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Trabajo Original

Otros

Combined intervention strategy for reversing iron-deficiency anaemia and deficiency in psychomotor development in chronic malnutrition

Estrategia de intervención combinada para revertir la anemia ferropénica y la deficiencia en el desarrollo psicomotor en la desnutrición crónica

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Abstract

Background: chronic iron-deficiency anaemia in children has a negative impact on neuronal and cognitive development. Despite current knowledge on this subject, in Bolivia iron intake along the psychomotor development stimulation as part of a comprehensive rehabilitation process for children with severe chronic malnutrition is not yet used.

Objective: to evaluate the effect of a neurorestorative diet, consisting of iron supplements and other micronutrients, along with psychomotor stimulation in preschool children with chronic malnutrition, iron-deficiency anaemia and severe psychomotor delay.

Patients and methods: twenty-four children between 1 and 56 months of age admitted to the integral nutritional recovery centre (INRC), Paediatric Hospital of Cochabamba, Bolivia were included. A strategy of intervention was applied consisting of nutritional replenishment through the administration of elaborated meals prepared from local foods with high heme and non-heme iron concentration, added with vegetables plus the administration of micronutrient´s supplementation and the psychomotor stimulation. Anthropometric indices, psychomotor and biochemical parameters were measured at four times points, during the hospitalisation period.

Results: at the beginning, the anthropometric and psychomotor parameters were decreased (between -2 and -3 z score and below 50 % respectively). Combined strategy intervention with iron and other micronutrients together photons produced significant changes between the evaluated time points, both in anthropometric and psychomotor parameters, although these changes were less than expected.

Conclusions: the combined strategy used in this study allowed recovery from the anaemia and minimal growth due to the low birth weight or chronic malnutrition. However, the intervention was insufficient to achieve a complete recovery.

Keywords:

Anaemia. Iron replacement. Psychomotor development.

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Resumen

Antecedentes: la anemia ferropénica crónica en niños tiene un gran impacto negativo en el desarrollo neuronal y cognitivo. A pesar del conocimiento actual sobre el tema, en Bolivia aún no se utiliza la ingesta de hierro más estimulación del desarrollo psicomotor como parte de un proceso de rehabilitación integral de niños con desnutrición crónica severa.

Objetivo: evaluar el efecto de una dieta neuro reparadora, consistente en suplementos de hierro y otros micronutrientes, junto con estimulación psicomotora en niños preescolares con desnutrición crónica, anemia por deficiencia de hierro y retraso psicomotor severo.

Pacientes y métodos: se incluyeron veinticuatro niños entre 1 y 56 meses de edad ingresados en el centro de recuperación nutricional integral (CRIN), Hospital Pediátrico de Cochabamba, Bolivia. Se aplicó una estrategia de intervención consistente en la reposición nutricional mediante la administración de comidas elaboradas a partir de alimentos locales con alta concentración de hierro hemo y no hemo, adicionados con vegetales más la administración de suplementación con micronutrientes y la estimulación psicomotora. Se midieron índices antropométricos, parámetros psicomotores y bioquímicos en cuatro momentos del tiempo de hospitalización.

Resultados: al principio, los parámetros antropométricos y psicomotores estaban disminuidos (entre -2 y-3 puntuación z; y menor a 50 % respectivamente). La estrategia combinada de intervención con hierro y otros micronutrientes junto con fotones produjo cambios significativos entre los momentos evaluados, tanto en los parámetros antropométricos como psicomotores, aunque estos cambios fueron menores a lo esperado.

Conclusiones: la estrategia combinada utilizada en este estudio permitió la recuperación de la anemia y un crecimiento mínimo debido al bajo peso al nacer o la desnutrición crónica. Sin embargo, la intervención fue insuficiente para lograr una recuperación completa.

Palabras clave:

Anemia. Reposición de hierro. Desarrollo psicomotor.

INTRODUCTION

Iron-deficiency anaemia affects nearly half of preschool children and one-third of pregnant women worldwide, included Bolivia (1,2). Anaemia in children has a great physiological repercussions due to the lack of tissue oxygenation and therefore decreased energy production, contributing to the delayed growth and interfering in the development of vital tissues, including the brain, with a negative impact on neuronal, psychomotor and cognitive development, as it causes alterations in neurotransmitters and dopamine receptors, engaging the affective responses, cognitive function, GABA-receptors, as well as, movement coordination and memory patterns (3-10).

