diet and cancers of the larynx and hypopharynx: the IARC multi-center study in southwestern Europe. *Cancer and Causes and Control*, 1996, 7:240-252.
4. Mataix J y Manas M: Tablas de composición de alimentos españoles. 3.ª Ed. Ed: University of Granada, 1998.
5. De Stefani E, Ronco A, Mendilaharsu M y Deneo-Pellegrini: Diet and risk of cancer of the upper aereodigestive tract-II. Nutrients. *Oral Oncol*, 1999, 35:22-26.
6. Gao YT, McLaughlin JK, Gridley G, Blot WJ, Ji BT, Dai Q y Fraumeni JF: Risk factors for esophageal cancer in Shanghai, China. Role of diet and nutrients. *Internat J of Cancer*, 1994, 58:197-202.
7. Freudenheim JL, Graham S, Byers: Diet, smoking, and alcohol in cancer of the larynx: A case-control study. *Nutr Cancer*, 1992, 17:33-45.
8. Zatonski W, Becher H, Lissowska J y Wahrendorf J: Tobacco, alcohol, and diet in the etiology of laryngeal cancer: a population-based case-control study. *Cancer Causes Control*, 1991, 2:3-10.
9. Graham S, Mettlin C, Marshall J Priore R, Rzepka T y Shedd DP: Dietary factors in the epidemiology of cancer of the larynx. *A J Epidemiol*, 1981, 113:675-680.
10. Notani PN, Jayant K. Role of the diet in upper aerodigestive tract cancers. Nutr Cancer 1987; 10:103-113.
11. Steinmetz KA y Potter JD: Vegetables, fruit and cancer II-Mechanisms. *Cancer Causes and Control*, 1991, 2:427-442.
12. World Cancer Research Fund in association with American Institute of Cancer Research: Food, Nutrition and the Prevention of Cancer: a Global Perspective. World Cancer Resarch Fund, 1997.
13. Zheng W, Blot WJ y Shu X: Diet and other risk factors for laryngeal cancer in Shangai, China. *AM J Epidemiol*, 1992, 136:178-181.
14. Riboli E, Kaaks R y Esteve J: Nutrition and laryngeal cancer. *Cancer Causes and Control*, 1996, 7:147-156.
15. Rogers MAM, Thomas DB, Davis S, Vaughan TL y Nevissi AE: A case control study of element levels and cancer of the upper aerodigestive tract. *Cancer Epidemiol Biomark Prev*, 1993, 2:305-312.

Nutr. Hosp. (2001) XVI (6) 284-285
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Nutrición Hospitalaria

Carta al director

Conocimiento y actitud sobre la desviación en la práctica clínica médica

F. González Hermoso* y A. Jiménez Sosa**

* *Departamento de Cirugía. Hospital Universitario de Canarias.* ** *Unidad de Investigación. Hospital Universitario de Canarias. España.*

Sr. Director:

El concepto de error médico tiene diferentes acepciones[1-7]. En la actualidad se prefiere la denominación de *desviación* al término error, por la posible implicación legal asociada a este significado.

En 1991 investigadores de la Harvard Medical School publicaron una serie de artículos sobre los eventos adversos, o simplemente desviación en la práctica médica[8, 9]. En conjunto, en estas publicaciones se concluye que la frecuencia de la desviación médica oscila entre un 2,9% y un 3,7%. En España el problema no ha sido abordado.

En una encuesta transversal describimos el conocimiento y la actitud que tienen los médicos de un hospital español de tercer nivel acerca de la desviación en la práctica médica.

De una población de 370 médicos de plantilla y residentes del Hospital Universitario de Canarias se seleccionó por muestreo aleatorio simple una muestra representativa de 270 médicos, incluido el 20% asumido de pérdida (54 médicos). El error de estimación se estableció en el 3%, la potencia se estableció en el 80% y el nivel de confianza en el 95%.

Cada médico de la muestra recibió un cuestionario. Éste consta de dos partes, unas instrucciones y 8 preguntas con formato variable. En las instrucciones se indica que es anónimo y fecha y lugar para entregar una vez cumplimentado. Se realizó en septiembre de 2000.

Las preguntas 1 y 2 aluden a la frecuencia y gravedad con la que piensan que ocurren las desviaciones médicas. La pregunta 3 cuestiona sobre el concepto de desviación médica. Las preguntas 4 y 5 intentan medir las causas de falta de comunicación sobre el problema y la repercusión que tiene el problema en la conciencia del médico, la pregunta 6 pretende medir cómo se toma las decisiones en presencia de un caso problema. Por último, las preguntas 7 y 8 cuestionan sobre el mejor método para informar, registrar y analizar los casos de desviación.

La muestra se estratificó de acuerdo con los años de ejercicio profesional en dos categorías: superior o inferior a 10 años. Las comparaciones de proporciones de respuesta entre ambos grupos se realizaron con la prueba χ^2. Se consideraron significativos el contraste con $p < 0,05$.

Contestaron al cuestionario y lo entregaron 86 médicos (23,2% de la población médica del centro), que es un 39,8% de la muestra calculada. Debido a esto, la potencia queda finalmente en el 63%. Por tanto, la capacidad de generalización de los resultados queda restringida a los médicos que entregaron el cuestionario y sus datos analizados.

La tabla I muestra los porcentajes de respuesta en cada pregunta. Podemos concluir que, por un lado, los médicos interesados lo consideran un problema frecuente, que afecta el sentido de responsabilidad y culpabilidad del 90% de los facultativos, por otro lado las decisiones diagnósticas o terapéuticas se realizan individualmente, con el asesoramiento de los compañeros en las sesiones clínicas, no reconociéndose para la toma de decisiones la antigüedad, la experiencia o la jerarquía. Por último, desconocen quien es el responsable del control y registro de la desviación médica.

Correspondencia: *F. González Hermoso*
Departamento de Cirugía.
Hospital Universitario de Canarias.
38320 La Laguna. Santa Cruz de Tenerife.
Correo electrónico: fgonzale@ull.es

Recibido: 25-VI-2001.
Aceptado: 25-VI-2001.

