

*Full length Research paper*

# **Artesunate versus Quinine : comparative analysis of efficiency clinic and Biologic in the treatment of complicated malaria in the north eastern of democratic republic of Congo**

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The measure of parasitary density in severe forms of malaria remains a true indicator in the assessment of the new techniques performances of a quick diagnostic of paludism and mainly of efficiency of the new antipaludic molecules as artesunate recommended in the treatment of severe forms of malaria since 2011. Hence our study aims at comparing the clinic and biologic efficiency of artesunate and quinine in the treatment of paludism complications in Kisangani, from the period of January 1st ,2015 to December 31, 2017. Our study being transversal and exhaustive sampling ; wehad analysed 117 surveying forms of children aged of 0 to 16 years of which 34 patients under artesunate and 83 patients under quinin treatment. After the examination, the treatment and data analysis in Microsoft, Excel ; word Software 2010 ; it was concluded : Children of 6 to 12 years old was the mostly concerned with 48.7%. Male sex predomine at 56.4% and the sex ratio of 1.3.The age bracket of 5- 10years old to parasite density of 76 532 P/ $\mu$ L. This density is more present to boys 86 492 P/ $\mu$ L. The thermic lyse as well as the reduction of parasitary density is observed in the concordent way as well as under artesunat and under quinin. This study concluded that artesunate and quinine present a similar clinic and biologic efficiency. Nevertheless were commended a maintainance of the strict observance of biologic density of malaria at look different varieties there are antipaludic molecules proposed on the market.

**Keywords :** Parasitary, density, efficiency, compared, antipaludic molecules,

## **INTRODUCION**

The complicated forms of paludism remain a major problem of public world health and a main concern of pедиатry. In 2015, half of world population was exposed to the risk of paludism contamination and on 214 millions of new cases recorded this year, we have noticed 438 000 deaths of which 66 % of victims were children under 5 years old according to world health organization [1-3]. In the same year, 88 % of world paludism was observed in Sub-saharian countries and 90 % world death due to

paludism falciparum [4,5].Childern under 5years old represent the tagretted preferential sever forms, mainly in endemic tyalustre zone [6,7]. In Democratic Republic of Congo, this affection situation represents the first cause of infanto- juvenile morbidity and mortality. The number of deaths was changed from 84 000 in 2010 to 42 000 to 2015. The reduction of this palustre mortality required an immediate aces in emergency to efficient antipaludic molecules of the cost first and available[9]. Hencefrom 2011, world health organization(WHO) has proposed the therapeutic choice that is the use of injectable of artesunate at first intention, the quinin and artemetherin respectively second and third choice. [10].This way is adopted and integrated in the national program of fight

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against paludism in Democratic Republic of Congo. The absence of compared study on efficiency of artesunate and quinin injectable in the treatment of the complicated forms of malaria in our study area justified this last research.

## MATERIALS AND METHODS

### Materials

Our study is transversal, which covers a period from January 1st, 2015 to December 31, 2017. It took place at the village pediatric Hospital center of Kisangani, located in the North – Est of Democratic Republic of Congo; Kisangani town. During this period 117 cases of complicated forms of malaria were colliges and analysed of which 34 child under intravenous artesunate in four doses of 2,4 mg/kg(Oh, 12h, 24h and 48 h) followed by a full course of either oral ACT and 89 child under intravenous quinin at loading dose of 20mg /kg over four hours followed by 10mg/kg every 8 hours until oral treatment was deemed possible with a total treatment period of seven days. Our sample being exhaustive and convenance, we have included in this study all cases of severe paludism according to the gravity criteria of paludism defined by WHO [10,11].

### Parasitologic Methods

The preparation of blood test and codified smear as well as their microscopic reading were looked by laboratory technicians experimented, trained; controlled and supervised. In case of cloubt the reading of the slide was done by two persons including the supervision. The determination of parasitary palustre density was conformed to world health organization procedures adopted by the fight national programme against paludism in Democratic Republic of Congo. The calculation of parasitary density at all patients by quantitative methods from the number of leucocyte by microliter; fixed at 800/  $\mu$ L [15], was systematically precised at admission and density parasitary evolution of patients mainly on the second, third and four day of treatment. The rapid test of paludism diagnostic used was on the bases of antigens of plasmodium falciparum: Histidine Rich Protein II and PLDH ( Lactate Deshydrogen) , this test was systematically done to all patient from the admission. [16,17],

The morning the body temperature was taken to electronic thermometer in respecting carefully the procedure of taking pediatric temperature[18].

### Data Collection and Treatment

A survey form has helped us in the collection of differents variables in this study which were the age, sex, clinic

signs and biologic signs. The data obtained was analyzed with the SPSS 20.0 and Excel 2010 software. The results were expressed as percentages and averages.

