The Internet Journal of Tropical Medicine
Volume 3 Number 1

Effects Of Vitamin A And Iron Supplementation On The Treatment Of Malaria In Cameroonian Preschool Children

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Citation

C Teugwa Mofor, D Zofou, P Amvam Zollo. *Effects Of Vitamin A And Iron Supplementation On The Treatment Of Malaria In Cameroonian Preschool Children*. The Internet Journal of Tropical Medicine. 2005 Volume 3 Number 1.

Abstract

This study investigated the effect of vitamin A and iron on the treatment of malaria, when they are given as supplements to infected preschool children. In a placebo-controlled supplementation trial, 132 children aged between 6 and 60 months were recruited and divided into 4 groups: the first group received 68mg (6-30 months) or 102mg (30-60 months) iron daily and the second, 30mg (6-12 months) or 60mg (12-60 months) of vitamin A in single dose at the beginning of the treatment. The third group received both vitamin A and iron while the placebo received no supplement. Completed data was obtained on parasitaemia, clinical (weight, vitality) and haematological parameters (red blood cells, white blood cells and haemoglobin) using WHO (1982) methods, and micronutrients status (serum vitamin A and iron) respectively by spectrofluorimetry and atomic absorption spectrophotometry.

From this study, it was observed that about 40.15% of the children suffering of malaria were anaemic (haemoglobin level from 9.02 ± 1.60 to 10.72 ± 1.21 g/dl and red blood cells level less than 3500000/ mm3 among 40.15% of infants recruited). They also had moderate to severe vitamin A deficiency (serum vitamin A between 0.53 ± 0.14 and 0.66 ± 0.24µmol/l). Compared with placebo group, infants receiving supplements improved considerably, for clinical and sub clinical parameters (weight gain from 0.49 ± 1.48 to 0.64 ± 1.97Kg, as against – 0.76 ± 2.17Kg in placebo group), iron status (haemoglobin level varied from 0.63 ± 1.33 to 0.94 ± 1.2.10 g/dl as against – 0.68 ± 0.98 g/l). A significant improvement of vitamin A status was observed within groups receiving vitamin A supplementation (serum level 0.08 ± 0.20 to 0.11 ± 0.17µmol/l), while there was a notable decrease in the non supplemented group (– 0.04 ± 0.05µmol/l within the group that received iron, and – 0.07 ± 0.13µmol/l in the placebo group). The improvement was most important in the group receiving either vitamin A or iron supplements than those who received iron or vitamin A alone.

This study showed that vitamin A and iron could remarkably improve the treatment of malaria when they are given as supplements to infected children.

BACKGROUND

The malaria infection during the young age is a major public health problem occurring in all tropical and sub-tropical area. In sub-Saharan Africa, 75% of infantile deaths are caused by malaria and children have as from 1.6 to 5.4 infections annually (WHO, 2004). The main reasons of this disaster include the increasingly frequent resistances to anti-malarial drugs aggravated by poverty, the insufficiency of sanitary infrastructure and the very widespread civil instabilities in these regions (Snow, 1999). Facing the wild progress of this illness, researches have increased and followed in various axes as Pharmacology, Haematology, Immunology and Entomology. However, in spite of enormous efforts, it always remains difficult to master the curse. Since some decades, a particular attention is granted to the importance of nutrition in the development of malaria. Malaria causes anaemia, as well as the decrease of the blood level in antioxidants including vitamin A. The investigations of Shankar and collaborators in 1999 revealed a considerable reduction in the frequency of falciparum malaria episodes in children under a vitamin A suplementation. Otherwise, thanks to the works done in vitro, it is established today that the retinol molecule can also act directly by inhibiting the development of Plasmodium (Hamzah et al, 2004). Although several authors worked on the impact of the vitamin A and iron deficiency on malaria as well as the use of the supplementation as means of prevention of malaria, very little have been done on the persons already infected by Plasmodium. Our study aims to evaluate the potential of vitamin A and iron supplementation on the treatment of malaria in Cameroonian preschool children.