Referencias

1. Wilson RM, Runciman WB, Gibberd RW, Harrison BT y cols.: The quality in Australian health care study. *Med J Aust,* 1995, 163:458-471.
2. Interin report of the taskforce on quality in Australian helth care www.health.gov.au/pubs/hlthcare/append.htm.
3. Classen DC, Pestonik SL, Evans RS, Lloyd JF y Burke JP: Adverse drug events in hospitalized patiens: excess length of stay, extra costs, and attributable mortality. *JAMA,* 1997, 277:301-306.
4. Gawande AA, Thomas EJ, Zinner MJ y Brennan TA: The incidence and nature of surgical adverse events in Colorado and Utah in 1992. *Surgery,* 1999, 126:1 66-75.
5. Thomas EJ, Studdert FM, Burstin HR, Orav EJ, Zeena T, Williams EJ, Howard KM, Weiler PC y Brennan TA: Incidence

Tabla I
Resultado al cuestionario enviado a médicos de un hospital terciario sobre lo errores médicos

N.º de pregunta		*Respuesta más significativa*
1.ª	¿Qué frecuencia estimas que hay de errores médicos en un hospital?	Un 65% de los encuestados estiman la frecuencia entre el 10 y 21% de los ingresos.
2.ª	¿Qué frecuencia estimas, de éstos, ocurren casos con resultado grave o muerte por los errores médicos en los ingresados?	Un 73% estiman que hay una mortalidad entre 1 y 10‰ de los errores.
3.ª	¿Qué o cuáles definición(es) te gustan más para el error médico?	Un 65% aceptan la propuesta de definiclón de error médico "un fallo o complicación en la evolución clínica de un paciente por equivocación del médico en una orden o actuación terapéutica".
4.ª	¿Por qué crees que no se comentan los errores médicos?	Un 46% estiman que no se comenta habitualmente el error médico por vergüenza y un 33% por miedo a una demanda judicial.
5.ª	¿Repercute interiormente la conciencia de un error propio?	Un 84% aceptan la conciencia de un error médico, les afecta en conciencia si ha habido repercusión clínica.
6.ª	¿En un caso problema con cuál o cuáles de las siguientes afirmaciones estás más identificado?	Un 47% afirma que un médico de plantilla puede decidir la conducta oída la opinión del equipo en sesión clínica.
7.ª	¿Cómo deben manejarse los errores médicos en tu opinión?	Un 48% contesta que los errores médicos deben analizarse aisladamente por el médico responsable sin darle publicidad.
8.ª	¿Debe haber constancia de los errores?	No hay ninguna propuesta dominante, e incluso se considera imprudente.

and types of adverse events and negligent care in Utah and Colorado. *Med Care*, 2000, 38: 3 261-271.

6 Kohn LM, Donaldson MS: EDS To err is human. Building a safer health system. Institute of Medicine. Washington, DC: National Academy Press, 1999.

7. Whem primun non nocere fails (editorial). *The Lancet*, 2000, 355:2007.

8. Brennan TA, Leape LL, Laird NM y cols.: Incidence of adverse events and negligence in hospitalised patients: Results of the Harvard Medical Practice Study II. *N Engl J Med*, 1991, 3214:370-376.

9. Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes BA, Hebert L, Newhouse JP, Weiler PC y Hiatt H: The nature of adverse events in hospitalised patients. Results of the Harvard Medical Practice Study II. *The New England Journal of Medicine*, 1991, 324(6): 377-384.

Nutr. Hosp. (2001) XVI (6) 286-292
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Nutrición Hospitalaria

CLÁSICOS EN NUTRICIÓN

Comentario al artículo

Long-term total parenteral nutrition with growth, development and positive nitrogen balance. Surgery 1968. 64:134-142

Dudrick SJ, Wilmore DW, Vars HM, Rhoads, JE

José Antonio Irles Rocamora, Sevilla.

En este artículo, los autores resumen la experiencia de sus estudios en pacientes y animales de experimentación alimentados con nutrición parenteral total (NPT), demostrando, por primera vez, la posibilidad de mantener el crecimiento y metabolismo tisular durante períodos de tiempo prolongados solamente con nutrición parenteral y que, desde el punto de vista de la nutrición celular, hay escasa diferencia entre la administración enteral o parenteral de los nutrientes.

En este trabajo se describe la evolución de 30 pacientes quirúrgicos o con enfermedades gastrointestinales que reciben nutrición parenteral total hasta un máximo de 200 días. El tratamiento consistió en una solución de hidrolizado de fibrina y glucosa, preparada en la farmacia del hospital, con un contenido calórico de 2.400 a 4.500 kcal/día, que se instauró de forma progresiva. La solución contenía además 15 vitaminas y 12 minerales. Cuando fue posible, se añadieron pequeñas cantidades de nutrición oral para favorecer el trofismo intestinal. La perfusión de esa solución se realizó durante un período de 21-23 horas al día, mediante el acceso percutáneo a través de la vena yugular o subclavia, cuidando el catéter con solución iodada cada 3 días. Se realizaron controles diarios de peso, balance hídrico y controles metabólicos periódicos. En estos pacientes se observó la curación de las heridas quirúrgicas o de fístulas enterales, junto con aumento de peso corporal, de fuerza muscular y de actividad física.

En el estudio experimental con seis perros (cachorros beagle de 12 semanas) pudo demostrarse durante un período de 256 días un desarrollo corporal normal hasta alcanzar el peso y talla del adulto, siendo el crecimiento similar con una nutrición isocalórica-isoproteica administrada por vía oral o parenteral.

Por primera vez en la década de los años 60 se abre la posibilidad de obtener la cicatrización de heridas quirúrgicas y de un desarrollo postoperatorio normal cuando la alimentación oral enteral es imposible o insuficiente. La administración por períodos cercanos a 24 h/día, superiores a los hasta entonces empleados, mejoraba la tolerancia y eficiencia metabólica de los nutrientes y además permitía cierto tiempo para el ejercicio físico y el juego diariamente, considerados como factores contribuyentes al anabolismo celular. Simultáneamente se demuestra además la posibilidad de conseguir el desarrollo y crecimiento corporal normal desde las primeras etapas de la vida, exclusivamente con nutrición parenteral.

