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Intravenous vitamin b – complex and ferrous dextrane in malaria induced anemia: a single center prospective study

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Abstract

Background: In sub - Saharan Africa countries Plasmodium falciparum malaria is the most important parasitic disease. Accordingly, malaria induced anemia is one of the main public health burden. Treatment for anemia depends on severity and cause. In severe cases a blood transfusion may be necessary. Blood supplies in Africa are not able to meet the demand and this often leads to high maternal and child mortality rates in the continent. Also, it has been estimated that 5 – 10% of HIV transmission in Africa is brought by contaminated blood transfusions. **Aim of the Study:** Was to explore the hemoglobin increase, clinical benefits and safety of intravenous administration of vitamin B – complex and ferrous dextrane combination in patients with acute moderate to severe malaria induced anemia in rural African setting. **Methods:** With the hypothesis of obtaining a hemoglobin increase of ≥ 1g/dl in at least 50% of patients, 89 patients were included in the study after diagnosis of malaria and moderate to severe anemia (Hb: 6 – 10 g/dl) was confirmed. Patients were treated twice daily for three consecutive days. **Statistics:** Analysis were undertaken on per-protocol basis. Wilcoxon rank test was used to compare the average hemoglobin value at baseline and end of treatment course. Correlation between patients' age and average hemoglobin increase was assessed by Spearman's rank correlation test. All tests were two-tailed and significance was reported at the 5% level. **Results:** 49 patients (55%) showed a treatment response, 21 (23,6%) improved clinically and 19 (21,3%) failed to respond to the treatment. The difference was found statistically significant. Average hemoglobin concentration at the end of treatment was found higher than baseline and the difference was considered statistically very significant (9 g/dl vs. 8 g/dl; $p < 0,0001$). **Conclusion:** The results of the present study show that this treatment should be considered a useful first line intervention in healthcare settings, especially in rural sub Saharan Africa where blood transfusion is a hardly available option.

Keywords: Intravenous vitamin B - complex, Intravenous iron therapy, Iron deficiency anemia, Malaria induced anemia, Blood transfusion in sub Saharan Africa, Hemoglobin increase.

INTRODUCTION

Malaria

Malaria is an infectious disease caused by protozoan organisms of the genus Plasmodium (falciparum, ovale, vivax, malariae). It is characterized by high fever and erythrocitic infection resulting in malaria induced anemia (MIA). In pregnant women it causes a placental infection that impacts the fetus development [1]. It is the world's most important parasitic infection, ranking among the major health and developmental challenges for the poor countries of the world [2]. More than a third of the world's population (about 2 billion people) live in malaria-endemic areas. In Africa alone there are an estimated 200 - 450 million cases each year [3]. In sub - Saharan Africa countries, where stable transmission is common, Plasmodium falciparum malaria is the most important parasitic disease. Accordingly, in these parts of the world MIA accounts to be one of the major public health burden [4]. Current WHO recommended treatments range from oral artemisinin combination therapy (ACTs) up to intravenous quinine in severe cases [5].

Anemia

Anemia is a decrease in number of red blood cells (RBCs) or less than the normal quantity of hemoglobin in the blood. However, it can include decreased oxygen-binding ability of each hemoglobin molecule due to deformity or lack in numerical development as in some other types of hemoglobin deficiencies [6 - 8]. Anemia is the most common disorder of the blood. The three main classes of anemia include excessive blood loss (acutely such as a hemorrhage or chronically through low-volume loss), excessive blood cell destruction (hemolysis) or deficient red blood cell production (ineffective hematopoiesis) [9].

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Mild to moderate anemiapresents with non-specific symptoms such as: asthenia, fatigue, general malaise and sometimes poor concentration. In severe anemia, the body may compensate the lack of oxygen - carrying capability of the blood by increasing cardiac output giving rise to symptoms such as dyspnea and tachypnea [10]. Treatment for anemia depend on severity and cause. It includes oral and intravenous iron therapy, vitamins (vitamin B - complex, folic acid, vitamin C), recombinant erythropoietin, and in severe cases, or with ongoing blood loss, a blood transfusion may be necessary [11 - 13].