MATERIAL AND METHODS

TYPE OF THE SURVEY

The present work is based on clinical and para-clinical data of children received for consultation in two health centers of the Mbouda town (West - Cameroon) from September to December 2004: The Mbouda District Hospital and the Health Center of Lepi.

CHILDREN ENROLLED

The target population was constituted of the children of 6 - 60 months old filling each of the following criteria :

- Having a positive result to malaria diagnosis (thick Drop showing the presence of the Plasmodium in the blood stream),
- Not requiring a blood transfusion during the treatment,
- Not suffering simultaneously from typhoid fever nor chronic illness,
- Voluntarily acceptance to participate for the survey.

CLINICAL SURVEY

Patient with a positive malaria test was submitted to other biomedical tests : blood counting (White blood cells, red blood cells, haemoglobin). In the same way, the serum was prepared for the ulterior assessment of the serum parameters (vitamin A and iron). Following this was the follow up of the treatment, according to the experimental group to with the patient was affected. We used Quinine as anti-malarial drug.

In this way, 132 children were recruited and randomly distributed into four groups: The Group 1 received iron as supplement, the group 2 vitamin A; Children of the third group received both vitamin and iron while the last one (Group 4 was treated without any supplementation. Parameters analysed during this survey include: weight, parasitaemia, blood counting (haemoglobin, red blood cells and white blood cells), serum vitamin A and serum iron.

THE SUPPLEMENTS

We used the Vitamin A provided by the Canadian Fund for International Development. The vitamin as retinyl-palmitate was given at beginning of the treatment: 30mg for children below 12 months; 60mg for those of at least 12 months old.

Iron was of Sodium Feredetate (FERROSTRANE) syrup form. It was given as followed: 68 mg per day for the children of less than 30 months and 102 mg for those aged of 30 months at least.

METHOD OF DIAGNOSIS

For the malaria diagnosis, following the clinical observations, we used the Thick drop method with Giemsa as stain (WHO, 1982).

METHODS OF DOSAGE

The children were weighed at the beginning and the end of the survey and the weight variation evaluated. The clinical status, haematological characteristics (haemoglobin, red blood cells and white blood cells) was evaluated by the WHO (1982) methods. The serum vitamin A and serum iron was determined respectively by spectrofluorimetry and Atomic Absorption spectrophotometry.

STATISTICAL ANALYSES

The data (different parameter averages) were analysed by parametric ANOVA test, followed by the Student–Newman–Keuls and Duncan tests. These tests were carried out using the software SPSS in its 12.0 version, and the different figures were done with EXCEL 2003.

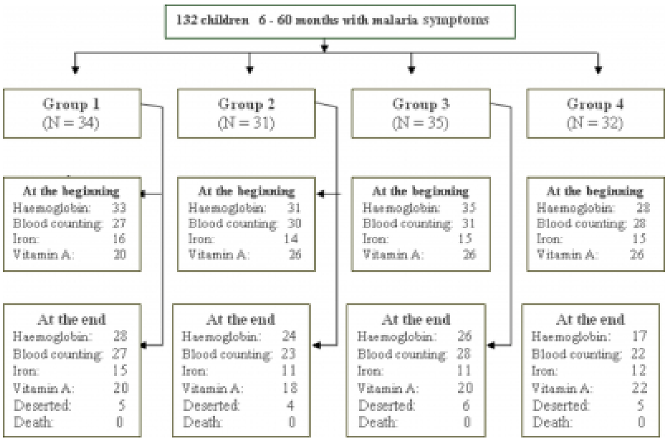
RESULTS

GENERAL PROCEDURE

Figure 1 summarizes the involvement of the patients at the different stages of the survey. Among the recruited children, 84.84% regularly followed the survey. 17 children, that is 13.07%, deserted and 3 children (2.30%) were excluded because they required blood transfusion during treatment.

