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Effect of an additive treatment based on micronutrient on the health and deductive and inductive functions of children in the High North of Morocco (Chefchaoune Region)

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Abstract: *Micronutrient deficiencies are recognized as a major public health problem, affecting more than 2 billion people worldwide. (1) The magnitude is much larger in low- and middle-income countries. (2) The objective of our study is to study the impact of a nutritional supplement on the nutritional and neurocognitive health status of anemic children. Our study population is made up of 49 students diagnosed with anemia in Chefchaouen province. The school children were 8 to 14 years old, including 14 girls and 35 boys with an average weight of 37.63 kg ± 7.76 and an average height of 145.96 cm ± 9.53. Each student was clinically examined by the team doctor for signs suggestive of anemia, and received a multi-micronutrient daily for one month. A battery of measurements and tests was performed at the beginning and at the end of the treatment. According to the results of the study a statistically significant difference between hemoglobin of the first measurement 11.4 [10.2; 11.65] and that of the second measurement 12 [10.90; 12.75] g / dl was found with p <0.001. There is also a statistically significant difference between the Raven of the first measurement 17,24 ± 5,774 and that of the second measurement 25,22 ± 11,37. (P<0.001). Most of our results support our hypothesis and confirms the data of the literature in a field little studied in Morocco. Our study focused on the positive effect of nutritional supplementation evoking an increase with highly significant values, hemoglobin improved between the two phases of the pre- and post-treatment study and the test score of deductive and inductive functions. of the progressive matrix of Raven. These results are encouraging and suggest that larger trials should be carried out over a longer period of intervention with more sophisticated means.*
Keywords: *multi-micronutrient, hemoglobin, deductive, inductive, neurocognitive*

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I. Introduction

Micronutrient deficiencies are recognized as a major public health problem, affecting more than 2 billion people worldwide. (1) The magnitude is much larger in low- and middle-income countries. (2)They can be caused by a series of common factors, in part related to poverty and adverse health environments, such as under-nutrition, dietary habits and practices, and infections. In addition, periods of rapid growth are particularly vulnerable because nutritional needs are high. (3)Among micronutrient deficiencies, iron deficiency is by far the most common]. . At an advanced stage, the depletion of iron results in a decrease of the hemoglobin itself responsible for anemia. An estimated 600 million preschool and schoolchildren worldwide have anemia, and at least half of these cases are thought to be caused by iron deficiency. (4) (5)In addition, iron deficiency anemia is associated with an increase in infant morbidity, the growth dynamics in these children would be slowed down and their height decreased (6) (7). Iron deficiency even in the absence of anemia, can lead to cognitive and behavioral development disorders as well as a drop in school performance. (8)Epidemiological and experimental data indicate that such disorders that occur at an early age are sometimes irreversible, even after recovery of iron stores. This highlights the importance of preventing iron deficiency anemia (8) (9) (10). Indeed, the magnitude of the consequences of iron deficiency and anemia on health, justifies the implementation of interventions. Our exploratory and interventional study aims to study the impact of a dietary supplement on the nutritional and neurocognitive health status of anemic children in the Chefchaouen region. In addition, the treatment of these deficiencies and deficits of the associated neurocognitive functions requires nutritional education programs and cognitive remediation. The hypothesis postulates that micronutrient nutritional supplementation will improve the neurocognitive performance and health status of this population.

II. Methodology

2.1 Subjects and methods

This is an interventional study. The target population is students from 3 public institutions; two schools and a college, located in the rural district of Kaa Asras, in the province of Chefchaouen in the far north of Morocco. It was carried out during the period from January 2016 to April 2016. In this study, 49 children enrolled at the basic level, were recruited by the medical team, their age varies between 8 and 14 years. Sociodemographic information, anthropometric and biological measurements were collected at the health center. The study was approved by the Ministry of Health after approval of the ethics committee.

2.2 Inclusion criteria

To be included in the study, children should be aged between 8 and 14, have a height for age or weight for age less than 2 Z score, hemoglobin less than 11.5 g / dl for older children less than 11 years and less than 12 g / dl for children over 12-14 years of age (11), and not showing any intolerance or allergy to the components of the nutritional solution proposed in the study.

2.3 Criteria of non inclusion

Children with a hemoglobin greater than 11.5 g / dl in children younger than 11 years and greater than 12g / dl in children over 12 are excluded from the study, and are excluded from the study if any child has received a martial treatment or a vitamin B12 or folate supplementation, or having benefited from a recent blood transfusion, or having an underlying disease during the recruitment, The non signature of the consent is also a criterion of exclusion.

2.4 Clinical examination and general questionnaire

The participants were clinically examined for suggestive signs (fever, asthenia, vertigo, difficulty concentrating, cutaneo-mucous paleness, jaundice, hepatosplenomegaly ...) and anthropometric measurements, based on the standardized method of WHO and United Nations Children's Fund. (12), (13), (14). Size for age and BMI for age, were estimated by Z-scores and calculated with the anthro-plus software (15). Stunting and wasting are defined by the WHO for Z-scores less than -2 (16). Each participant responded to a general questionnaire including socioeconomic data and medical history.