Después de más de 30 años los principios de este trabajo pionero siguen manteniendo su vigencia, si bien la modificación de los materiales y soluciones empleados y el tiempo de tratamiento con NPT se ha prolongado notoriamente. La NPT continúa siendo una parte esencial del tratamiento en situaciones de estrés y catabolismo así como de anabolismo en pacientes de cualquier edad. La composición de las soluciones y mezclas de NPT son más completas tanto en macronutrientes, que han incorporado diferentes tipos de grasas, soluciones de aminoácidos y nutrientes esenciales. En los últimos años ha surgido el concepto de fármaco-nutriente en la idea de que aprovechar el efecto "farmacológico" de algunos nutrientes con la intención de favorecer el metabolismo celular, especialmente en situaciones catabólicas así como la utilización de sustancias como la hormona de crecimiento y el IGF-1 como factores estimuladores del anabolismo y de la retención de nitrógeno. Aunque los resultados iniciales no son optimistas, indican las nuevas oportunidades de controlar la respuesta metabólica al ayuno y la agresión.

La duración de la nutrición se ha prolongado, pasando de pocas semanas a años, existiendo en la actualidad casos de niños y adultos con más de 27 años de tratamiento. En esta situación de nutrición parenteral prolongada, han emergido nuevos problemas como la osteopatía metabólica, sin una solución óptima, o las complicaciones de las técnicas del abordaje ve-

noso que en ocasiones limitan la eficacia de la NPT, por las complicaciones infecciosas del catéter o la trombosis venosa, cuando el tratamiento debe prolongarse durante años. En el abordaje de estos problemas conviene recordar una frase de uno de los autores de este artículo: "los clínicos, con la ayuda de personas preparadas en ciencias básicas, deben buscar en el laboratorio soluciones a los problemas de los pacientes, para después aplicarlas a los enfermos".

La NPT, un método de tratamiento desarrollado inicialmente por cirujanos, se ha convertido en una técnica de inestimable valor con la incorporación de equipos profesionales multidisciplinares de nutrición clínica, que han permitido extender el uso de la NPT, en la mayoría de los hospitales en los países desarrollados, hasta el propio domicilio del paciente convirtiéndose en un método de soporte vital en los enfermos con intestino corto o fístulas digestivas e incluso permitiendo una vida social activa de los pacientes que antes tenía una esperanza de vida muy corta.

Bibliografía

American Society for Parenteral and Enteral nutrition. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *JPEN J Parenter Enteral Nutr*, 1993, 17 (4 suppl) 1S-52S.

Buchman AL y Ament ME: Fifteen-year survival of a Broviac catheter used for home parenteral nutrition. *JPEN J Parenter Enteral Nutr*, 1993, 17(5):489.

Klein S, Kinney J, Jeejeebhoy K, Alpers D, Hellerstein M, Murray M, Towney P y cols.: Nutrition support in clinical practice: review of published data and recommendations for future research directions. *Clin Nutr*, 1997, 4:193-218.

Rhoads JE: Memoir of a surgical nutritionist. *JAMA*, 1994, 272:963-966.

Wilmore DW y Dudrick SJ: Growth and development of an infant receiving all nutrients exclusively by vein. *JAMA*, 1968, 203:860-864.

Long-term total parenteral nutrition with growth, development, and positive nitrogen balance*

Stanley J. Dudrick, M. D.; Douglas W. Wilmore, M. D.; Harry M. Vars, Ph. D.; Jonathan E. Rhoads, M. D.

Philadelphia, P.A. From the Department of Surgery and the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania

The best route for satisfying nutritional requirements is the gastrointestinal tract. However, when its use is precluded for prolonged periods, parenteral alimentation becomes necessary and is common clinical practice with the use of carbohydrate, amino acid, vitamin, and electrolyte solutions. Limited positive nitrogen balance has been achieved in several short-term periods of total intravenous feeding.[1, 5]. However, rarely if ever, has a patient gained weight and passed into a significant and continuing anabolic state with parenteral nutrition alone.[6]

The purpose of this work has been to determine if tissue maintenance and synthesis and growth could be achieved exclusively by intravenous infusion of basic nutrients for prolonged periods of time.

This study supported by United States Public Health Service Grants No. 5-P01-AM-04825-07 and No. 5-201-GM-01540-02.

Presented at the Twenty-ninth Annual Meeting of the Society of University Surgeons, New York, N. Y., Feb. 8-10, 1968.

Laboratory studies

Six male pedigreed beagle puppies were fed entirely intravenously for 72 o 256 days and compared with their orally fed littermates. After weaning at 8 weeks of age, the puppies were paired according to their size and compared with their orally fed litterately in metabolic cages, and fed a standard oral ration to determine their individual growth rates. At 12 weeks of age a No. 24 vinyl catheter was inserted into an external jugular vein and threaded in to the superior vena cava of one member of each pair. The proximal end of the catheter was directed subcutaneously with a trocar and brought out through a puncture wound in the skin between the scapulas. A blunt No. 21 needle was inserted into the catheter and secured to the puppy's back by a stainless stell support assembly and canvas harness.

A peristaltic pump propelled the nutrient solution through a counterbalanced delivery apparatus which allowed the animal freedom of movement in his cage.

The solutions, infused over a 21 to 23

hour period daily, consisted of glucose, fibrin hydrolysate, and all the vitamins and minerals recommended for frowth in dogs. In the dietary regimens which included fat, the emulsion was infused separately over a 2 to 3 hour period. The experimental animals were disconnected from the delivery apparatus the remaining 1/2 to 1 hour daily for exercise and play. The littermate controls were fed orally at the same caloric level. The compositions of the three intravenous rations studied and the oral control diet were modified from the recommended oral requirements for growing puppies (Table I). The vitamin and mineral content of all the intravenous diets were constant (Tablas II and III).