Chronic malnutrition and anaemia are determined by dietary deficiency of micronutrients and proteins primarily, and are also conditioned by social, economic, cultural factors, and/or the presence of underlying conditions that affect the ability to ingest, digest and absorb nutrients (11,12).

The acquisition of neuromotor, cognitive and psychosocial abilities occur around the first 2 - 3 years of life, that requires the maturation of the central nervous system and a pleasant psychoaffective environment with active intervention of the parents (13). There are multiple causes for deficiency in psychomotor development; different authors indicate the biological factors such as prematurity, neonatal anoxia, hereditary genetic factors, prenatal infections, and also the socio-environmental factors as conditioning to this, such as parental illiteracy, unemployment, social and geographical difficulties for accessibility to the health system (14-16). Despite actual knowledge of the neuroplasticity in children during the first years of life, supervised iron intake combined with psychomotor development stimulation as part of a comprehensive rehabilitation process for children with severe chronic malnutrition has not yet been considered in Bolivia. The purpose of this study was to evaluate the effect of a neurorestorative diet, based on iron and micronutrients supplementation along with psychomotor stimulation in preschool children with low birth weight and/or chronic malnutrition, iron deficiency anaemia and severe psychomotor delay.

METHODOLOGY

STUDY DESIGN AND POPULATION

An exploratory, descriptive, longitudinal study was conducted. Twenty-four children male and female between 1 to 56 months of age, were included in the study. They were admitted into Integral Nutritional Recovery Centre (INRC) at Manuel Ascencio Villarroel Paediatric hospital in Cochabamba, Bolivia according to the following criteria.

INCLUSION CRITERIA

Diagnosis of low birth weight (lower than 2500 g) and severe chronic malnutrition, defined thus, according WHO standards (17) [-3 z score Height/Age (≤ 3 SD) and -2 z score Weight/Height: (≥ -2 SD)]; evidence of severe delay in psychomotor development (Denver test: less than 50 %); presence of iron-deficiency anaemia (haemoglobin concentration: < 11 mg/dL); and absence of severe infectious process or serious complication. Informed consent signed by parents and mandatory hospitalisation period into INRC for 8 weeks. It was decided 2 weeks period between admission and the starting the combined intervention strategy for rutinary procedure to evaluate and monitoring for possible infections that need to be controlled. The next three post-assessments were conducted every 2 weeks after the first assessment. The values obtained in the previous assessment were used as comparison pattern.

EXCLUSION CRITERIA

Presence of one or more of the following criteria: Acute infectious disease; severe acute malnutrition defined thus, according WHO standards, (17) (-3 z score Weight/Height and ≥ -2 z score Height/Age); Anaemia due to deficiency of vitamin B9 and B12 (MCV > 100 fL); hypothyroidism; parental rejection; Children over 5 years old; premature discharge.

ASSESSMENTS

Anthropometry

Included the measurement of anthropometric indices Weight/Height; Weight/Age; Height/Age; Arm circumference/Age; Cephalic perimeter/Age and Triceps skinfold thickness/Age using WHO standards (17), at four time points, starting from the second week of admission to the INRC (first time); and ending at medical discharge (fourth time), corresponding to the week eight of hospitalization. The evaluations during intervention period were every 2 weeks, and the comparison of subsequent evaluations was made with the values of the first evaluation and also between them.

Haematology and biochemistry

Haemoglobin concentration, haematocrit, mean corpuscular volume and the biochemical parameters (glucose, albumin, total proteins, ferritin) were measured at two time points: the first measurement taken in the second week of admission and the second at medical discharge. Plasma concentration of TSH measurement was only performed upon admission to the INRC.

Psychomotor development

It included the measurement of Personal social area, Language, Gross motor area and Coordination through the Denver test at four time points, every 2 weeks, starting from the second week after admission to the INRC and concluding at medical discharge.