Figure 1

Figure1: Enrolment of children at different stages of the survey



CLINICAL AND SUB - CLINICAL PARAMETERS

There was not a significant difference between the four experimental groups, for some parameters like age and the sex (p = 0.21; ANOVA). The parasitaemia level was less in patients of the Group 4 compared with the other groups (p = 0.04). The bodily temperature varied 38 to 40°C with an average of 38.96 °C.

Considering the declarations of parents during the consultation, more than the half of children presented a lack of appetite and fever at their arrival for consultation.

VARIATION OF DIFFERENT PARAMETERS DURING THE SURVEY

CLINICAL AND SUB CLINICAL STATUS

Figure 2 presents the weight averages in the different groups, at the beginning and the end of the survey. In the each of the three test groups, we observed a weight increase. Children receiving supplements presented an increase of 0.49 to 0.64Kg, while the unsupplemented patients presented rather a meaningful weight loss. The weight gain was more important in the group having receiving vitamin A combined with iron. But this difference between the supplemented groups was not significant (p = 0.06). Nevertheless, the difference between each of the test groups and placebo was highly significant (p = 0.016).

Ten children, 5.30% (of which 7 from Placebo group and 3 receiving iron as supplement) remained positive to malaria test at the end of the experiment.

WHITE BLOOD CELLS

The average values of white blood cells in the different groups is summarized in Figure 3. In general, we observed a significant decrease of the white blood cells level in the Group 3, receiving both vitamin A and iron (-5657.08 ±76993.17 µmol/l). In the other groups, variations were not significant.

ANAEMIA STATUS

The Figures 4, 5 and 6, present respectively, haemoglobin, red blood cells and serum iron averages, summarizing the anaemia status in the different experimental groups during. In the supplemented groups, we recorded a significant increase of the haemoglobin level, while the Group 4 was constant. The increase was more considerable in Group 3 that received both vitamin A and iron compared with any of groups receiving only one supplement. We didn't observe any significant variation in red blood cells level during the experimentation in all the groups.

Variations in serum iron in the different experimental groups are presented in Figure 6. There was a significant increase of the serum iron level in groups receiving this micronutrient as supplement, unlike Placebo group.

VITAMIN A STATUS

Figure 7 presents the average of serum vitamin A level in the different groups. This result shows a significant decrease in groups that were not supplemented in this micronutrient (Group 1 and Group 4) and a very significant increase in the vitamin A supplemented groups.