Blood transfusion in sub - Saharan Africa

In industrialized "high income" countries current guidelines put between 6 and 10 g/dL of hemoglobin concentration the accepted triggers for transfusion. In Africa accepted indications for blood transfusion are an Hb level ≤ 5 - 6 g/dL (or PCV - packed cells volume less than 15-18%) and the presence of signs of respiratory distress, profound prostration and / or altered consciousness. Blood supplies in Africa have never been able to meet the demand; this is reflected in the high maternal and child mortality rates in the continent [14, 15]. Transfusion practices in most African countries are hospital based (decentralized) and rely on donors recruited from family members. Sometimes the provision of a replacement unit is either a condition of having the patient transfused or provides a significant financial discount of the costs incurred in receiving blood. As is often the case when family members are unwilling to donate, commercial (paid) donors are contracted and these constitute a particularly high risk group for transmission of diseases [16, 17]. It has been estimated that 5 – 10% of HIV transmission in Africa is by contaminated blood transfusions [18]. While transfusion - transmissible diseases continue to attract considerable attention from transfusion medicine professionals (blood group incompatibility, HIV, hepatitis B, hepatitis C, Cytomegalovirus) no significant advances have been made to minimize preventable transfusion errors in developing countries. Transfusion errors always remain underreported owing to a lack of awareness about transfusion-related adverse events among the hospital staff and an inadequate feedback system in most of the transfusion centers [19, 20].

Vitamin B - Complex

B vitamins are a group of water – soluble molecules that play important roles in cell metabolism. Their deficiencies give rise to neurological, endocrine and cardiovascular symptoms. Research showed that they are a group of eight chemically distinct vitamins that often coexist in the same foods, Table 1. In general, oral supplements containing all eight are referred to as vitamin B complex. They must be replenished regularly, since any excess is excreted in the urine. B vitamins are found in whole unprocessed foods. Vitamin B - complex may also be delivered by injection to reverse deficiencies [21]. They are particularly concentrated in meat such as turkey and tuna, in liver and red meat products. Good sources for B vitamins include, whole grains, potatoes, bananas, lentils, chili peppers, beans, nutritional yeast, brewer's yeast, and molasses [22]. Although the yeast used to make beer results in being a source of B vitamins, their bioavailability ranges from poor to none as drinking ethanol inhibits absorption of thiamine. In addition, studies further emphasize that elevated consumption of beer and other ethanol-based drinks result in a net deficit of B vitamins and the health risks associated with their deficiencies [23 – 25].

Table 1:vitamin B group and related deficiencies*

Vitamin	Name	Deficiency effects
Vitamin B1	thiamine	Deficiency causes beriberi. Symptoms of this disease of the nervous system include weight loss, emotional disturbances, Wernicke's encephalopathy, weakness and pain in the limbs, periods of irregular heartbeat, and edema. Heart failure and death may occur in advanced cases. Chronic thiamine deficiency can also cause Korsakoff's syndrome, an irreversible psychosis characterized by amnesia and confabulation.
Vitamin B2	riboflavin	Deficiency causes ariboflavinosis. Symptoms may include cheilosis, high sensitivity to sunlight, angular cheilitis, glossitis, seborrheic dermatitis or pseudo-syphilis, pharyngitis, hyperemia, and edema of the pharyngeal and oral mucosa.
Vitamin B3	niacin	Deficiency, along with a deficiency of tryptophan causes pellagra. Symptoms include aggression, dermatitis, insomnia, weakness, mental confusion, and diarrhea. In advanced cases, pellagra may lead to dementia and death the 3 Ds: dermatitis, diarrhea, dementia, and death.
Vitamin B5	pantothenic acid	Deficiency can result in acne and paresthesia, although it is uncommon.
Vitamin B6	pyridoxine	Deficiency may lead to microcytic anemia, depression, dermatitis, hypertension, water retention, and elevated levels of homocysteine.
Vitamin B7	biotin	Deficiency does not typically cause symptoms in adults but may lead to impaired growth and neurological disorders in infants. Multiple carboxylase deficiency, an inborn error of metabolism, can lead to biotin deficiency even when dietary biotin intake is normal.
Vitamin B9	folic acid	Deficiency results in a macrocytic anemia, and elevated levels of homocysteine. Deficiency in pregnant women can lead to birth defects. Supplementation is often recommended during pregnancy.
Vitamin B12	cobalamin	Deficiency results in macrocytic anemia, elevated homocysteine, peripheral neuropathy, memory loss and other cognitive deficits. It is most likely to occur among elderly people, as absorption through the gut declines with age; the autoimmune disease pernicious anemia is another common cause. It can also cause symptoms of mania and psychosis. In rare extreme cases, paralysis can result.