INTERVENTION STRATEGY

Nutritional supplementation

It starting in the 2nd week and involved the administration of meals prepared with selected local foods with high concentrations of hem and no-hem iron, combined with fruit and vegetables rich in vitamins A and C in children older than 4 months. The children younger than 4 months received an oligomeric milk formula. Additional micronutrients were administered as supplements, at the following doses: Iron sulphate: 5 mg/kg/weight, omega-3: 0,7 or 1,4 mg/day (18), prebiotics: 1 x 10^8 CFU *(Lactobacillus rhamnosus; acidophilic lactobacilli; streptococcus thermophilus)* as commercial formula; zinc: 2 mg/kg/weight; selenium: 5 µg/kg/weight; Cooper: 20 µg/kg/weight; B12 vitamin 2.4 mg/day and folic acid: 200 μg/day. The nutritional supplementation is summarised in figure 1.

During the two first weeks after admission, the children received standardized stabilizing diets (liquid and soft), either for infants or preschoolers. The liquid diets were dairy formulas that vary for each patient, because they had specific intolerances, so anti-reflux and/or lactose-free dairy formulas were used.

Nutritional stabilization and supplementation were carried out individually according to the children's admission to the INRC.

Psychomotor stimulation

The psychomotor stimulation was carried out twice session per day, and included the application of mechanical procedures to stimulate sensory, motor and language reflexes. The procedure was organised in three phases: a) environmental phase, assisted with intentional, epigenetic stimulation (mother-child relationship), environmental improvement and use of sound waves; b) management of psychomotor development delay based on an algorithm that considered sensory, sensorimotor and formal logic stimulation; and c) photon stimulation for 20 minutes using a light-emitting diodes (LED) (19,20) with a 6 w/0.5 ampere of electrical power by twice per day during 6 weeks, progressively in the patients individually, in pairs and also in groups. There were used a single colour, two colours, three colours and a range of colours with a great proportion of red-light pulsations, while avoiding excessive blue light. The psychomotor development progress was measured with the Denver test.

DATA COLLECTION

The relevant clinical information was collected by the clinical records at admission in the INRC. The anthropometric data collected included the ratios Weight-for-Height; Height-for-Age; Arm circumference-for-Age; Cephalic perimeter-for-Age; Triceps skinfold thickness-for-Age and Body Mass Index using WHO nutritional assessment tables for children under 5 years old, 2007 version (17). The collected psychomotor development data included Personal social area, Language, Gross motor area and Coordination expressed as an average in percentage (Denver test).

DATA ANALYSIS

The anthropometric data were processed using Anthro-2010 software (https://whonutrition.shinyapps.io/anthro), and the overall analysis of all variables was performed using SPSS software version 25.

The Student's t-test was used to evaluate the same variables at four time points measured every 2 weeks, from admission to the INRC to medical discharge.

ETHICAL PERMISSION

The study has been approved by the ethics committee of the Faculty of Medicine, Universidad Mayor de San Simón, Bolivia, number: C-BE-39/19. The parents of the children admitted to the

INRC and selected for the study signed written consent indicating their voluntary participation and the right to withdraw their children from the study at any time.

RESULTS

The twenty-four children who underwent nutritional replenishment and psychomotor stimulation showed average weight (SD) at birth of 1.9 (0.2) and 2.7 (1.4) kg (female and male respectively) and an Apgar score of 5.82 (0.19) and 6.37 (0.37) (female and male respectively). The anthropometric index, psychomotor and biochemist parameters taken 2 weeks following the hospitalisation (first time point assessment), were below. Only glycemia and total protein were within the normal reference range [87.41 (18.85) mg/dL and 6.07 (0.68) g/dL respectively] (Table I).

The nutritional intervention through iron supplementation, iron-fortified diet along the addition of other micronutrients (third phase) during the stay in the INRC (Fig. 1) produced significant changes between the evaluated time points, in anthropometric indices (Table II) and psychomotor parameters assessed (Fig. 2).

Between the anthropometric parameters evaluated, the index: Height/Age; Weight/Age and Arm circumference/Age, showed significant statistical differences (Student's t-test, $p < 0.05$) between the assessment time points: first vs. fourth; first vs. second and third vs. fourth. The skinfold thickness/Age showed significant statistical differences within the assessment time points: first vs. fourth and second vs. third. On the other parameters, it showed significant changes on the comparison first vs. fourth assessment (Table II).