The Chi- squared test was used when necessary to assess signficance and statistical significance was at a P value less than 0.05.

### Ethical considerations

Authorization to carry out the study, and ethical clearance were obtained from the Pediatrics village Hospital Center of Kisangani authorities and the hospital ethics committee (Table I).

From this chart 58.1 % of patients are 6 yearsold and more with significant difference.(  $P < 0, 00012$ ). Male predominates 56 ,4% with sex ratio of 1.3.

Figure 1 : Shows athermic lys quasi- identique 24 hours after administration of the first dose of artesunate and quinin schema.

GRAPHIC 1 : The thermic evolution under artesunate treatment compared to treatment.

Rapid reduction effet of parasitary density is quasi perceptible almost in proportion alway 24 hours after administration of the first doses of Artesunate and Quinin. In both cases reduction rate is identically to 79,1 %.

GRAPHIC 2 : Distribution of Parasitary density according Artesunate versus Quinin treatment.

It clairly appear the high parasitary density average of 106 374 Parasites/  $\mu$ L in the pre school age.

Figure 3 : Distribution Parasitary Density according Age.

We have realized on figure N°4 that boys present a strong parasitary density average of 864,924 Parasites / $\mu$ L comparatively to girls who have a parasitary average of 34 705Parasites / $\mu$ L at the admisiion and parasitary density decrease in proportion alway 24 hours after administration of the first doses of Artesunate and Quinin.

Figure n°4- Distribution of parasitary density according to gender and its evolution density during the treatment de la densité parasitaire selon le genre et son évolution au cours du traitement.

Figure 4 show the parasitarydensityaverage138 274 Parasite/ $\mu$ L at admission with external values of (560 Parasites/ $\mu$ L - 1 470 584 Parasites/ $\mu$ L).

Figure 4- The parasitary palustre density average and evolution.

## DISCUSSIONS

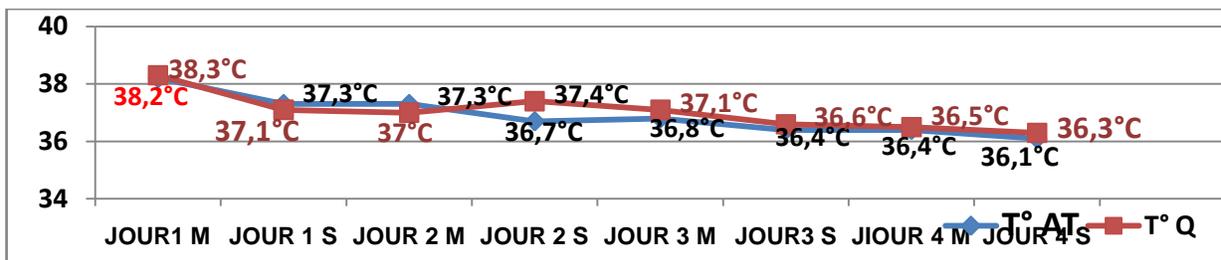
Contrary to a symptomatic malaria which has received less attention [47], the symptomatic malaria rested a global public health problem with serious consequences for children health and it's associated to several iron deficiency [48-52] and malnutrition [53-55]. Among

**Table 1 : Characteristics Of The Patients Artesunate Quintintotal**

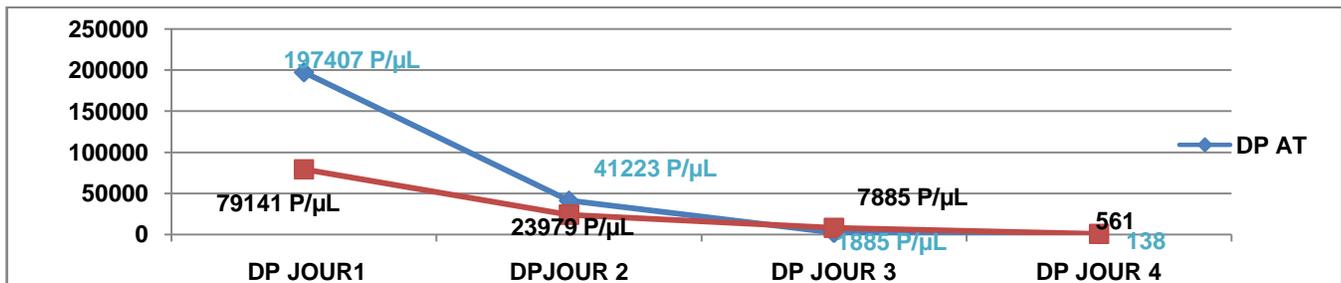
Characteristics	n= 34	n=83	N=117 (100%)
<b>Age(Year)</b>			
0- 2	04	16	20(17.1)
3 - 5	12	17	29 (24.8)
6 - 12	17	40	57(48.7)
13 et plus	01	10	11(09.4)
<b>Gender</b>			
Male	24	42	66(56.4)
Female	10	41	51(43.6)
<b>Bilan</b>			
TDR+ PF	33	75	108(92.3)
TDR+PAN	18	51	69 (59.0)
Achieved Density P.	34	83	117 (100)

From this chart 58.1 % of patients are 6 year sold and more with significant difference. ( P< 0, 00012). Male predominates 56 ,4% with sex ratio of 1.3.