Figure 2

Figure 2: Weight averages according to supplements

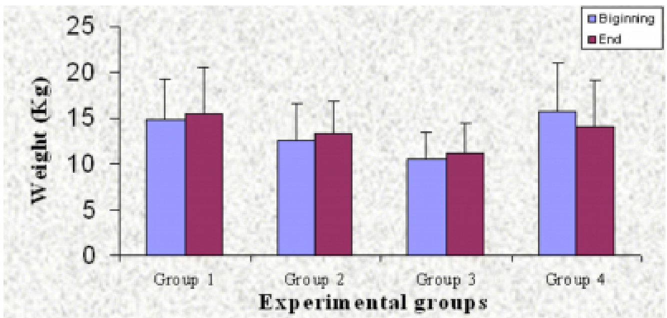


Figure 3

Figure 3: White blood cells averages according to supplements

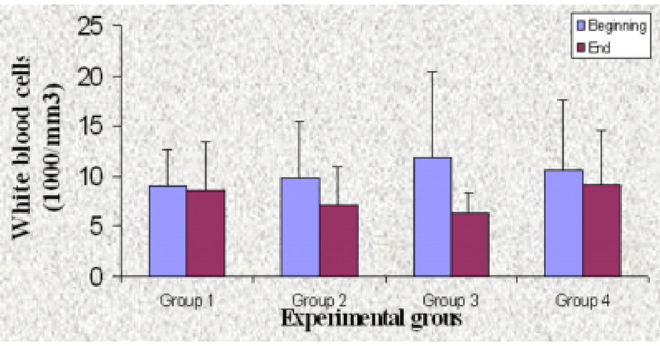


Figure 4

Figure 4: Red blood cells averages according to supplements

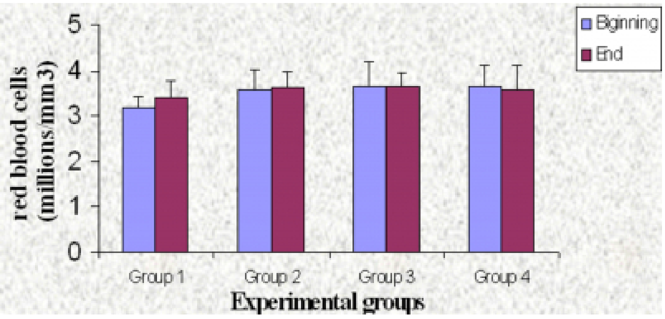


Figure 5

Figure 5: Haemoglobin averages according to supplements

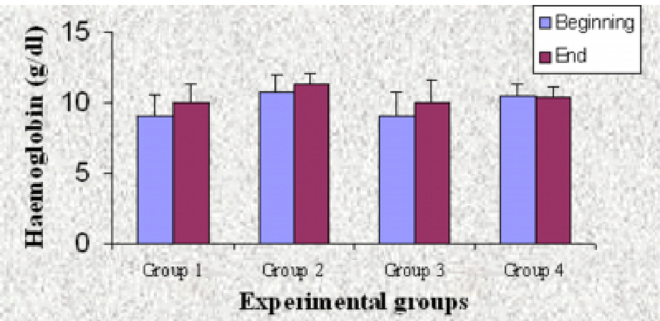


Figure 6

Figure 6: Serum iron averages according to supplements

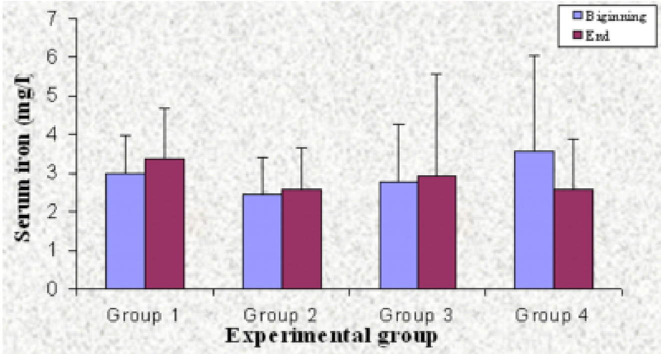
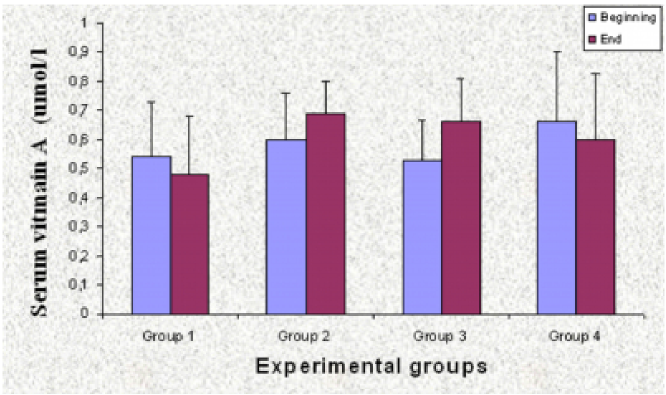


Figure 7

Figure 7: Serum vitamin A averages according to supplements



DISCUSSION

At the beginning of the survey, 28 children (21.21%) had white blood cells level over than the normal values included between 6000 and 10000/mm3 according to Aubert and Guittard in 1990. Indeed, when the organism is infected, the parasite secretes hemozoin that, when in contact with lymphocytes, induces a massive production of antibodies; this toxin also stimulates the white blood cells production (Gentilini, 1993).