*Adapted from B vitamins. Wikipedia, the free encyclopedia. http://en.wikipedia.org/wiki/B_vitamins

Aim of the study

In consideration of the confirmed shortages in blood transfusion supply in most sub Saharan Africa countries, the health risks associated to the practice itself and last but not least the infrastructural and socio - economic hurdles met by patients in reaching referral centers from rural settings, we decided to investigate in a single center prospective case study, the benefits associated to a cost-effective and readily available emergency therapy such as the intravenous administration of vitamin B – complex in association to ferrous dextrane in patients presenting with acute moderate to severe malaria induced anemia.

The primary outcome measure of this study was to assess the hemoglobin increase induced by the intravenous administration of vitamin B – complex and ferrous dextrane combination.

The secondary outcome measure was to evaluate patients' clinical response and tolerability to the treatment.

PATIENTS AND METHODS

Patients

Between January and November 2014, 100 patients of both sexes presenting to the Emergency Unit of the Life for Africa Clinic (Kiyonza village, southwest of Uganda) met the inclusion criteria and were enrolled consecutively in the present study after providing written informed consent.

Inclusion criteria were: diagnosis of malaria confirmed by either thick smear microscopy or histidine rich protein - 2 test (HRP – 2), diagnosis of moderate to severe anemia (Hb: 6 – 10 g/dl), HIV negative status, at least 18 months of age.

Exclusion criteria were: diagnosis of malaria excluded by both methods and /or; Hb ≤ 5 g/dl, signs of respiratory distress (in infants: respiratory rate ≥ 40 b / min; in adults: respiratory rate ≥ 25 b / min), signs of cerebral malaria (coma, diplopia, stiff neck, treatment resistant convulsive state or intractable cry in infants), HIV positive status, age < 18 months, recent history of blood transfusion (≤ 12 weeks), current oral multivitamin supplementation including vitamin B – complex and ferrous products (< 4 weeks) for any reason, medical record of a chronic disease or any severe organ disease such as heart, liver or renal failure at the time of assessment.

The Local Ethics Committee approval was provided by the District Health Authority in Rakai, and study was conducted according to the principles of Good Clinical Practice (GDP).

Assessment

As patients presented to the Emergency Unit, they underwent routine critical care such as vital parameters measurement (blood pressure, respiratory rate, heart rate, clinical signs of anemia), parenteral antipyretics, intravenous fluids and a panel of laboratory tests including: thick smear microscopy for malaria parasites, those negative were confirmed with the HRP- 2 strip test, Widal test (antigens 0 and H), Brucella antigen test (abortus and melitensis), hemoglobin estimation by the Sahli's Hemometer optical method, blood grouping reagent (ABO + Rh) and HIV rapid test. A detailed medical history was obtained from the parents or attendants in case of children (< 18yrs) or adults, respectively. Patients found with a Hb estimation of 5 g/dl or below, signs of respiratory distress and/or cerebral malaria were referred to the nearest hospital for whole blood transfusion and oxygen therapy (Rakai Hospital). Where the patient met the inclusion criteria, oral and written explanation was provided to patient's attendants regarding theaim of the study and written informed consent obtained.

