



## Trabajo Original

Nutrición artificial

### Clinical nutrition prescription using a mathematical method to assess industrialized formulas

*Prescrição de nutrição clínica utilizando um método matemático para valorar as fórmulas industrializadas*

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#### Abstract

**Background:** the planning of nutritional therapy depends on restrictions defined by the prescriber, in a way that nutrients and calories levels are placed at appropriate intervals. Since industrialized formulas (IF) have fixed compositions of macro and micronutrients, there is a high risk of not meeting the set of restrictions in a given clinical scenario, i.e., attendance of the caloric, but not of the protein target.

**Objective:** the objective of this study is to identify under what conditions it is possible an industrialized formula to meet the clinical restrictions of calories, macro and micronutrients.

**Methods:** we deduced a mathematical relationship that must be met in order to satisfy such constraints. Using as variables: a) the necessary volume of an FI to meet the energy goal; b) the energy density of the FI; c) upper limit of calorie or nutrient; and d) the lower limit of calorie or nutrient.

**Results:** a first degree inequality was developed that if attended allows to discriminate if a prescribed volume  $v$  of an IF meets the set of restrictions placed by the prescriber, in order to previously select viable formulas among a portfolio. Clinical vignettes are presented.

**Conclusion:** the viability condition of an industrialized formula for the attendance of a system of constraints can be identified with the aid of a mathematical formula of the first-degree inequality type.

#### Keywords:

Linear model.  
Nutrition therapy.  
Formula.  
Macronutrient. Target.

#### Resumen

**Introducción:** la planificación de la terapia nutricional depende de las restricciones definidas por el prescriptor, de manera que los niveles de nutrientes y calorías se coloquen a intervalos apropiados. Como las fórmulas industrializadas (IF) tienen composiciones fijas tanto de macronutrientes como de micronutrientes, existe un alto riesgo de no cumplir con el conjunto de restricciones en un escenario clínico dado; es decir, la consecución del objetivo calórico, pero no del objetivo proteico.

**Objetivo:** el objetivo de este estudio es identificar bajo qué condiciones una fórmula industrializada puede cumplir con las restricciones clínicas de calorías, macronutrientes y micronutrientes.

**Métodos:** dedujimos una relación matemática que debe cumplirse para satisfacer tales restricciones. Usando como variables: a) el volumen necesario de un FI para alcanzar la meta de energía; b) la densidad de energía del FI; c) el límite superior de calorías o nutrientes; y d) el límite inferior de calorías o nutrientes.

**Resultados:** se desarrolló una desigualdad de primer grado que, si se atiende, permite discriminar si un volumen prescrito  $v$  de un IF cumple con el conjunto de restricciones impuestas por el prescriptor para seleccionar previamente fórmulas disponibles dentro de una cartera. Se presentan viñetas clínicas.

**Conclusión:** la condición de viabilidad de una fórmula industrializada para el cumplimiento de un sistema de restricciones puede identificarse con la ayuda de una fórmula matemática del tipo de desigualdad de primer grado.

#### Palabras clave:

Modelo lineal. Terapia nutricional. Fórmula. Macronutriente. Objetivo.

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*Clinical Relevancy Statement: The achievement of caloric, protein and micronutrient targets has been discussed in various publications. Industrialized formulas are default in provision of nutrition support for hospitalized patients, delivering a stable proportion of macro and micronutrients per volume unit. Goals are achieved by determination of a flow rate of industrialized formulas per unit of time. The flowrate necessary for attending the goals is found by trial and error until the constraints are met, or by the prescriber's choice to prioritize one constraint over others. Not infrequently, the final prescription delivers nutrients out of the desired limits.*

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**INTRODUCTION**

For nutrients to have beneficial effects on health, they must be offered in adequate doses, within maximum and minimum limits. The establishment of what is appropriate (maximum and minimum limits) for each patient is determined by the prescriber and constitutes a critical part of the decision-making process. In other words, the decision-making process consists in establishing maximum and minimum ranges not only for the calories but also for each of the macro and micronutrients. Societies of experts compile recommendations based on the best evidence, also expressing them through constraints, with upper and lower limit limits, for example caloric supply between 25 and 30 kcal.kg<sup>-1</sup>.d<sup>-1</sup> (1).