The biochemical parameters: total protein, albumin, ferritin, haemoglobin, haematocrit and mean corpuscular volume within first and fourth-time points assessment (Table II), showed significant statistical changes (Student's t-test, $p < 0.05$).

Regarding the psychomotor parameters, they also had significant changes (Student's t-test, $p < 0.05$) between the four assessment time points for: Coordination, Personal social area and Language. Besides, the indoor Gross motor area has shown significant changes on the second vs- third and first vs. fourth assessment time points (Fig. 2).

Table I. Characteristics of Children at the time of starting combined intervention strategy in INRC

Characteristics of children		Values	Reference ranges
Gender[a]	Female (%)	10 (42)	
	Male (%)	14 (58)	
Age[b] (months)		16.75 (1-56)	
Anthropometric indices (z score)			
Weight/Height		-2.43 (2.03)	
Weight/Age		-3.65 (2.04)	
Height/Age		-3.39 (1.92)	
Arm circumference/Age		-2.99 (1.95)	
Cephalic perimeter /Age		-1.76 (2.40)	
Triceps skinfold thickness/Age		-2.18 (1.19)	
BMI		-2.64 (3.16)	
Psychomotricity (%)			
Personal social area		33.78 (18.67)	90-95
Language		43.60 (23.09)	
Gross motor area		35.97 (25.14)	
Coordination		44.83 (18.76)	
Biochemical parameters			
Thyroid stimulating hormone (TSH) (µUI/mL)		0.42 (0.06)	0.8-6
Glycaemia (mg/dL)		87.41 (18.85)	70-140
Total protein (g/dL)		6.07 (0.68)	6-8,3
Albumin (mg/dL)		2.77 (0.34)	3.2-3.5
Ferritin (ng/mL)		11.25 (8.86)	15-150
Haemoglobin (mg/dL)		9.30 (1.14)	11.25-12.75
Haematocrit (%)		28.02 (4.83)	34.5-37.5
Mean corpuscular volume (MCV) (fL)		77.66 (2.07)	80-100

Data are presented as mean (SD); n *= 24. INRC: integral nutritional recovery centre; SD: standard deviation. [a]Frequency (%); [b]Mean (range in months).*

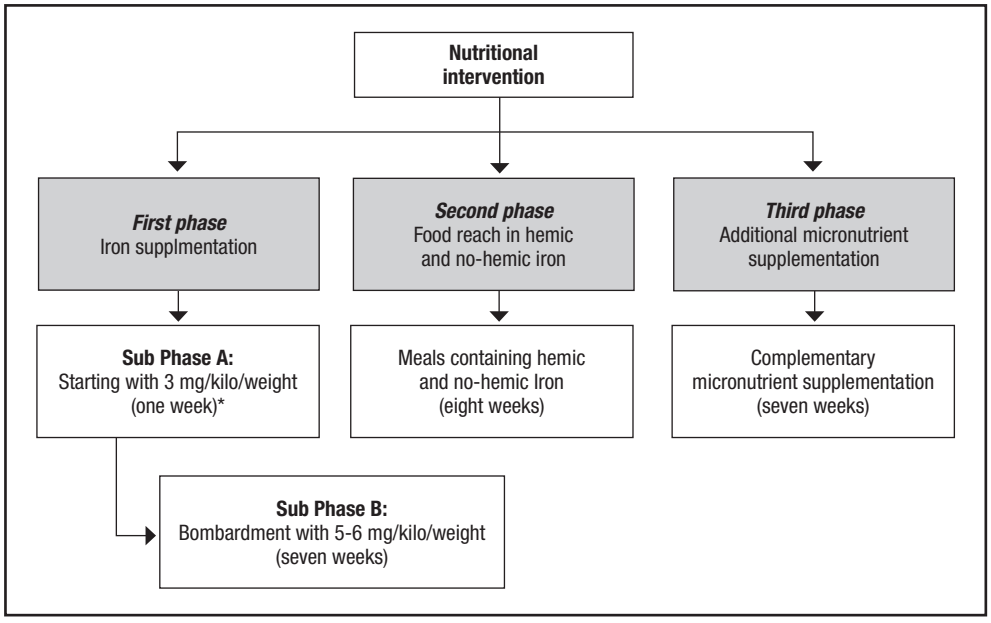

Figure 1.