Treatments

All patients underwent intravenous volume repletion with either 5% dextrose, Ringer lactate or 0,9% normal saline at a thirty minutes infusion rate, this was followed by intravenous quinine treatment adjusted by age and weight at a four hourly infusion rate. After this, blood samples were withdrawn to repeat a thick smear microscopy, HRP – 2 strip test, and hemoglobin estimation. Those found free of malaria parasites, were then selected to enter the study treatment. It consisted of adding a vial (2 ml) of vitamin B – complex and a vial of ferrous dextrane (100 mcg) in an infusion bottle (either 5% dextrose or 0,9% normal saline) of 250 ml (for children under 5 years and/or weighing less than 20 kgs) or 500 ml (for children weighing more than 20 kgs and adults) twice daily at an infusion rate of two hours, for three consecutive days. Patients who showed laboratory (Hb estimation increase of at least 1g/dl) and clinical signs of improvement (walking, eating, drinking, urinating, defecating and playing in case of children) were then switched to oral multivitamin supplementation (vitamin B – complex, vitamin C, ferrous sulphate) along with their oral antimalarial treatment. Patients who did not show signs of laboratory and clinical response were then referred to the district hospital for further management. The study was kindly funded by the Italian humanitarian Fundraising Organization *"Youandmetogether".*

Tolerability and Follow – up

Patients were monitored throughout the infusion treatment by means of regular blood pressure, heart rate and respiratory rate measurement and general clinical assessment for signs of toxicity or intolerance to the treatment regimen. Toxicity was considered as: bradycardia or tachycardia (decrease or increase of more than 20 b/min), tachypnea (increase of more than 15 b/min), anaphylactic reactions, infusion site infection, idiopathic hyperpyrexia, facial and body edema, oliguria and body rashes. Intolerance was considered as: vomiting, diarrhea, anorexia, hemicranias, restlessness, etc. After discharge, patients were followed up for three consecutive months in order to assess their hematological and clinical status.

Results analysis

Treatment response was defined as: hemoglobin increase of at least 1 g/dl associated to clinical signs of improvement; clinical response was defined as: unchanged or increase of hemoglobin less than 1 g/dl associated to clinical signs of improvement; failure was defined as: a decrease of hemoglobin of at least 1 g/dl associated to clinical conditions of worsening and/or signs of systemic toxicity; drop – out was defined as: patient discharged before repeating Hb estimation and/or before completing seven days of admission.

Statistical analysis

A Medline search on the placebo response in clinical trials, revealed an average 25% treatment response [26, 27]. On the other side, average treatment response to blood transfusion in malaria induced anemia, which is considered a gold standard, proved an 85% treatment response [28 - 30]. With the hypothesis of obtaining a treatment response inferior to the gold standard but superior to placebo, at least a 50% response was expected. Based on this assumptions, 100 patients were required to detect this difference at a 5% level of significance with 95% power. Sample size calculations were made using Graph Pad Stat Mate software V2.0.

Chi square test was employed to compare the trend of treatment response in children, women and men. Fisher's exact test was employed to compare treatment response in different groups of patients: children vs. women; children under 5yrs vs. over 5yrs; pregnant women vs. non pregnant. Wilcoxon signed rank test was used to compare the average hemoglobin value at baseline and end of treatment course. Correlation between patients' age and average hemoglobin increase was assessed by Spearman's rank correlation test.

Analysis were undertaken on per-protocol basis. Statistical calculations were made using Graph Pad In Stat software V3.0. Numerical results are expressed as the median and inter quartile range. All tests were two-tailed and significance was reported at the 5% level.

Only patients who met the inclusion criteria, underwent Hb estimation before and after treatment and were admitted for at least seven days, were included in the final analysis.

RESULTS

Of the 100 patients assessed and entered into the trial, 11 were considered drop – outs and excluded from the final analysis. Of these, 3 did not repeat hemoglobin estimation whereas 8 requested discharge before completing seven days of admission. The study flow is presented on Figure 1.

In total, 89 patients were included in the analysis. Patients' baseline characteristics in relation to sex, age, weight and blood group are presented on Table 2. In total, 49 patients (55%) showed a treatment response, 21 patients (23,6%) showed a clinical response and 19 (21,3%) failed to respond to the treatment. According to the preliminary assumptions these data were considered statistically significant ($p < 0,05$), Table 3.