The 6 intravenously fed puppies outstripped their controls in weight gain and matched them in skeletal growth, development, and activity for study periods of 72, 100 (3 puppies), 235, and 256 days[2, 3] (Figs. 1 and 2). No significant differences were observed in growth rates or weight gain when results of the three intravenous diets studied were compared.

Tabla I. *Compositions of the oral control diet and the three intravenous diets studied compared with the diet for growing puppies recommended by the Food and Nutrition Board, National Research Council*

	Oral	*Intravenous*			*Oral*
	(recommended)	*Balanced*	*Essential*	*Fat-free*	*(control)*
Protein (Gm./Kg./day)	8.8	4.0	4.0	4.0	10.5
Carbohydrate (Gm./Kg./day)	15.9	25.0	30.0	31.0	18.0
Fat (Gm./Kg./day)	2.6	2.6	0.6	0.0	3.3
Calories (Kcal./Kg./day)	140-200	140	140	140	140
Water (c.c./Kg./day)	–	130-190	130-160	130-160	100-140

Table II. *Vitamins**

	Oral recommended	*Intravenous*
A (I.U./Kg./day)	200	100
D (I.U./Kg./day	20	10
E (I.U./Kg./day	2.2	0.05
Thiamine (mg./Kg./day)	0.03	0.5
Riboflavin (mg./Kg./day)	0.09	0.1
Pyridoxine (mg./Kg./day)	0.05	0.15
Niacin (mg./Kg./day)	0.4	0.1
Pantothenic acid (mg./Kg./day)	0.1	0.25
C (mg./Kg./day)	–	5.0
B_{12} (mg./Kg./day)	0.0013	0.003
K (mg./Kg./day)	–	0.1
Folic acid (mg./Kg./day)	0.009	0.015
Choline (mg./Kg./day)	60	25
Biotin (mg./Kg./day)	–	0.007
PABA (mg./Kg./day)	–	2.0

*The dosages of the first nine vitamins were determined by their rations in a commercially available preparation (M.V.I.-U.S. Vitamin and Pharmaceutical Corporation, New York, N. Y.).

Clinical studies

Thirty patients with chronic complicated gastrointestinal disease have been supported exclusively by vein with 2,400 to 4,500 calories per day for 10 to 200 days. The parenteral solution, consisting of 20 per-

Table III. *Minerals*

	Oral recommended (mg./Kg./day)	*Intravenous (mg./Kg./day)*
Sodium	210	100
Potassium	440	115
Chloride	315	225
Calcium	530	72
Phosphorus	440	58
Magnesium	22	4
Iron	1.3	0.058
Cooper	0.16	0.065
Cobalt	0.055	0.041
Manganese	0.22	0.14
Zinc	0.22	0.14
Iodine	0.066	0.046

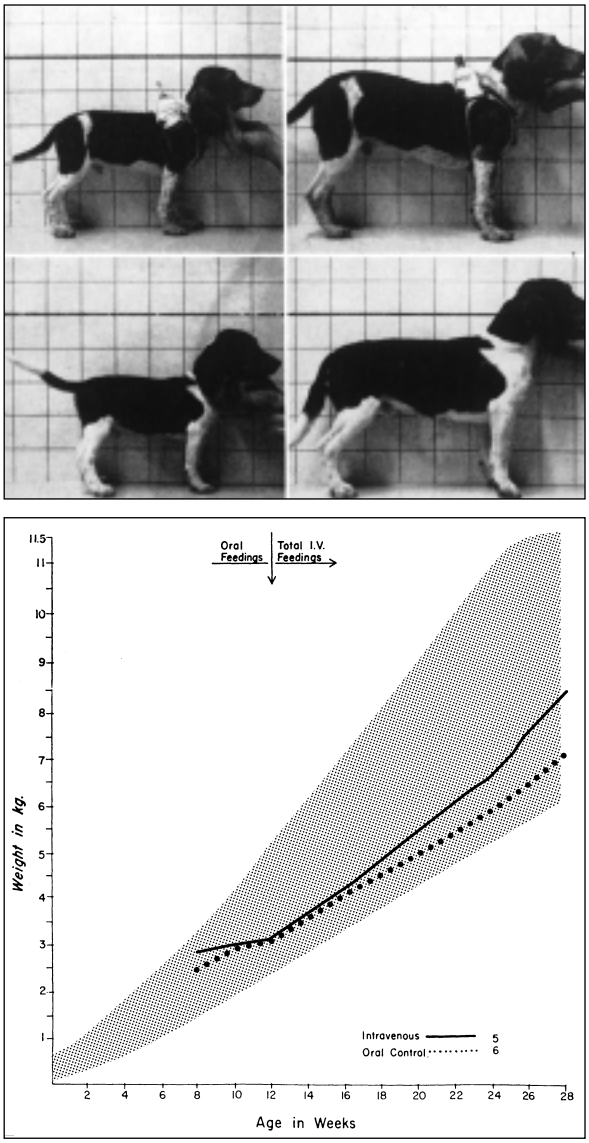


Fig. 1. Animal receiving total intravenous nutrition (*above*) for 100 days compared with the isocalorically fed oral control. Stippled area on weight curve indicates normal range of growth for beable puppies.