For patients in nutritional therapy industrialized formulas (IF) constitute the means to supply nutrients and to meet nutritional goals is necessarily related to a daily flow given by the volume infused per unit of time.

However, since calories, proteins or any other nutrients that may become clinically relevant are linked to this flow, there is a risk of not meeting the restrictions for a given clinical circumstance. An example is the difficulty of meeting current protein targets with the formulas available in the market, usually with less protein than necessary, thanks to the use of protein supplement (2), complementary modalities such as supplementary parenteral nutrition (3), or acceptance of a nutritional load above the desired level in order to allow the fulfillment of currently important restrictions.

The IF flow prescription is found by trial and error, erratically, until the constraints are met, or by the prescriber's choice to prioritize one constraint over others. Not infrequently, the final prescription delivers nutrients out of the desired limits.

In order to improve the efficiency of the IF selection process, it is convenient to have prior knowledge of its potential adequacy to the proposed system of restrictions for each patient.

The objective of this study is to show under what conditions it is possible an industrialized formula to meet the clinical restrictions of calories, macro and micronutrients. To do so, we deduce a mathematical relationship that must be met in order to satisfy such constraints.

**METHODS**

The energy prescriptions place the energy (or caloric) supply between two extremes:

$$e^{min} \leq \rho^e \cdot v_e \leq e^{max} \quad (I)$$

where

- v<sub>e</sub>*: volume required by energy ∈ IF
- ρ<sup>e</sup>*: energy density ∈ IF
- e<sup>max</sup>*: superior limit of energy
- e<sup>min</sup>*: inferior limit of energy

Rewriting equation I, we obtain the volume effect of the energy restriction:

$$\frac{e^{min}}{\rho^e} \leq v_e \leq \frac{e^{max}}{\rho^e} \quad (II)$$

Similarly, any and all nutrients will be placed between two extremes in the medical prescription:

$$n_j^{min} \leq \rho_j \cdot v_j \leq n_j^{max} \quad (III)$$

where:

- v<sub>j</sub>*: volume required by nutrient j ∈ IF
- ρ<sub>j</sub>*: density of nutrient j ∈ IF
- n<sub>j</sub><sup>max</sup>*: superior limit of nutrient j
- n<sub>j</sub><sup>min</sup>*: inferior limit of nutrient j

Rewriting equation III, we obtain the volume effect of the nutrient restriction:

$$\frac{n_j^{min}}{\rho_j} \leq v_j \leq \frac{n_j^{max}}{\rho_j} \quad (IV)$$

The volume administered to the patient, however, is not something hypothetical or a thing of imagination. There is, for example, no negative volume. Thus:

$$v_e \geq 0$$

$$v_j \geq 0$$

In the same way, it is a real and equal quantity for all constraints, be they nutrients or energy. Thus;

$$\frac{e^{min}}{\rho^e} \leq v \leq \frac{e^{max}}{\rho^e} \quad (V)$$

$$\frac{n_j^{min}}{\rho_j} \leq v_j \leq \frac{n_j^{max}}{\rho_j} \quad (VI)$$

To meet all minimum constraints, we have to choose a volume such that:

$$max \left\{ \frac{e^{min}}{\rho^e}, \frac{n_j^{min}}{\rho_j} \right\} \leq v \quad (VII)$$

To satisfy all the maximum constraints, we have to choose a volume such that:

$$v \leq min \left\{ \frac{e^{max}}{\rho^e}, \frac{n_j^{max}}{\rho_j} \right\} \quad (VIII)$$

Therefore, we have the following restriction:

$$max \left\{ \frac{e^{min}}{\rho^e}, \frac{n_j^{min}}{\rho_j} \right\} \leq v \leq min \left\{ \frac{e^{max}}{\rho^e}, \frac{n_j^{max}}{\rho_j} \right\} \quad (IX)$$

Since the chosen volume must be a positive real quantity, the condition of existence of a solution to a formula becomes:

$$max \left\{ \frac{e^{min}}{\rho^e}, \frac{n_j^{min}}{\rho_j} \right\} \leq min \left\{ \frac{e^{max}}{\rho^e}, \frac{n_j^{max}}{\rho_j} \right\} \quad (X)$$

Or stated literally: the condition for an industrialized formula to meet a constraint system is that the maximum volume between the minimum service volumes of each restriction is less than or equal to the minimum volume between maximum volumes to meet each restriction.