When stratifying the different groups of patients (children, women and men) in terms of treatment response, the trend was found statistically significant, Table 4. The different treatment response found in children compared to women (37 vs. 11; $p < 0,05$) was considered statistically significant. Comparing treatment response obtained in children under to over 5 years the difference was not statistically significant (28 vs. 9; p = ns). Pregnant women compared to the unpregnant showed a higher treatment response, this difference was found statistically significant (17 vs. 2; $p < 0,05$). Average hemoglobin concentration at the end of treatment was found higher than baseline and the difference was considered statistically very significant (9 g/dl vs. 8 g/dl; $p < 0,0001$).

An inverse correlation was found between the patient age and average hemoglobin increase from baseline, Figure 2.

Three patients complained mild symptoms such as gastritis, diarrhea and excessive sweating. Patients were managed symptomatically and did not require treatment discontinuation.

Table 2: Patients' characteristics

Sex (M / F)	37 / 52
Age (years) (median, range)	8 (1,5 - 45)
Weight (kg) (median, range)	23 (8 - 73)
Blood group (ABO, Rh*) (number of patients)	A+ (50); A- (12); B+ (4); AB+ (2); AB- (1); O+ (14); O- (6)
Children (total) (≤ 5yrs / > 5 yrs)	54 (36 / 18)
Women (total) (pregnant / non)	29 (21 / 8)

*Rh: Rhesius

Table 3: Treatment results by group of patients

Pts (%)	Treatment response	Clinical response	Failure	P
General	49 (55 %)	21 (23,6 %)	19 (21,3 %)	0,0001
Children (≤ 5yrs)	28 (77,7 %)	5 (13,9 %)	3 (8,3 %)	0,0001
Children (> 5yrs)	9 (50 %)	7 (38,9 %)	2 (11,1 %)	ns
Pregnant women	9 (42,9 %)	9 (42,9 %)	4 (14,2 %)	ns
Unpregnant women	2 (25 %)	0	6 (75 %)	ns
Men	1 (16,6 %)	1 (16,6 %)	4 (66,6 %)	ns

Table 4: Number of patients in each group after stratifying for treatment response

Group	Treatment response	P
Children	37 (61,8 %)	
Women	11 (30,9 %)	0,0001*
Men	1 (7,3 %)	

* P value is given by the Chi square test for Trend
Chi squared value = 16,12 with 1 degree of freedom