Schematic representation of nutritional intervention performed in children admitted to INRC to revert the anaemia. The doses of Iron and other micronutrient supplementation are described in methodology. *Corresponds to the first week post admission.

Table II. Evolution of anthropometric and biochemical parameters during period of intervention (8 weeks), stating at second week of admission in INRC

Anthropometric indices (z score)	Evaluation times (n = 24)				
	First (2nd week)	Second (4th week)	Third (6th week)	Fourth (8th week)	*p* values
Height/Age	-3.39 (1.92)	-3.10 (1.89)	-2.88 (1.97)	-2.58 (1.92)	0.010 (1st/4th) 0.028 (1st/2nd) 0.010 (3rd/4th)
Weight/Height	-2.43 (2.03)	-1.69 (2.00)	-1.63 (2.17)	-1.58 (2.32)	0.066 (1st/4th)
Weight/Age	-3.65 (2.04)	-3.24 (1.99)	-2.99 (1.98)	-2.51 (1.85)	0.001 (1st/4th) 0.028 (1st/2nd) 0.010 (3rd/4th)
Cephalic perimeter/Age	-1.76 (2.40)	-1.75 (2.22)	-1.55 (2.22)	-1.36 (2.22)	0.197(1st/4th)
BMI	-2.64 (3.16)	-2.16 (2.13)	-1.94 (2.24)	-1.79 (1.71)	0.143 (1st/4th)
Arm circumference/Age	-2.99 (1.95)	-2.30 (1.77)	-1.95 (1.60)	-1.63 (1.62)	0.006 (1st/4th) 0.023(1st/2nd) 0.015 (3rd/4th)
Triceps skinfold thickness/Age	-2.18 (1.19)	-1.96 (0.98)	-1.68 (0.88)	-1.05 (2.39)	0.032 (1st/4th) 0.025 (2nd/3rd)
Biochemical parameters					
Glycaemia (mg/dL)	87.41 (18.85)			86.54(10.38)	0.083
Total protein (mg/dL)	6.07 (0.68)			7.99 (0.92)	0.001
Albumin (mg/dL)	2.77 (0.34)			3.96 (0.40)	0.001
Ferritin (µg/L)	11.25 (8.86)			20.05 (11.59)	0.002
Haemoglobin (g/dL)	9.30 (1.14)			12.28 (0.80)	0.001
Haematocrit (%)	28.02 (4.83)			37.10 (2.40)	0.001
Mean corpuscular volume (fL)	77.66 (2.07)			85.25 (1.56)	0.001

Data are presented as mean (SD); n = *24.*

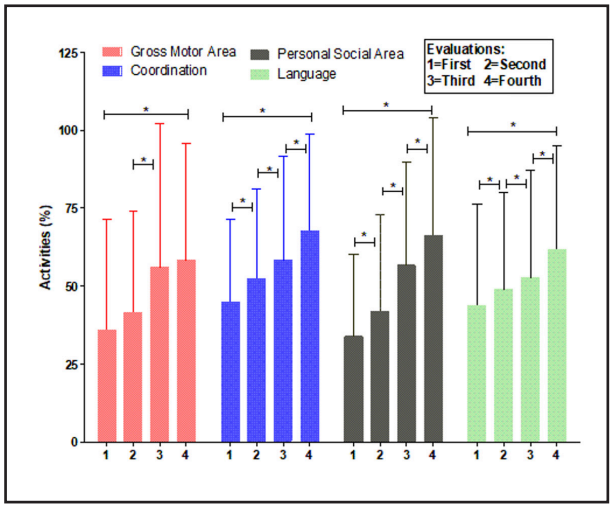

Figure 2.