2.5 Hematological measurements

2.5.1 Blood sample

Blood samples were taken on an empty stomach, by venous blood collection in tubes containing anticoagulant EDTA (ethylene diamine tetraacetic acid) and were analyzed on site by a haematological analyzer type MINDRAY BC 2800). at our disposal by the delegation of health of the province of Chefchaouen.

2.5.2 Measuring hemoglobin

It was performed using a HemoCue® device (HemoCue 201, Angelholm, Sweden). After carefully disinfecting the end of the finger chosen for puncture, a drop of capillary blood is obtained by stinging with a sterile lancet. This drop of blood is collected in a microcuvette, then the whole is introduced into the HemoCue for reading. This method is recommended by WHO (WHO, 2001) because of its simplicity, reliability, accuracy and reproducibility in the field confirmed in various publications (11). Children are considered anemic if they have hemoglobin levels <11.5 g / dl (7-11 years) or <12 g / dl (12-14 years) (WHO, 2001 and 2008). (11, 17)

2.5.3 Product used

This is a powder to mix with water to make a chocolate flavor drink tested and accepted in children of the same age. Each nutritional preparation is low in sodium and salt, and is a source of fiber and rich in protein and micronutrients.

Each dietary preparation of 64 g brings on average

- **Energy value: 253 Kcal**
- **Protein: 15.6 g (25% of total energy)**
- **Fat: 5.5 g (20% of total energy)**
- **Carbohydrates: 31.4 g (50% of total energy)**
- **Fiber: 6.3 g (5% of total energy)**
- **Calcium 174 mg (22% of DC : daily contribution)**
- **Phosphorus 97.4 mg (14% DC)**
- **Zinc 2.6 mg (26% of DC)**
- **Magnesium 8 mg (2% of DC)**
- **Vitamins 30% DC**
- **Potassium 23.3 (1% of DC)**
- **Sodium 369 mg**
- **Iron: 5.3 mg (38% of DC)**

The contributions provided by this supplement are sufficient to correct the deficiencies of macronutrients (proteins, carbohydrates and lipids) and micronutrients (especially iron) reported in this population of children according to FAO recommendations. The drink was prepared daily, for each child individually, by mixing a sachet of powdered product with mineral water.

Children were encouraged to consume their usual diet during the intervention period. Parents were advised not to give their children fortified products or dietary supplements during the study period. In order to study the impact of this dietetic preparation on the different statuses of these children, a battery of measurements and tests were carried out at the beginning of the supplementation and a month later.

2.6 Neurocognitive test

Raven Progressive Matrix Test

This test was designed to assess nonverbal intelligence, intellectual ability and general mental skill through the comparison of forms and reasoning by analogy. It includes 60 problems distributed in five series (A, B, C, D and E), each composed of 12 problems, of an order of increasing complexity, being realized in two phases; the first phase comprising the series A, B and C (in 30 minutes) and the second phase comprising the series D and E (in 20 minutes). The test was individually administered, the scores were established according to a percentile scale based on age (18), (19).

2.7 Statistical analysis

All statistical analyzes were performed using the statistical software for the social sciences (SPSS, version 20.0). . Anthropometric indicators were calculated from the Anthroplus software using the WHO / NCHS 2007 reference (20). The normality of the distribution of the variables was tested by the Kolmogorov-Smirnov test. Values of $p < 0.05$ are considered significant. The mean values of the various parameters sought in children were compared using the non-parametric Mann-Whitney test. The de2 test was used to test the independence between qualitative variables. The Spearman correlation test was used, p values less than 0.05 were considered statistically significant.

Table 1	
Characteristics of students at the beginning of the study N = 49	
Age	12.65 ± 2.03 *
Boys	35 (71.4) *
girls	24 (28.6) *
Weight	37.63 ± 7.76 *
Size	145.96 ± 9.53 *
Z-score T / Age	-1 [-2; 0.115] **
stunting	21 (42.9)
Normal size	28 (57,1)
Z-score BMI / Age	-0.45 ±, 843 *
Hemoglobin 1 (before intervention)	11.40 [10.20; 11.65] **
Hemoglobin 2 (after surgery)	12 [10.90; 12.75] **
Breakfast	
Yes	25 (51) *
No	24 (49) *

* mean ± standard deviation or% depending on the type of variable

** median [quartiles]

III. Results

The average age of participants was 12.65 ± 2.02 with extremes between 8.5 and 14; they are predominantly male with 71% (35) boys and 28.6% (14) girls, the sex ratio is 2.5: the characteristics of the population are shown in Table 1. The average weight of the population was 37.6 ± 7.76kg and the average height was 145.96 ± 9.53cm. The median hemoglobin before the intervention was 11.4 [10.2-11.65] and the median after intervention was 12 [10.90; 12.75] g / dl.