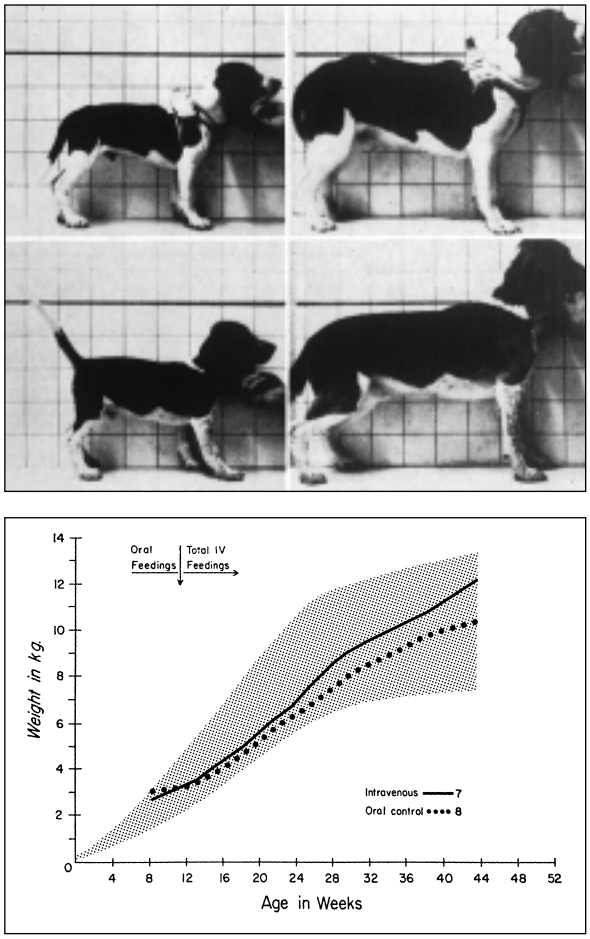


Fig. 2. This animal (*above*) fed intravenously for 235 days doubled his weight on the balanced diet in 12 weeks. At that point, fat was omitted with no apparent change in his growth rate or development.

cent glucose, 5 percent fibrin hydrolysate, electrolytes, trace minerals, and vitamins, was infused continuously through an indwelling catheter placed percutaneously in the external jugular or subclavian vein and directed into the superior vena cava. To preserve long-term catheter sterility and minimize contamination by way of the catheter tract, every 3 days an iodine solution was used to prepare the skin, antibiotic ointment was applied tot he catheter exit site, and an occlusive sterile dressing was replaced.

The basic nutrient solution, containing 1,000 calories and 6 Gm. of nitrogen per 1,000 c.c., was prepared by the hospital's manufacturing pharmacist from fibrin hydrolysate and anhydrous glucose. Each morning the mineral requirements were determined, and appropriate electrolyte concentrates, vitamins, and trace elements were added. Starting at established levels of fluid metabolism and carbohydrate utilization (2,400 c.c.), the parenteral mixture was gradually increased to levels of tolerance (up to 4,500 c.c.). For maximum efficiency, the solution was administered as constantly as possible. Daily determinations of the patient's weight, fluid balance, urine sugar concentration, and regular serum electrolytes were basic guides for safe administration of the intravenous solution.

Positive nitrogen balance was achieved in all patients with associated wound healing, fistula closure (Fig. 3), weight gain

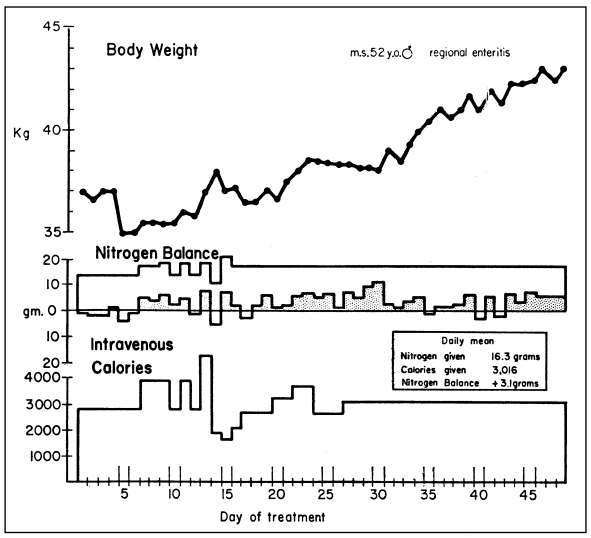


Fig. 3. Metabolic events accompanyng parenteral nutrition in a patient with multiple fistulas and short bowell syndrome. Eleven of 14 enterocutaneous fistulas closed during total intravenous therapy.

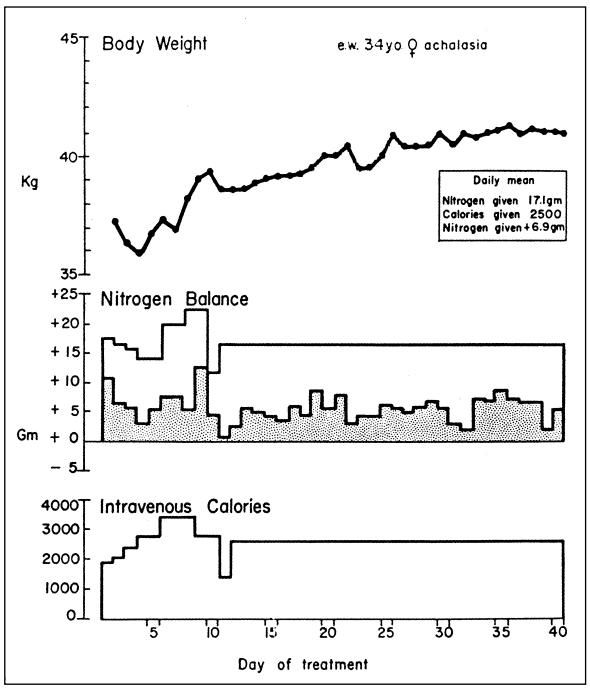


Fig. 4. Continued weight gain and positive nitrogen balance accompanied complete healing of a 250 c.c. staphylococcal abscess in this patient with achalasia and tuberculosis.

(Fig. 4), and increased strength and activity. In the first 6 patients with long-term treatment, metabolic studies demonstrated significant positive balance in the presence of a variety of generally catabolic clinical situations (Table IV).

The most dramatic result of total intravenous nutrition was the normal growth and development of a 1.8 kilogram infant with near-total small bowel atresia. During the first 44 days when gastrointestinal dysfunction precluded enteral feeding, total parenteral alimentation was accompanied by increases of 1.4 kilograms in weight, 6.3 cm. in length, and 5.0 cm. in head circumference.[8] At this time, small enteral feedings were started to stimulate small bowel adaptation. However, intravenous alimentation was required to provide sufficient nutrients to double the infant's weight in 75 days (Fig. 5).