About 40% of children were anaemic, with haemoglobin level less than 11g/dl. This was associated with a low red blood cells level (less than 3500000 / mm^3 for 40.15% of children). In presence of the parasite, the macrophages react by generating the active oxygen that attack infected erythrocytes as well as uninfected cells, causing haemolysis and other disorders (Clyde et al, 1975; Bernard et al, 1990; Kulkarni et al, 2003).

We couldn't note any clinical sign of vitamin A deficiency during this study. However, the serum level in general was lower than 0.70µmol/l that is the minimum value according to WHO for vitamin A deficiency in human (Kempe et al, 1978; Mc Laren and Frigg, 2002). Approximatively all of the children participating to this survey presented as from moderate (serum vitamin A of 0.56 to 0.63µmol/l; 34.09% for) to severe vitamin A deficiency (serum vitamin A level less than 0.56µmol/l for 62.12% of total cases).

Along the experiment, we noted a progressive restoration of the health status in all groups, but at different rates: 5.30% of recruited children remained infected at the end of the study. However, considering the different clinical and par-clinical parameters, we noted a net improvement in the groups receiving the supplements, compared with placebo group. The supplements would have a positive impact on the treatment of malaria. Vitamin A could act by improving the absorption of iron in the digestive tract (Garcia – Casal and Larisse, 1998). Otherwise, it is knowm that retinol inhibits the in vitro growth and the development of Plasmodium (Hamzah et al, 2004). The present survey done in vivo, confirms this previous findings therefore. Considering its antioxydant properties, vitamin A could also act by eliminating the free radicals produced due to Plasmodium and interfere with the pathological activity as well as the parasite's growth and development. This hypothesis is especially plausible, since Plasmodium uses essentially haemoglobin as source of amino acids and energy (Kulkarni et al, 2003). However, the mechanism of such an inhibition of Plasmodium development by the retinol molecule remains unclarified.

MICRONUTRIENTS STATUS

Vitamin A and iron supplements would have contributed to reduce the deficiency caused by Plasmodium. This facilitates the restoration of the haemoglobin level as well as the red blood cells synthesis, resulting in the improvement noted in children receiving iron supplementation (Kulkarni et al, 2003).

The association of iron and vitamin A permits to have values distinctly higher than those of each of the supplements taken individually. Beneficial interactions exist therefore between iron and the A. Vitamin A improves the mobilization of iron, driving to an increase in the intestinal absorption of iron and its utilization by the organism (Sommer and West, 1996). This is why vitamin A deficiency also constitutes a major handicap in the fight against anaemia in infants as well as in pregnant women (Stuijvenberg et al, 2003; Tanumhardjo, 2002).

We observed an important decrease of the serum vitamin A level in the groups not receiving supplements in this micronutrient (Groups 1 and 4) and a relative increase in the supplemented groups. Thus the supplementation would have contributed to fill the deficit created by the infection, raising the level serum retinol (Muslimatum et al, 2001, Flora et al, 2003). Otherwise, during the treatment, the losses due to the different physiological and metabolic disruptions are reduced progressively, increasing the food intake, as well as the metabolic use of food vitamin A. The association of these two factors would to the improvement vitamin A status as observed in this survey.

CONCLUSION

The vitamin A and iron suplements considerably improved the treatment of the malaria in the children of 6 to 60 months. The association of vitamin A and iron had an impact distinctly higher than the one of each supplement considered separately.

We recommend to everyone living in malaria endemic region a usual consumption of food sources of these micronutrients as papaya, yellow potato, carrots, yolk and liver, considering the virtues of vitamin A and iron in the malaria prevention and treatment. Further researches are need to optimise the use of vitamin A and other micronutrients in the treatment of malaria, as wall as to determine their mechanism of action.

ACKNOWLEDGEMENTS

We thank all the children and parents for their participation to this survey. We also thank Dr KAMGA Abel Christian and Mrs TENGOU Veronique of the Mbouda District Hospital, Dr. YOTA Daniel of the NDOP District hospital because they highly contributed to the achievement of this work.

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