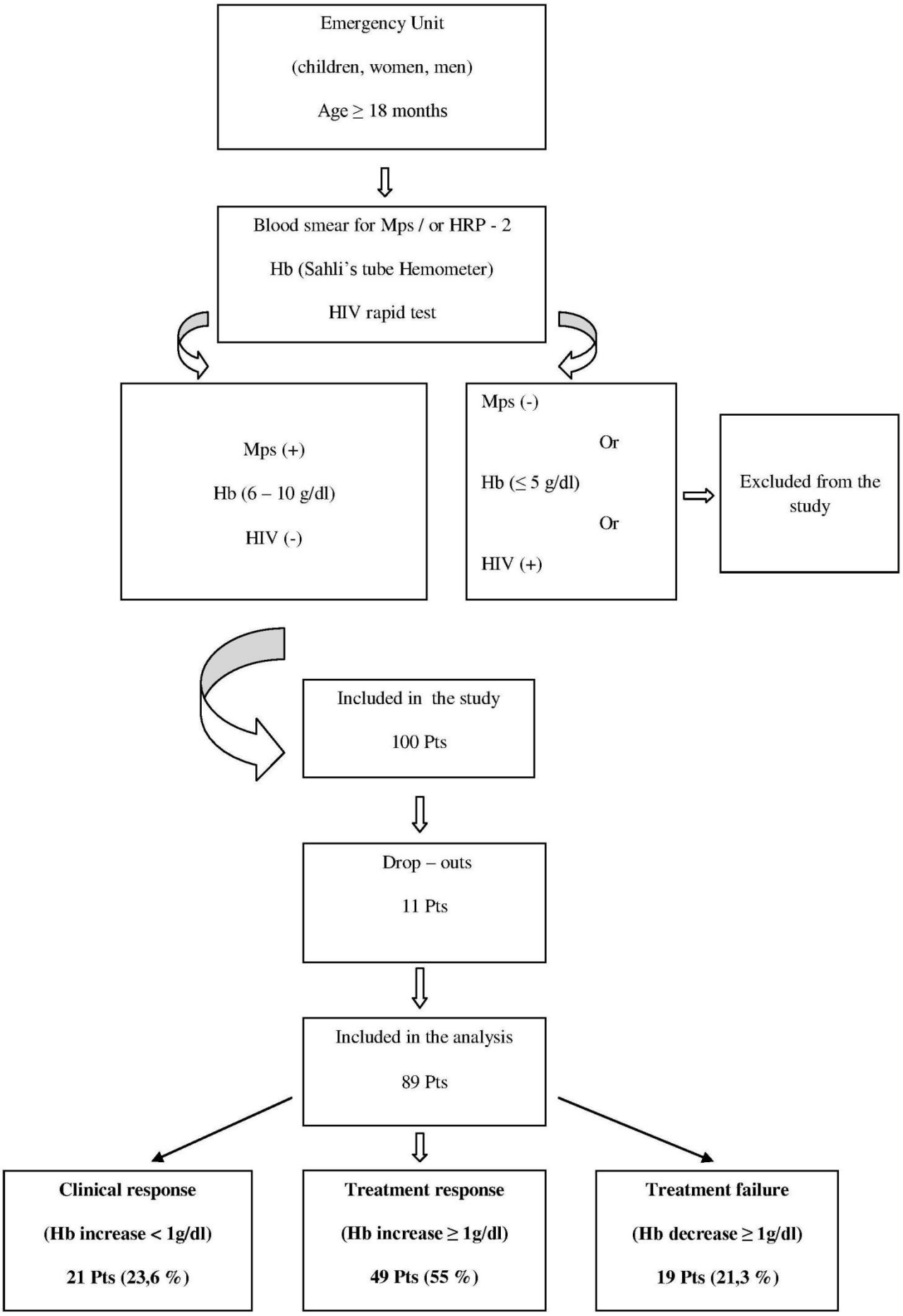

Figure 1: Study flow diagram

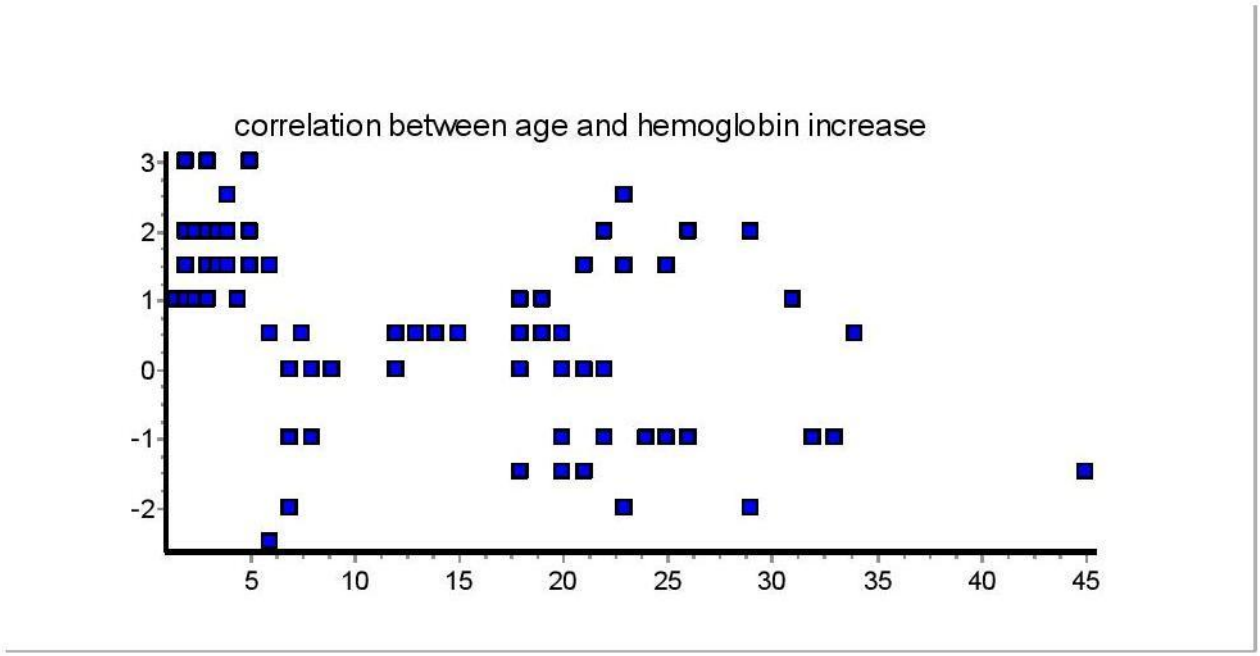

Figure 2: Spearman's rank correlation test (age vs. hemoglobin increase)

