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Influence of Parasitaemia on Anaemia in *Plasmodium Falciparum* Treated Children at Lake-Alau, Borno State

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Abstract: ***The relationship between malaria parasite density and anaemia was investigated on 313 children (6-59) months. Drug resistance in Plasmodium falciparum malaria is a major obstacle to malaria control. Plasmodium falciparum infection is a major contributory factor to the etiology of anaemia in malaria endemic areas of world, and this resulted in parasite resistance to drug therapy. Drug combinations for the treatment of P. falciparum malaria can delay the emergence and spread of resistance. Most of the monotherapies of anti- malarial drugs have gradually become less efficacious over time, while the most efficacious ones gradually lost their efficacies. The present study assessed packed cell volume (PCV level) as indicators for recovery from malaria anaemia (PCV≤ 33%) in children treated with AT+SP and AQ+SP between days 0,3,7,14 and 28 days follow- up. The standard protocol for therapeutic efficacy studies by the World Health Organization was strictly followed, parasite densities and PCV on days 0, 3, 7, 14 and 28 in children (6-59 months) treated for Plasmodium falciparum malaria with AT+SP and AQ+SP. There was a sharp parasite clearance phase between days 0 to 3 after treatment then a more stable clearance from 7 to 28 days. Similarly, for each µl of blood / parasites cleared there was a PCV recovery of 0.0214% versus 0.018% for AT + SP versus AQ + SP, respectively over 28 days of follow – up.***

Keywords: influence, Malaria, Parasitaemia, PCV, *Plasmodium, falciparum,* Efficacy

1. Introduction

Malaria is a systematic protozoan parasitic disease of the genus Plasmodium that causes infections of the red blood cells [20]. It is a major cause of morbidity and mortality in children under the age of five years in Sub-Saharan Africa and responsible for the death of over one million children annually [22]. The risk associated with malaria infection constitutes 10% overall disease burden which accounts for 40% public expenditure, 30-50% of inpatient admissions and up to 50% outpatient visits in areas with high malaria transmissions of Africa [18]. Drug combinations for the treatment of *P. falciparum* malaria might delay the emergence and spread of resistance [1]. Anaemia is relative to *Plasmodium falciparum* malaria especially severe in younger (<5 years) children [7] than pregnant women [10] as compared to normal adults [13] and really associated with increased risk of death due to malaria of *Plasmodium falciparum* infections [4]. Anaemia as a result of *Plasmodium falciparum* infection in children could impair cognitive and motor development [21], growth and immune function in children malaria [12]. Changes in haematological profiles such as PCV ((PCV<33%) are strongly associated with malaria infections because of red blood cells destruction [30] and a phenomenal process [21] which is linked to the frequency and degree of anaemia in malaria infected children and varies with intensities of parasite densities in malaria infected children during follow-up periods [3].

2. Literature Survey

In a study conducted in Nigeria on the relationship between Packed Cell Volume (PCV) and malaria parsitaemia showed a marginally significantly (P>0.05), results further showed that parasitaemic positive (33.8±5.0) children had lower PCV compared to negative parasitaemia (35.7±5.0) [29]. Anaemia is caused by increased hemolysis or a decreased rate of erythrocyte production [25]. Anaemia is associated with changes in hemoglobin among malaria cases and reports from Gambia and Nigeria indicated significant decreases in haemoglobin and packed cell volume [3]. Malaria-related anaemia is more severe in younger children and pregnant women rather than adults [10]. Anaemia may vary with level of malaria endemicity, background hemoglobinopathy, nutritional status, demographic factors, and malaria immunity [7]. Severe anaemia is associated with an increased risk of death [20]. A recent study in two large hospitals in Malawi indicated that cases of malaria associated with severe children anaemia were 5.2 to 8.5% of all paediatric admissions and accounted for 32 to 54% of malaria related deaths and malaria associated severe anaemia peaked at the age group 6 to 11 months [31]. Anaemia and possibly iron deficiency can impair cognitive and motor development [14], growth [21] immune function [17] and physical capacity [12].

3. Materials and Methods

3.1. Study site

This study was carried out at primary Health Center of Kayamla village settlement, Lake-Alau in Konduga Local Government Area of Borno State Nigeria. It is located at Lat: 120N and 130N; Long: 110E and 130E (Fig. 1) Prior to the commencement of the project, ethical clearance was sought from the Borno state ministry of health.

3.2. Recruitment Procedure

A complete physical examination was performed and a full medical history obtained by the clinical personnel. Detailed information's concerning the history of present illness, past and present drug history such as hypersensitivity to anti-malarial drugs were recorded into case record form (CRF) according to [26] as modified [27].