Let's exemplify in clinical vignettes.

### CLINICAL CASE 1

Let patient P with the following weights and goals to be met:

- weight = 70 kg
- caloric goal  $e = 25$  a  $30 \text{ kcal.kg}^{-1}.\text{d}^{-1}$
- protein goal  $p = 1.2$  a  $1.5 \text{ g ptn.kg}^{-1}.\text{d}^{-1}$

Let a proposed enteral formula to meet the goals described above containing

- caloric density  $\rho = 1500 \text{ kcal.l}^{-1}$
- protein density  $j = 60 \text{ g ptn.l}^{-1}$

The system of restrictions to be met by the formula will be composed of the following intervals:

- $25 \leq e \leq 30$
- $1.2 \leq p \leq 1.5$

Replacing in the equation X the terms, we have in the term of the left or "maximum volume" among minimal volumes:

$$\text{máx} \left\{ \frac{25 \times 70}{1500}, \frac{1.2 \times 70}{60} \right\}$$

$$\text{máx} \{1.17 \text{ l}; 1.4 \text{ l}\} = 1.4 \text{ liters of l}$$

Replacing in the equation X the terms, we have in the term of the right or "minimums" among maximal volumes:

$$\text{mín} \left\{ \frac{30 \times 70}{1500}, \frac{1.5 \times 70}{60} \right\}$$

$$\text{mín} \{1.4 \text{ l}; 1.75 \text{ l}\} = 1.4 \text{ l}$$

Since  $\text{Max} \{1.4\} \leq \text{Min} \{1.4\}$ , then we have that the formula meets the constraint system and can comply.

### CLINICAL CASE 2

Let patient P with the following weights and goals to be met:

- weight = 120 kg
- caloric goal = 12 to 14  $\text{kcal.kg}^{-1}.\text{d}^{-1}$
- protein goal  $p = 1.8$  to  $2.2 \text{ g ptn.kg}^{-1}.\text{d}^{-1}$

Let a proposed enteral formula to meet the goals described above containing

- caloric density  $\rho = 1280 \text{ kcal.l}^{-1}$
- protein density  $j = 75 \text{ g ptn.l}^{-1}$

The system of restrictions to be met by the formula will be composed of the following intervals:

- $12 \leq e \leq 14$
- $1.8 \leq p \leq 2.2$

Replacing in the equation X the terms, we have in the term of the left or "maximum volume" among minimal volumes:

$$\text{máx} \left\{ \frac{12 \times 120}{1280}, \frac{1.8 \times 120}{75} \right\}$$

$$\text{máx} \{1.73; 2.88\} = 2.88$$

Replacing in the equation X the terms, we have in the term of the right or "minimums" among maximal volumes

$$\text{mín} \left\{ \frac{14 \times 120}{1280}, \frac{2.2 \times 120}{75} \right\}$$

$$\text{mín} \{1.31; 3.52\} = 1.31$$

Since  $\{2.88\} \leq \text{Mín} \{1.31\}$  is a false statement, then we have that the formula does not meet the constraint system and cannot comply.