DISCUSSION

In this single center, prospective case study, the intravenous administration of vitamin B – complex in combination with ferrous dextrane showed relevant clinical benefits in most of the patients treated. In fact, the proportion of patients showing a hemoglobin increase of 1 g/dl or more, was even higher than the expected ratio hypothesized during study design. Moreover, when we combine data of patients treated to those who improved clinically though without relevant laboratory changes, the cumulative effect (78,6 %) becomes more interesting by embracing almost 8 out of 10 patients included in the study. This findings give rise to other interesting observations. For example, we found a significantly higher proportion of children treated compared to adult women. This can be interpreted as a greater hematopoietic response of growing organisms, however is to be noted that children represented the majority of patients. Two other findings act as a confirmation of this hypothesis: when we further stratified the children population into under 5 vs. over 5, again we found a greater effect among the youngest, though this difference was not considered statistically significant, the limited sample size must have underestimated this difference; in second place, an inverse relationship between age and hemoglobin increase response was found [Figure 2]. Another important finding was the higher treatment response obtained in the pregnant women compared to the unpregnant. Several studies have demonstrated in pregnant women high vitamins, minerals and iron demand triggered by the increased metabolic activity of the expectant mother [31 - 33]. Of note is the poor representation of adult male population in our study, this confirms other studies that have shown the reduced hospitalization rate of the adult male population for malaria in sub Saharan Africa [34 - 36]. This is easily explained by the semi-immune state of the adult population to malaria parasites, though women are hampered by the frequent malnourished state to which they are exposed by pregnancies and breastfeeding. Also, treatment response among the male population was very low, possibly exposing an underlying chronic anemia due to endemic alcohol abuse among the adult male population in rural sub Saharan Africa, a known cause for reduced absorption of hematopoietic vitamins and minerals [24, 25].

As transfusion services in Africa continue to be a hospital initiative and rely more on paid than voluntary donors, the provision of blood supply still remain scarce and disorganized, nonetheless highly risky in terms of transmission of diseases [16, 17]. That notwithstanding, transfusion errors are still by large underreported as a result of health staff poor knowledge and inadequate policy guidelines around the matter [18, 19].

A recent study by Bhandal *et al.*[37], compared in a randomized controlled trial oral versus intravenous iron therapy in preventing postpartum iron deficiency anemia (IDA). The oral ferrous sulphate was given for six weeks, opposed to intravenous ferrous sucrose two doses daily for four days. The main outcome measures were serum hemoglobin and iron levels. After a week, the results showed that intravenous iron administration rose hemoglobin and iron levels more rapidly, though at six weeks no significant difference was found among the two groups. The authors conclude that intravenous iron administration is more effective when rapid hemoglobin and iron levels increases are expected as is the case for postpartum IDA.

The similarity of our study to Bhandal et al. is limited to the parenteral iron therapy in IDA, a condition much similar to the cause and /or consequences of malaria induced anemia in sub Saharan African population with the most vulnerable being children under 5 years and pregnant women, as a result of denutrition and /or malnutrition. However, in the latter study intravenous ferrous sucrose was preferred to ferrous dextrane which according to the authors was associated to several side effects when administered to patients, situation not confirmed by our experience as only three patients manifested mild

symptoms such as gastritis, diarrhea and over sweating, which did not lead to treatment discontinuation.

Several studies have shown the risks and benefits of intravenous administration of vitamin B compounds or iron separately [38 - 40], but our study is the first of its kind, to the authors knowledge, to investigate the benefits of the combination in malaria induced anemia.