Evaluation of four psychomotor parameters by Denver Test in four times. All parameters. Present differences statistically significant (Student's t-test). Gross motor area: first/fourth and second/third evaluation times, $p = 0.001$ and $p = 0.028$ respectively. Coordination, first/second, third/fourth and first/fourth evaluation times, $p = 0.001$ in all cases. Personal social area, first/second, and third/fourth evaluation times, $p = 0.001$ for both cases; second/third, and first/fourth evaluation times, $p = 0.002$ and $p = 0.029$ respectively. Language, first/second, $p = 0,044$; second/third, $p = 0,034$; third/fourth, $p = 0,002$ and first/fourth evaluation times, $p = 0.001$.

DISCUSSION

A suitable and stimulating environment, that includes conversation, full of images, light, music, interaction with toys, friendly treatment, as well as nutrition are important factors that take part in the growth and neural development stimulation of children (21,22). On this matter, the findings presented here have shown significant statistical changes on the anthropometric and psychomotor parameters measured between the fourth time points evaluated during application of combined intervention strategy. Nevertheless, the intervention, produced scant modifications on any of the measured parameters (anthropometric and psychomotor development), which reflects neuronal plasticity and its recovery capacity. This behaviour responds to the short intervention period (8 weeks) and it is expected that after hospital discharge the children will continue to recover growth until a measurable improvement is achieved. However, progressive changes are highlighted as result of the intervention with nutrient supplementation (minerals, vitamins and probiotics), not administering them as part of the therapy constitutes a risk factor because it makes possible the alteration of systemic metabolic homeostasis and the consequent cellular stress, including neuronal cells (23,24). Particularly, iron administration is essential for reversing anaemia and guaranteeing neuronal functioning (25), which enables development of neural, cognitive and psychosocial capabilities (6,25,26) achieved about the age of 2 to 3 in the suitable psychoaffective environment (13,26).

The brain becomes iron deficient before the onset of anaemia due to the prioritisation of iron available to red blood cells (RBCs) over other organs (27). Such deficiency will then lead to alterations in neurotransmitters and dopamine receptors that compromise affective responses, cognitive functioning and GABA receptors in children, before anaemia itself manifests (6,27). Even so, the use of photons through light of different colours of low intensity had a positive impact on the different areas of the child's psychomotor development due to its improvement on cognition and social and interpersonal skills, because it stimulates the brain tissue oxygenation, as previously was reported by others (20,28,29).

The increase in the values of different parameters evaluated, between different time points, with more evident differences between the first and the last points, reflect the positive effect of the combined intervention strategy applied to stop the deleterious effect of nutritional iron and other micronutrients deficiencies on neurodevelopment and its biological and social consequences (4,8,30).

The iron deficiency anaemia must be assessed within the concept of supply and demand, in which the demands are created by erythropoiesis, tissue oxygenation, erythrocyte turnover, and erythrocyte loss from haemorrhage and erythrocyte half-life from anaemia are decreased (31). Small-for-gestational-age (SGA) new-borns have low iron stores, which increases the risk of anaemia in the offspring, and its support the findings of this research, and also developmental delay (32), as was found here, characterised by a history of low birth weight and low APGAR score, which indicates the probability of "some problems during birth" that reduced oxygen in the blood (32).

Additionally, as previously reported by others, chronic malnutrition and anaemia have as a determining factor the dietary deficiency of basic nutrients, in addition to being conditioned by social, economic and cultural factors and/or by the presence of base pathologies that determine the ability to ingest, digest food or absorb nutrients (11,12).

The limited progress in the nutritional recovery and psychomotor improvement, probably respond to the confluence of factors such as the low birth weight (Table I) and the unstimulating household environments, low purchasing power of the families, low level of parental education (33,34) and in the present study as additional characteristic the rurality of the families (35).

The children discharged post-intervention were followed for a year in the outpatient clinic to promote recovery of growth and information, education and communication sessions with their parents.

In conclusion, the first years of life are the ones with the biggest neuronal maturation, where the first neural connections are established and the nervous tissue network becomes more complex. The possibility of recovery in these first years will have a great impact on an appropriate intervention. Unfortunately, chronic malnutrition in such people were so severe that the combined strategies used in this study, despite the progress in the recovery (reversion of anaemia and improvement of psychomotor parameters), was not enough to achieve complete recovery.

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