Based on the results of our study, there is a statistically significant difference between hemoglobin at the first measurement and that of the second measurement. ($P < 0.001$)

The clinical signs characterizing the anemic syndrome were present in the students participating in our study to different degrees. Thus, 72% of them had cutaneo-mucous pallor, 67.3% had dyspnea of effort, 65.3% suffered from asthenia, while 58.7% were in difficulty to make an effort intellectual. Vertigo and visual disturbances were present in 58.3% and 40% of students, respectively.

Nutritional indices of height for age and BMI for age were -1 [-2; -0.115] and 1.16 ± 0.84. A total of 42.9% (n = 21) had a size insufficiency (z-score height / age ≤-2) and 4% (n = 2) had a leanness (z-score BMI / age ≤-2). We also note that nearly half of the participants do not eat breakfast.

Table II

Neurocognitif test (Raven PM 38) n=34		
	Before intervention	After intervention
PM 38 de Raven	17,24±5,77*	24,97±11,25*

* Mean ± SD

According to the results mentioned in Table 2, there is a statistically significant difference between the MPR score of the first measurement 17,24 ± 5,77 and that of the second measurement 24,97 ± 11,25. (P <0.001)

IV. Discussion

4.1 Hemoglobin

In light of the results, we noted a statistically significant difference between the first measurement of hemoglobin (11.40 [10.20; 11.65]) and the second measurement (12 [10.90; 12.75]) with p <0.001, indicating a good response to treatment. Our results are similar to those of studies using multimicronutrients (MMNs) for the treatment of anemia (21, 22); they showed that MMNs caused a further increase in mean hemoglobin compared with treatment. iron-based (23), and improved the iron status. The prevalence of anemia and iron deficiency has been reduced and their prevention has been improved (21, 24, 25, 26).

4.2 Growth retardation

The association between anemia and stunting is evident, and evidence suggests that anemia can lead to stunting (28). In a study conducted in Morocco in 2004, 65% of anemic school-age children were stunted (29). This study is delayed by 46% of participants. Treatment with MMN can have a beneficial effect on the growth of children, as the results of studies established in this direction are quite encouraging (22, 27); MMN would be more effective at improving child growth compared to placebo or a single nutrient (30) (31). The 4-week period was short enough to judge the effect of supplementation on the growth of our participants.

4.3 Anemia, cognitive function

The relationship / association between cognitive function and iron / anemia status has been widely demonstrated. Indeed, many cross-sectional studies have reported significant associations between hemoglobin concentrations and measures of cognitive function and academic achievement in school-aged children. (32, 33, 34). Iron anemia can impede psychomotor and cognitive development, lowering the IQ by nine points. (37) In general, all areas of cognitive functioning are affected by micronutrient deficiencies (36, 37, 38), but are sensitive to changes in micronutrient status in school-aged children. (38, 39, 40). In the same sense a iron supplementation alone or in combination with folic acid may improve cognitive function in children with iron deficiency anemia (39, 41, 42, 43), but this improvement has been better observed with the use of multi-micronutrients. (44) In our study we evaluated cognitive function in our patients using the Raven Progressive Matrix Test, which studies the nonverbal intelligence of subjects, and obtained an average score of 17.24 ± 5.77. This score is close to that of a study conducted by our laboratory of anemic children of the same age in the province of Kenitra in northwestern Morocco which was 21.01 ± 11.3. These rather mediocre scores placed them in very low percentiles of French calibration. However, this result can not be explained by the mere existence of anemia, but other factors may be involved. (45). With supplementation received by the participants, there was an improvement in RPM test score of 7.73 points, reflecting the beneficial effect of supplementation on the non-verbal intelligence and fluid intelligence (thinking skills).

This effect has been described in several studies postulating that performance in nonverbal tests would result in part from basic biological functions and may be influenced by diet. (44, 46) This result was promising as this supplement was able to improve IQ during a short treatment period.

Recalling that several mechanisms have been described to explain how micronutrients can influence cognition. Interactions between macronutrients and micronutrients may influence the optimization of cognitive development in children after infancy. Macronutrients are used as a source of energy while micronutrients play a vital role for the whole body (47) iron is required for myelination and neurotransmission (48), neurotransmission processes are altered in case of anemia iron deficiency probably caused by a reduction in the availability of oxygen (49). Zinc is a necessary coenzyme for neurogenesis, neuronal migration, and synaptogenesis (50); B vitamins are necessary for neurotransmitter synthesis, function (51, 52), energy metabolism of the brain (53), and myelination of the spinal cord and brain (52, 54).

These for this reason that the probable contribution of this dietary supplement seems promising especially as the result of the results of the study being analyzed including those relating to the analysis of digital traces in these children, especially that this diagnostic technique is already validated by the neuroscience unit (Ahami and collaborator).

V. Conclusion

This work has focused on the positive effect of nutritional supplementation evoking an increase with highly significant values of hemoglobin that improved between the two phases of the pre- and post-treatment study. Neurocognitive performance has also been improved; Raven's IQ improved by 7.73 points between the two periods. These results are encouraging and suggest that larger trials should be carried out over a longer period of intervention with more elaborate means..

Acknowledgements & Conflicts Of Interest

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