Discussion

From the standpoint of cellular nutrition, it makes little difference whether nutrients are given by the enteral or parenteral route.[4] With parenteral nutrients the problems of toxicity and availability are accentuated and the additional requirements of sterility and nonpyrogenicity are imposed. The toxicity problems are avoided by determining a safe level of infusion for each nutrient, based upon oral requirements and modified by knowledge of its absorption, utilization, and excretion. Because of the current unavailability of an intravenous fat emulsion for clinical use in this country, "complete" parenteral

Table IV. *Metabolic data obtained in the first 6 paients given long-term total parenteral nutritions*

Patient	*Sex*	*Age*	*Diagnosis*	*Operation*
J. J.	M	28	Regional enteritis	Bypass*
C. D.	M	77	Pyloric stenosis	Subtotal gastrectomy*
I. G.	F	47	Small bowel obstruction	Lysis of adhesions*
R. R.	F	23	Traumatic pancreatitis	Pancreatic drainage
E.W.	F	34	Achalasia	Esophagomyotomy
M. S.	M	52	Regional enteritis	Small bowel resection
Total for entire series				
Mean (total series)				

*Operation during study period.

Total intravenous therapy				
Days	*Fluid volume (c.c./day)*	*Calories (Kcal./day)*	*Nitrogen (Gm./day)*	*Nitrogen balance (Gm./day)*
15	4,000	2,760	25.1	+3.6
16	3,100	2,250	16.9	+2.2
25	4,500	3,300	18.7	+2.0
28	3,200	3,060	19.1	+4.8
40	3,100	2,500	17.1	+6.9
48	3,400	3,020	16.3	+3.1
172	598,900	490,350	3,116	+700
28.6	3,500	2,850	18.1	+4.1

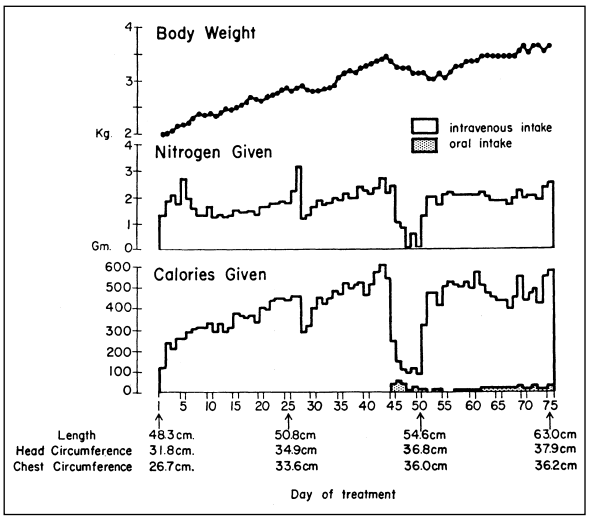


Fig. 5. Growth and development of an infant following intravenous nutrition. Small enteral feedings begun at 45 days to stimulate bowel adaptation provided negligible calories and nitrogen.

diets in isotonic form are generally not possible. Whit hypertonic solutions, all essential nutrients can be provided without exceeding daily fluid requirements. Infusion into the superior vena cava allows rapid dilution and peripheral distribution of the nutrients at isotonic concentration. Finally, development of a sterile technique for catheter placement,[7] together with aseptic safeguards in manufacture and administration of solutions, insures sterility during long-term intravenous infusions.

Summary

This is the first demonstration that growth, development, and positive nitrogen balance can be achieved by long-term total parenteral nutrition in animals and man.

Technical assistance was given by Jo Ann Nallinger, R.N., Merle Reidenberg, Laura D. Robinson, and Stanley Serlick, B.S.

References

1. Beal, J. M., Payne, M. A., Gilder, H., Johnson, G., Jr, and Carver, W. L.: Experience with administration of an intravenous fat emulsion to surgical patients, Metabolism **6:** 673, 1957.
2. Dudrick, S. J., Rhoads, J. E., and Vars, H. M.: Growth of puppies receiving all nutritional requirements by vein, Forschritte der Parenteral Ernahrung **2:** 16, 1967.
3. Dudrick, S. J., Wilmore, D. W., and Vars, H. M.: Long-term total parenteral nutrition with growth in puppies and positive nitrogen balance in patients, S. Forum **18:** 356, 1967.
4. Geyer, R. P.: Parenteral nutrition, Physiol. Rev. **40:** 150, 1960.
5. Holden, W. D., Krieger, H., Levey, S., and Abbott, W. E.: The effects of nutrition on nitrogen metabolism in the surgical patient. Ann. Surg. **146:** 563, 1957.
6. Moore, F. D.: Metabolic care of the surgical patient, Philadelphia, 1959, W. B. Saunden Company, p. 447.
7. Wilmore, D. W., and Dudrick, S. J.: Prevention of cannular sepsis preliminary report, New England J. Med. **277:** 433, 1967.
8. Wilmore, D. W., and Dudrick, S. J.: Growth and development of an infant receiving all nutrients exclusively by vein, J. A. M. A. **203:** 860, 1968.

Discussion

Dr. John Border (Buffalo, N. Y.). I think these are really fascinating results. However, the authors have not placed much stress on their use of a 24 hour infusion. I suspect this might constitute a major part of the difference between their successful use of intravenous infusions for caloric and protein maintenance and the previous failures. Serum amino acids are maintained physiologically within relatively narrow limits. This occurs, in part, because of storage in all tissues. However, the major part of this control resides in the tremendous capacity of the liver for deamination and glyconeogenesis. Thus, if we give our amino acids over a small fraction of the day, we can expect a major portion of them to be converted to glucose. Further, since the capacity for storage of glucose as glucogen is very limited, we can expect a significant portion of the glucose given over a small portion of the day to be irreversibly converted to fatty acids. All previous re-

ports of the use of intravenous calories and amino acids have been, to my knowledge, based upon giving the material over roughly 8 to 12 hours periods. These have rather uniformly failed to reveal use of the amino acids for protein synthesis. A second facet of this problem has been the demonstration that the amino acid hydrolysate must be given simultaneously with a sufficient quantity of glucose to get any utilization. This has now rather clearly been found to be dependent upon the insulin secretion produced by the glucose. Insulin stimulates the transport of amino acids into the cell and stimulates protein synthesis in the carcass at several levels.