3.3. Inclusion and Exclusion Criteria

The inclusion criteria for the admission into study was strictly based on [27] for evaluating anti-malarial drugs in children (6 – 59 months). Informed consent provided by patient or parent/guardian, mono-infection with a slide confirmed *Plasmodium falciparum* infected children with asexual blood stage parasitaemia, absolute absence of history of hypersensitivity reactions to either of study drugs, enrolment parasite density of > 2,000 and < 200,000 asexual parasites/µl of blood). Measured axillaries temperature ≥ 37.5 °C with the ability to attend the stipulated follow-up visits and a packed cell volume > 15%.

3.4.1. Group one

(AT+SP), each child orally received 4 mg⁄kg body weight Artesunate daily for three days and a combined 25 mg⁄kg body weight Sulphadoxine and 1.25 mg⁄kg body weight Pyrimethamine as single oral do se on the first day of treatment.

3.4.2 Group two

(AQ+SP), each child orally received 10 mg⁄kg body weights of Amodiaquine daily for three days and also a combined 25 mg⁄kg body weight Sulphadoxine and 1.25 mg⁄kg body weight Pyrimethamine as a single oral dose on the first day of treatment.

3.5 Experimental Procedures

3.5.1 Physical parameters

The age of each child was determined by interviews with the parents or birth certificates while the body weight (kg) was expressed in (kg) using weighing balance (Model: Hansen H60 5500/11494798, UK) [26].

3.5.2 Blood sampling

Blood was sampled by pricking the third phalanx with a sharp sterile needle after cleaning with spirit-moistened cotton, smear slides on days 0, 1, 2, 3, 4, 7, 14 and 28 for the assessment of parasite densities [11].

3.5.3 Determination of Parasite density (per µl)

The thick film slide was stained for 30 to 45 minutes with 3% Giemsa for the assessment of parasite density. The samples were examined using objectives of a research microscope (x100) asexual parasites were counted alongside with 200 leukocytes. In an even that parasite count was < 10 parasites/200 leukocytes; count was continued per 500 leucocytes. The parasite density was expressed as the number of asexual parasites per ml of blood by assuming a mean normal leukocyte count of 8000/µl of blood [11and modified by [28]. Parasitaemia (per µl) = number of parasites x 8000 / number of leucocytes (200/500)

3.5.4 Determination of packed cell volume (PCV %)

The EDTA anti coagulated blood sample in a glass capillary was centrifuged in a microhaematocrit centrifuge at 12000 xg (rpm) for 5 minutes to obtain constant packing of the red cells. The PCV value was then read-off using a hand held microhaematocrit reader and the values were expressed as percentages of the PCV (%) on days 0, 3,7,14 and 28 [23].

3.5.5 Data management and analysis: Data management and analysis

Data collected were subjected to descriptive statistics using the analytical software Staistix Version 8.0 (Microsoft, 2003). Measures of central tendencies (standard deviations and percentages) were determined. Charts were drawn using Microsoft Excel (2007) and the regression equations on the relationships between *P. falciparum* parasitaemia (per µl) and PCV (%) over 28 days of follow-up.

4. Results

4.1. Baseline Parameters Before the admonistraion of drugs

Table 1: Baseline characteristics of patients at enrolment

S. No	*Parameter*	*Baseline data*
1	No. enrolled (N)	313
2	Gender (No. /%)	
	Male	149 (47.6)
	Female	164 (52.4)
3	Age (months)	
	Mean ± SD	43.3 ± 14.4
	Range	Aug-59
4	Body weight (kg)	
	Mean ± SD	18.4 ± 8.5
	Range	3.0 - 50.0
5	Temperature (^{0}C)	
	Mean ± SD	38.15 ± 0.47
	Range	37.0 - 39.6
6	Haematological	
	a. Parasite count (µl)	
	Mean ± SD	20820 ± 5277.7
	Range	2304 - 36800
	b. Haematocrit (PCV %)	
	Mean ± SD	27.0 ± 0.5
	Range	14.0 – 48.0

Table - 1 shows the baseline characteristics of the patients at enrolment. A total of 313 children were enrolled for the study, 149 (47.6%) were males and 164 (52.4%) were females. Mean of standard deviation (SD) and measures of dispersion to estimate variability in the data set to observed ranges. Consequently, the age of the children was highly dispersed between 6 - 59 months from the mean of 43.3 + 14.4 months. Results showed a total mean parasite count of 2304 - 36800⁄µl on admission with a mean range of 20820 ± 5277.7⁄µl. The mean PCV of the children on admission was 27.0 ± 5.0%, with a range of 14.0 - 48.0%.

4.1. Influence of Parsitaemia on Anaemia:

Results of figures 1and 2 shows a relationship between the PCV build – up and parasite depletion over 28 days of follow-up, The initial (day 0) with mean PCV levels for AT+SP as (25.69%) while slightly higher for AQ+SP (25.87%) patients, both treated groups were almost at par at enrollment. Influence of parasitaemia on PCV was higher (98.41%) for AT+SP (fig-1) compared to AQ+SP (93.51%) (Figure 2). The results further draws a respective daily build-up in PCV by 0.0214% and 0.018% per microliter (µl) of blood, which depicts almost twice as fast rate of recovery from anemia in AT+SP than AQ+SP patients.