### CLINICAL CASE 3

Let patient P with the following weights and goals to be met:

- weight = 90 kg
- caloric goal  $e = 28$  to  $30 \text{ kcal.kg}^{-1}.\text{d}^{-1}$
- protein goal  $p = 0.8$  to  $1.2 \text{ g ptn.kg}^{-1}.\text{d}^{-1}$
- carbohydrate goal  $c = 100$  to  $150 \text{ g.d}^{-1}$  (new restriction added)

Let a proposed enteral formula to meet the goals described above containing

- caloric density  $\rho = 1000 \text{ kcal.l}^{-1}$
- protein density  $j = 40 \text{ g.l}^{-1}$
- carbohydrate density  $c = 81 \text{ g.l}^{-1}$

The system of restrictions to be met by the formula will be composed of the following intervals:

- $28 \leq e \leq 30$
- $0.8 \leq p \leq 1.2$
- $100 \leq c \leq 150$

Replacing in the equation X the terms, we have in the term of the left or "maximum volume" among minimal volumes:

$$\text{máx} \left\{ \frac{28 \times 90}{1000}, \frac{0.9 \times 90}{40}, \frac{100}{91} \right\}$$

$$\text{máx} \{2.52; 1.8; 1.23\} = 2.52$$

Replacing in the equation X the terms, we have in the term of the right or "minimals" among maximal volumes

$$\text{mín} \left\{ \frac{30 \times 90}{1000}, \frac{1.2 \times 90}{40}, \frac{150}{91} \right\}$$

$$\text{mín} \{2.70; 2.70; 1.85\} = 1.85$$

Since  $\text{Máx} \{2.52\} \leq \text{Mín} \{1.85\}$  is a false statement, then we have that the formula does not meet the constraint system and cannot comply.

## DISCUSSION

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In the present work we propose an equation to identify the conditions of existence so that a nutritional formula of defined composition meets the clinical restrictions established based on the medical judgment.

In an ideal theoretical model, where we have an ideal nutritional formula, all the proposed restrictions would be met and we would be facing the perfect nutrition. The perfect nutrition is not dependent on via, and encompasses the modalities of parenteral nutrition, oral nutritional therapy and even these strategies combined with each other, as well as use of supplements.

In real world, however, the solution applied by the prescriber is to simplify the number of restrictions considered, usually based only on protein and caloric needs, with the inclusion of new restrictions for other nutrients depending on the clinical conditions. This bedside solution is performed erratically, in which the prescriber can randomly select formulas that do not necessarily meet the constraints and pre-terminate the search by the most appropriate formula. In addition, this method is vulnerable to non-technical elements such as prescription, marketing and industry advertising habits or anchoring in the last prescription made. Furthermore, as stated by Hoffer, "enteral products that have replaced PN are designed for normal people and hence are protein-deficient for critically ill patients. The current situation requires the treating team to choose between 2 adverse consequences: severe protein deficiency during the first 7 to 10 days in the ICU, or toxic calorie overfeeding as the cost of providing a suitable amount of protein" (4).

The presented theorem that denominated "maximum of the *minimi* and minimum of the *maximi*" is a more assertive method, and allows to identify immediately among formulas of defined composition in a portfolio, that attend or not to the set of restrictions. The medical decision focuses only on the determination of the intervals, thus being robust against non-technical influences from marketing and propaganda.

The method can also be applied in the field of parenteral nutrition therapy and in a variety of scenarios whenever the clinical condition in the patient demands a change in the system of

restrictions, without restricting free choice of the prescriber in the determination of the restrictions.

An additional utility of the method is to allow that when finding the infeasibility of a formula it is possible to identify which of the restrictions hinders the viability of its use. In this sense, it may still be a useful method for the industry, when studying the ideal types of patients, for example the severe obese patient, to identify in each formula profile in which categories of restrictions there will be no viability.

In the examples studied, calories, proteins and carbohydrates were considered. The method may encompass the incorporation of other categories including micronutrients and fibers.

The theorem was developed assuming the total nutrient load per unit of time, for example, kcal per day. In mathematics, this mode of developing the calculation is based on integral method. However, the infusion of nutritional formulas occurs in the form of flow. Future research results should analyze the properties of the volume infused in a differential perspective and in this sense include other elements such as cost for example.

## CONCLUSION

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The viability condition of an industrialized formula for the attendance of a system of constraints can be identified with the aid of a mathematical formula of the first-degree inequality type.

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