Many of the same remarks may be made about the alternating cycles of overhydration and dehydration produced in our patients by the usual 8 hour infusion of fluids.

Thus, it seems to me that the crucial difference between your results and previous results is the 24 hour infusion. I wonder if you have compared your infusion on a 24 hour basis with the same quentity of material given over 8 or 12 hours.

Dr. Clarence Dennis (Brooklyn, N. Y.). My associates and I in Brooklyn have been very much interested in this program, and Dr. Grosz and I have been doing this over a period of more than 20 years. Although we have not used hydrolysates, we have used 15 and 20 percent glucose and covered it with insulin in the same infusion.

We have been very much impressed that we can maintain caloric intake such as has been described by Dr. Rhoads and his associates, and have had some very striking results.

Recently we had a patient weighing 69 pounds, with ulcerative colitis in the acute phase, who was taken in the course of 48 hours from a total protein concentration of 3.2 to 6.6 Gm. percent, and at 60 hours had a proctocolectomy followed by successful primary wound healing and an ultimate recovery which went very nicely.

One thing that has perplexed us very much about this problem has been that the insulin requirement is high at first`one unit per every 5 Gm., more or less, of glucose, but it goes down in the course of the next few days, and if one doesn't watch the situation, he will have trouble with hypoglycemic shock.

We have found many of our patients to have a total disappearance of the requirement for added insulin in the course of 3 or 4 days, and wonder if this group has had the same experience and whether they have any ideas about what the mechanism is.

Dr. Dudrick (closing). Dr. Dennis, we have not routinely added insulin to these infusions. We can generally administer 2,400 c.c. containing 2,400 calories initially to all patients without glycosuria, and we have not added insulin unless the patient had diabetes. In some patients with diabetes we have substituted fructose for glucose.

The solutions are infused continuously over 24 hours to take full advantage of the day. In this manner the rate of glucose infusion is regulated to comply with the inherent rate of maximum utilization, which varies between 0.5 and 0.9 Gm. per kilogram per hour. Should the infusion be interrupted or fall behind schedule, a compensatory increase in the infusion rate will not be tolerated by the patient`glycosuria with osmotic diuresis will occur`and should not be attempted. If a relatively large amount of glucose is not given, we believe that there is decreased amino acid utilization for protein synthesis, with oxidation of the amino acid substrates for energy. If hypertonic sugar is not given to satisfy caloric requirements, amino acids are not of much value because they wil be metabolized in the same fashion as glucose at greater expense.

We have not yet done endogenous insulin studies in any sophisticated manner, but we do know that if we start infusing 2,400 calories to a patient, and the next day or so increase to 2,800 calories, he might spill a trace to 2+ sugar in urine. If this a accepted for a day or 2, there seems to be a pancreatic adjustment of insulin secretion, the patient will stop spilling sugar, and then glucose can be increased again in stepwise fashion over a period of time as previously mentioned from 2,400 calories up to 5,000 calories in some selected patients.

Another thing that can be done, if a patient continues to "spill" after glucose is increased, is to increase potassium. This has been known to accompany sugar movement into the cell. In our patients we are giving as much as 200 to 250 mEq. of potassium daily, if we get up to the 4,000 calorie level. Large amounts of potassium must be given in order for the interrelationship of glucose, potassium, amino acids, and insulin to be optimal in incorporation of nutrients into the cells and tissues.

Nutrición Hospitalaria

Nutr. Hosp. (2001) XVI (6) 293
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Crítica de libros

Nutrición clínica: bases y fundamentos

Editor: Alberto Mijan de la Torre. Ediciones DOYMA. 2000. 588 páginas.
ISBN 84-7592-652-5

El libro editado por Mijan y en el que participan más de 50 autores españoles aparece prologado por Khursheed N. Jeejeebhoy, que también contribuye con un capítulo, escrito en inglés, sobre composición corporal y evaluación del estado nutritivo.

El libro está dividido en cinco secciones, introducción, nutrición y cuerpo humano, nutrición, órganos y sistemas, nutrición y nutrientes, nutrición y metodología de la investigación nutricional, apareciendo un total de 26 capítulos.

En la sección nutrición y cuerpo humano se incluyen siete capítulos que describen el efecto de la nutrición sobre la composición corporal y la función, la respuesta al ayuno y a la enfermedad crítica.

Aparece también la anorexia debida a la enfermedad orgánica y los conceptos recientes sobre termogénesis y los fenómenos de apoptosis.

La siguiente sección, compuesta por 10 capítulos, se dedica a la influencia de la nutrición sobre la función del organismo y en las enfermedades. Se tratan en profundidad los efectos positivos de la nutrición sobre la inmunidad, el sistema nervioso central, la función mental y el crecimiento, los efectos negativos como causa del síndrome de renutrición y el síndrome X.

Finalmente se analiza la nutrición e hipoxia celular, estudios metabólicos, lesión pancreática y envejecimiento.

En la siguiente sección, dedicada a nutrición y nutrientes, se habla de los nutrientes esenciales, de los radicales libres y nutrientes antioxidantes, enfermedades asociadas al estrés oxidativo, acción farmacológica de los nutrientes y los conceptos dinámicos de la interacción fármaco-nutriciente. La última sección, dedicada a la nutrición y metodología de la investigación nutricional, trata sobre el efecto de la malnutrición sobre la mortalidad, método científico en nutrición clínica, elección del tipo de estudio en investigación nutricional e interpretación clínica de datos y fuentes bibliográficas.

Este libro nos ofrece un punto de vista diferente de lo que es la nutrición artificial y es válido para todos los segmentos profesionales que hoy día tienen interés en la nutrición.