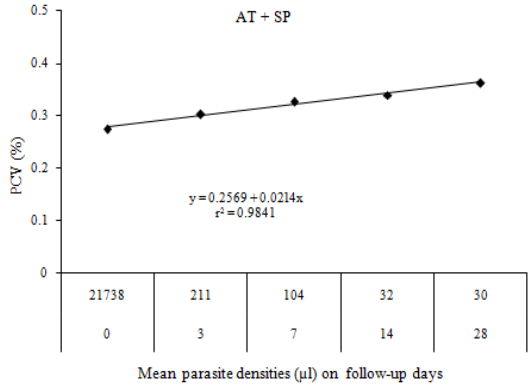

Figure 1: The influence of mean parasite densities (P. falcifarum) on treated (AT+SP) children during follow-up period (0-28).

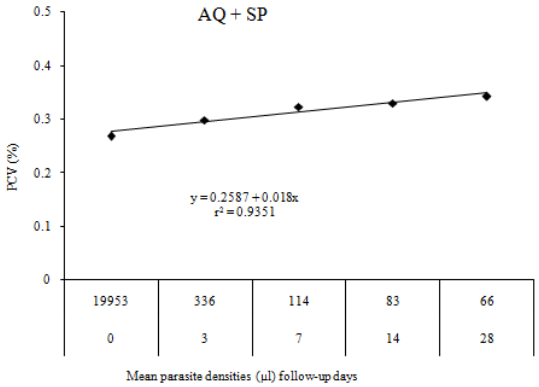

Figure 2: The influence of mean parasite densities (P. falcifarum) on treated (AQ+SP) children during follow-up days (0-28)

5. Discussion

The results of this study have clearly showed that anaemia has correlated directly with *Plasmodium falciparum* parasitaemia. The global malaria control strategy advocates a prompt and adequate treatment as essential measure to reduce morbidity and mortality arising from anaemia related complications [2]. *Plasmodium falciparum* infection is a major contributory factor to the etiology of anaemia in malaria endemic areas of the world (Kwadwo *et al*., 2000). The result trend shows that despite high mean parasite density at inception (day-0) in the two treated groups (fig. 1 and 2) and characterized by low PCV (<33%) there was a rapid parasite clearance in less than 72 hours in both treated groups, this coincides with observations by [9] in Rwanda, as further confirmed by the potentials of combination therapies in the clearance of parasites within the shortest possible time as reported by [5] in Uganda and [15] in Nigeria. This remarks on artemisinin derivatives on its efficacy and the rapid and substantial decrease in the parasite load when in used for treating malaria patients is in agreement with Rwagacondo *et al*. (2003).

5.1. Pattern of recoveries from anaemia

The mean recoveries from anaemia in the two treated groups showed a reciprocal recovery from anaemia between the two drug groups as evident from regression coefficient (r^2) values (fig 1 and 2), this is in congruent with [9] which lends credence to the fact that with ascending PCV level there will be a descending parasite density during the 28 days of follow-up period. Malarial infections normally relates with a decline in haemoglobin concentration of less than 8g/dl/ PCV (<33%) [20]. This further concurs with reported studies by [16] and using AQ+SP treatment of children *Plasmodium falciparum* malaria in relation to anaemia. The cumulative mean influence of parasite densities on PCV during the follow-up days was higher (98.41%) for AT+SP (fig- 1) compared to AQ+SP (93.51% (fig- 2). In a similar trend, the speed of parasite clearance was faster for AT+SP than in AQ+SP, as revealed by the coefficient of regression (r^2) with faster recovery from anemia in the older drug combination than in the later. The results further shows that parasitaemia had higher effects on the occurance of higher frequency of anaemia in AQ+SP than AT+SP which concurs with the findings by [20]and [3] on the relationship of parasitaemia to anemia frequencices in *Plasmodium falciparum* infected treated children.

5. 2. The speed of recoveries from anaemia

The results on the speed of recovery from anaemia (fig-1 and 2) showed a respective build-up in PCV by 0.0214% and 0.018% in the two respective drug combinations which depicts almost twice as faster rate of PCV recovery in AT+SP compared to AQ+SP patients (Dorsey *et al*.(2007). In a similar trend, the relative parasite clearance rate was generally faster within the early phase of days 0 – 3 compared to the later phase (days 7- 28) in AT+SP as compared to AQ+SP treated groups and equally corresponding PCV levels for the respective days(fig 1 and 2). The explanations for this strong reciprocal relationship

between and malaria parasite densities and the anemia (PCV < 33%) trends on follow-up days was malaria-induced [6], [9] and parasitaemia dependent.

6. Acknowledgment

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