**Figure 1\_**Shows athermic lys quasi- identique 24 hoursafter administration of the first dose of artesunate and quinins chema



**Graphic 1 :** The thermic evolution under artesunate treatment compared to treatment.



children in our study, contrary of several African authors who reports a significant predominance severe forms of paludism in the age bracket of 0 -5 years[19-25], we have founded in our series 58,1% more cases of complicated paludism in the age bracket of 6 years and but no significative difference (Table 1).Although the results of present study showed clearly that the preschool age has a high parasitary density average of 106 374 Parasites/ µL ( Figure 3), Several authors get similar results. [42, 45,46et 32], This category of children have palustre imminuty progressively acquired and relatively active in endemicity palustre stable zone as ours. [26,27 et 30,31]. This observation are confirmed in this study. Certainly infants in prescolaire age not

benefitted the maternal antibody protection immunity transmitted under one year,the absence of para-aminobenzoic acid in the breast milk essential factor of growth of plasmodium, the presence of secretory IgA, lactoferin and persistance of foetal hemoglobin in infants under one year. In our study, the results getting , this urged us to ask several questions on in efficiency or inexistant prevention measures of paludism in this children categorie. Hence Noor AM. And al. [28], and Shargie EB and all [29], proposed the correct usage of insecticide impregnated mosquito long duration which would have protective benefic effet as well as for children under 5 years and of school age. However we think that, in our study it could exist a conjugation of environmental

Graphic 2 :Distribution of Parasitary density according Artesunate versus Quinin treatment.

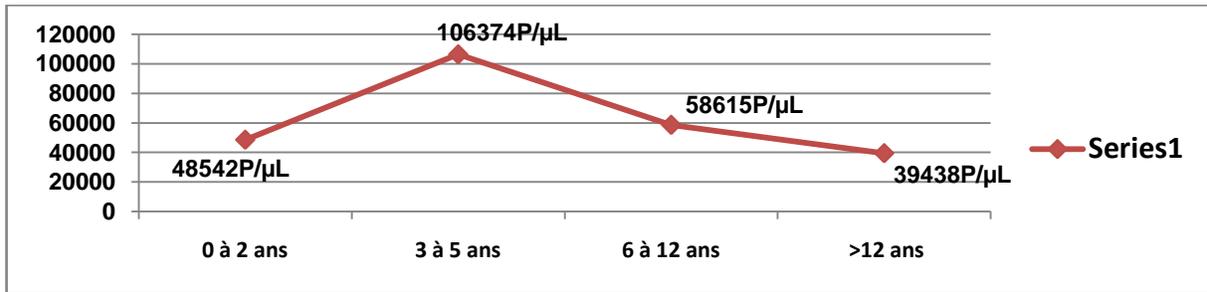
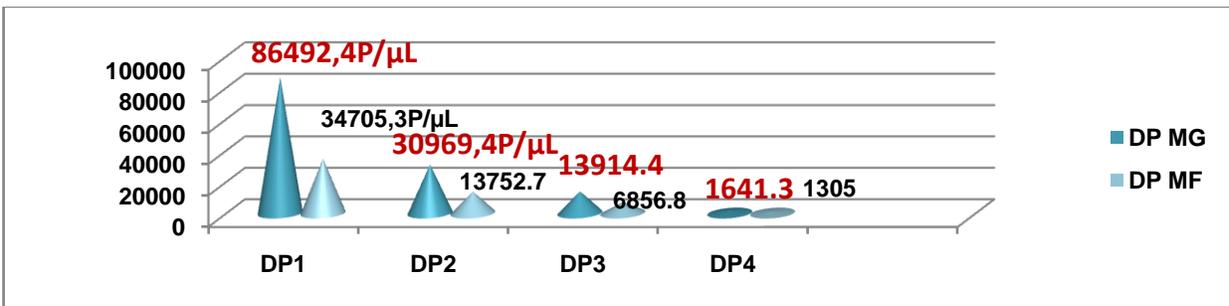


Figure 3 :Distribution Parasitary Density according Age.