El formato de cada capítulo es homogéneo y bien estructurado. Tanto el índice de comienzo como el índice de materias que aparece al final del libro son exhaustivos lo que confiere a este tratado una gran agilidad en su manejo.

La edición, realizada por Doyma y patrocinada por Nutricia, está muy cuidada. En su conjunto creo que es un libro que no debe faltar en nuestras bibliotecas para su consulta cotidiana.

Jesús Culebras

¿Qué es una alimentación sana? Reflexiones sobre alimentación y nutrición

E. Rojas Hidalgo. Grupo Aula Médica, S.A. 200 páginas. Madrid, 2001.
ISBN 84-7885-266-2

El libro de Rojas es el resultado de la recopilación de una serie de artículos, conferencias y reflexiones sobre alimentación y nutrición. Algunos de los temas que se exponen han aparecido ya en libros, revistas y periódicos y otros han sido expuestos en distintos foros académicos.

En total se recopilan 25 artículos incluyendo temas históricos (el fuego de la vida, descubrimiento de la vitamina C), aspectos básicos (agua, oligosacáridos, aceites, lípidos, fibra, vitaminas), temas clínicos (diabetes, arteriosclerosis) y recomendaciones sobre algunas alteraciones relacionadas con la alimentación (obesidad, desnutrición). El libro es fácil de leer porque el profesor Rojas se ha caracterizado siempre por su amenidad. En un momento dado cualquier capítulo por sí mismo resulta interesante.

Jesús Culebras

Nutriología Médica. 2.ª edición. Fundación Mexicana para la Salud.

Editores: Esther Casanueva, Martha Kaufer-Horwitz, Ana Berta Pérez-Lizaur, Pedro Arroyo. Editorial Médica Panamericana. 720 páginas. Año de edición: 2001. PVP con IVA: 12.500 pesetas.
ISBN 84-7903-629-X

La primera edición de Nutriología Médica fue concebida como un libro de texto para introducir a los estudiantes de medicina en el conocimiento nutriológico general; sin embargo, en la práctica ha resultado ser un libro de consulta para todos los médicos, nutriólogos, odontólogos, enfermeras y psicólogos, entre otros, e incluso para profesionales en pleno ejercicio laboral. Por lo anterior, esta segunda edición ha profundizado más en algunos temas con el fin de ofrecer a los lectores una visión más amplia sobre la forma como influyen la alimentación y la nutrición en la expresión del potencial genético a lo largo del ciclo de la vida, sin perder la visión preventiva y aplicativa de la obra; es decir, sin dejar de hacer énfasis en aquellas prácticas que han mostrado ser efectivas tanto en el campo clínico como en el epidemiológico para promover la salud en el amplio sentido del término y al mismo tiempo evitar o retardar la aparición de las enfermedades más comunes en los diferentes grupos de edad. En este sentido es importante llamar la atención sobre la inclusión de un capítulo dedicado a la actividad física. Ésta se debe tomar en cuenta no sólo por ser el componente más importante y variable del gasto energético, sino porque cada vez con mayor frecuencia resulta ser un factor fundamental en la prevención de las enfermedades crónicas, de manera tal que su evaluación y su promoción deben ser actividades obligatorias, junto con el estudio de los hábitos alimentarios, en la atención tanto del individuo sano como del enfermo.

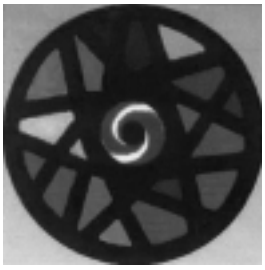
Empresas de restauración alimentaria. Un sistema de gestión global

M.ª del Mar Araluce Letamendía. 2001, rústica, 15 x 21,5 cm, 262 páginas, 400 gramos, 3.400 pesetas.
ISBN: 84-7978-460-1.

Resulta incuestionable el gran cambio y enorme crecimiento que el sector de la alimentación está experimentando en los países desarrollados. Los cambios sociales, las nuevas formas de vida y sus hábitos de consumo, el incremento de los viajes, las constantes variaciones en los horarios de trabajo, el aumento del poder adquisitivo hacen del comer fuera del hogar una necesidad más del hombre contemporáneo. Sin embargo, son pocos los estudios que tratan de aplicar técnicas de gestión a empresas de restauración, y los que lo hacen, se quedan en un estudio parcial sobre aspectos concretos.

La publicación de este libro tiene fundamentalmente dos objetivos, el primero: que sirva de texto a los alumnos de la Diplomatura de Nutrición Humana y Dietética que se cursa actualmente en varias universidades; el segundo: transmitir los conceptos de bechmarking y mejora continua de la calidad, proporcionando a las empresas de restauración una metodología de análisis y organización que puedan aplicar. El trabajo se apoya en el modelo de dirección estratégica que permite una dirección flexible que, analizando las necesidades del entorno, define productos y servicios de gran valor añadido para los clientes —reales y potenciales— y el modo de gestionarlos.

Índice resumido: Conceptos básicos de gestión de empresas de servicios. El sector de la restauración colectiva. El diseño del producto. La gestión de las actividades. Logística de entrada. Operaciones. Logística de salida. Comercialización y ventas. Servicio. Compras. Diseño y desarrollo de la tecnología. Política de personal. Infraestructura.



XVIII Congreso Nacional
de la Sociedad Española
de Nutrición Parenteral y Enteral
y
IX Reunión de la
Sociedad Española de Nutrición

León 14 - 17 Mayo 2002

Información completa en:
www.tilesa.es/senpe

SENPE
sociedad española de nutrición parenteral y enteral

SEN

Noticia de ULTIMA HORA

PREMIO DE LA REAL ACADEMIA NACIONAL DE MEDICINA A "NUTRICIÓN HOSPITALARIA"

La Real Academia Nacional de Medicina ha acordado conceder el premio *José García Sicilia* a la revista NUTRICIÓN HOSPITALARIA. El galardón será entregado a su director en la Sesión Solemne de Apertura del Curso Académico, el próximo día 15 de Enero de 2002. En el siguiente número daremos información completa de la concesión del premio.