Most of our patients presented to the Emergency Unit with clinical signs such as lethargy, bradycardia, hypotension and jaundice being the most common. As a rurally based health centre, due to bioethical considerations patients with life threatening symptoms were excluded from the study regardless of the hemoglobin status. Similarly, HIV positive cases who are demonstrated by several studies to be more difficult to manage when presenting with malaria induced anemia. [41 - 43]. Children below 18 months of age were deemed inappropriate for the trial. Patients had to be confirmed with malaria to be included in the study but had to first undergo intravenous antimalarial treatment and later confirmed parasites free before undergoing research treatment, as the circulating parasites could have influenced the study results.

The rationale of the study was that of combining a known cell metabolism booster as vitamin B – complex, and a fundamental hematopoietic element such as iron intravenously in order to stimulate patient hematopoiesis and recovery process, where vitamins play active part by enhancing energy production. Also, the intravenous route was preferred in order to bypass the digestive tract thus avoiding possible intolerance or malabsorption which are common in severe malaria especially among the pediatric and pregnant women patients. The choice of high volume intravenous fluids, was aimed at recovering the volume loss as a result of acute anemia and febrile state, so in a way tamponade the hypovolemia and improve the cardiac output. The slow infusion rate of approximately two hours was to limit the possible cardio toxicity or other unknown reactions, and three days were considered sufficient to produce results if any, and on the other side, avoid patients excessive infusion treatment and related infectious risk.

The clinical strengths of the present study are: its capacity to demonstrate the benefits of the vitamin B – complex and ferrous dextrane combination when administered intravenously in an endemic condition such as malaria induced anemia by increasing hemoglobin levels and providing general clinical improvement to patients treated without significant side effects throughout the study; secondly, it proved to be a useful treatment alternative to blood transfusion in managing patients with acute blood loss. The methodological strengths are: the laboratory diagnosis of malaria was based on two systems: smear microscopy and histidine rich protein – 2 strip test, being the latter more sensitive in detecting parasites especially at low concentration rates or in patients under treatment thus reducing the risk of misdiagnosis and also discriminates Plasmodium falciparum infection from other species;

secondly, in consideration of the abundant and diffuse availability of this pharmacological products, it proved to be a cost – effective and easily reproducible option compared to the routine blood transfusion at a rural level.

The clinical limits of this study are mainly: its incapacity to provide a control population with a placebo which of course would have been unethical in a life threatening situation as malaria induced anemia, or alternatively blood transfusion, due to unavailability of the clinical setting; secondly, the fact of excluding other causes of anemia limits the generalization of the findings. The methodological limit is related to the hemoglobin determination which was performed with a Sahli's tube Hemometer, an operator dependent estimation keen to inaccuracy, however this was partly adjusted by entrusting the same expert laboratory technician in all the estimates for all the patients

In summary, the results of this study highlight three important considerations: first of all, the capacity of preventing serious outcomes of malaria disease in sub Saharan Africa, if only, an appropriate diet, or where not feasible, a regular multivitamin supplementation to children and women population became a national or continental policy; the availability of a healthier and natural blood transfusion option by providing the organism with the necessary molecules in order to generate independently the required body necessity and in a self - regulated model, avoiding all the hazards and inaccuracies (under or over transfusion) of the standard transfusional process; from the socio - economic point of view, this would reduce the costs of patients' mobilization from the rural setting to the few town – based hospitals in Africa, and as a direct consequence, reduce the burden in the referral hospitals, that receive the bulk of cases within and outside the town setting without an appropriate filtering system.

CONCLUSION

The intravenous administration of vitamin B – complex in combination with ferrous dextrane proved to increase hemoglobin levels and provide clinical recovery fastly in patients with acute malaria induced moderate to severe anemia, especially in the children population. Also, it proved to be safe, as no serious side effects were documented throughout the study. The results of the present study show that the treatment should be considered a useful first line intervention in healthcare settings, especially in rural sub Saharan Africa where infrastructural and socio - economic obstacles added to the limited blood supply, render blood transfusion a hardly available option. However, further studies with a larger patient population are highly recommended in order to confirm the findings of the present study.

Competing interests

The authors declare that they have no competing interests.

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