factors as the residence place, the season, the marginal used of MIILD, the appearance of the new vectors and probability immuno-genetic factor in our country. Several authors showed genetic role in several malaria that the CD-40 ligand, CD-36, the FC gamma receptor II, complement receptor-1, the tumor necrosis factor gamma; the interleukins-4; -12;-13; intracellular cell adhesion molecules-1;platelet; endothelial cell adhesion molecule-1; toll-like receptor; mannose binding lectin 2 [56-59]; the variants of haemoglobin; ABO blood group antigen; G6PD deficiency; oval ocytosis [60-63].There is strong evidence that O blood group provided protection in several malariaby mechanism of reducing rosetting and sequestration [71] and other authors showed a significant association between several malaria and A blood group [64,65]. Such protection roles are much less clear for mild and a symptomatic malaria [66], All these genetic factors are highly depending on ethnical background population and geographical region in world. Studies on the genetic differences between population may provide a better understanding of the role of these genes. Malaria infection induces also polyclonal immunoglobulin production proportionally which determines protection against the blood stages of P.Falciparum. Evidence suggest that antibody dependent mechanisms play an important role in reduction of parasitama and this alleviates clinical symptoms as demonstrated by the passive transfert of hyper-immune immunoglobulin G (IgG). [67,68]. Among the various of IgGisotypes, cytophillic antibody IgG1 and IgG3 has been consistently correlated with uncomplicated malaria and even offer protection. While IgG4 does not protected

against malaria [69,70].However, one of the most challenging issues with studying malaria immunology is that individuals at risk for malaria infection are typically at riskfor other parasitic or non-parasitic diseases.The average age of the children was 7,5 years with variations of age extreme of 3 months and 16 years old. This average age is largely superior to 4.1 years (3 months and 14 years) described by Dembelé DE [42] at Bamako.In our study we have observed a predominance of masculine sex at 56.4% (Table) , this result join those of Bagayogo KN and Bamba K [33,40]. And we have also noticed a sex ratio of 1.3 near these of Diarra D . 1.32 [34] inferior to Daffé H 1.44 at Bamako. Taking into account the clinic evolution and biologic of patients, we have realized the thermiclyse (Figure N°1) and a rapid reduction of parasitemia quasi identique 24 hours after administration of the first dose of Artesunate and Quinin in both cases the reduction rate of parasitary density is 79,1 % within 24 hours. This result coincides with Noubiap and WHO observation. The Artesunate being schizonticides and gametocides with the capacity to reduce more than 50 % cytoadherence and rosetting phenomena about 2 hours after[36,37].The administration of the first dose contrary to Quinin which is solely schizonticide hasn't any action on cytoadherence phenomena but reduces of 50 % of rosetting phenomena 4 hours [38].Boys presents high parasitary density average of 86 492,4 Parasites /μL comparatively to girls who have an average parasitemia with a significant difference statistic P< 0,0000 at admission . This hyper parasitemia reduce in both sexes under Artesunate and Quinin treatment. The main reasons of this significative

difference are not cleared in this study and in different literature revised. It's resorts in our study that parasitary charge average at admission was 138 274 Parasite/ $\mu$ L at with external values of (560 Parasites/ $\mu$ L - 1 470 584 Parasites/ $\mu$ L).

This parasitemias comparable to what was reported in Nigeria by Rougemot A and Al which could reach 100 000 Parasite / $\mu$ Lat the children some times totaly apyretic [41].

On the contrary our parasitary charge in far superior to that of Dembelé DE [42].

That records an average parasitary charge of 47 888 Parasites / $\mu$ L with variation extreme (75 Parasites/ $\mu$ L– 997 800 Parasites/ $\mu$ L) at the children of 3 months to 14 years in hisstudy. These difference could be correlated to palustre environnemental typography different in two studied areas. The effect of thermiclyse and reduction of parasitary density was reported by Dossou GB and Al in their studies [43].

## CONCLUSION

In general, this study reveals that artesunate and Quinin injectable present a clinic efficiency and biologic similar in treatment of acute of pediatric paludism in our area of study.

However we recommend permanent surveillance of parasitary charge at look different molecules of artesunate proposed on market, also the observance of individual and collective prophylactic measures mainly at the children in preschool age.

The authors declare that they have no competing interests.

## Authors' contributions

N. Ngbona conceived the study and all authors participated to collect the data, performed the statistical analysis; wrote the draft of the paper and were involved in critically revising the manuscript for important intellectual content. All authors read and approved the final manuscript.

## Ethical considerations

Authorization to carry out the study, and ethical clearance were obtained from the Pediatrics village Hospital Center of Kisangani authorities and the hospital ethics committee.

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