

Comparative Evaluation of the Effects of Artemisinin-based Combination Therapy and Amodiaquine Monotherapy in G6PD Activity, Fasting Glucose Level and Parasite Clearance Rate in Malaria-infected Adults in Abakaliki, Nigeria.

Ewenighi Chinwe O^{1*}, Ukwa BN¹, Dimkpa Uchechukwu², Onyeanusu JC¹, Onoh Linus U. M.³, Ezeugwu Uchechukwu⁴, Onoh Gladys O.⁵, Ibeagi Ogubuike O.⁶, Eze Chukwuemeka O.⁷, Uzo Simon¹

1 Correspondence Author: Ewenighi Chinwe O, Medical Laboratory Science Department, Ebonyi State University, Abakaliki, Ebonyi State, Nigeria; E mail: ectabiel@yahoo.com.

2 Physiology Department, Nnewi Campus, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.

3 Dept. of Community Medicine, Enugu State University of Science and Technology, Enugu, Nigeria.

4 Department of Physiotherapy, University of Nigeria Teaching Hospital, Enugu, Nigeria

5 Nursing Science Department, Ebonyi State University, Abakaliki, Ebonyi Nigeria

6 Federal Teaching Hospital, Abakaliki, Ebonyi State, Nigeria

7 Dept. of Medicine, Federal Teaching Hospital, Abakaliki

Abstract:

Background: Antimalaria combination therapy with regimen containing an artemisinin-based compound has been recommended as a gold standard and first-line treatment for malaria by WHO. Studies have also proven the effectiveness of Artemisinin-based Combination Therapy (ACT) in the treatment of uncomplicated *Plasmodium falciparum* and delaying the emergence of drug resistance. However, limited reports exist on the effects of ACT on some vital biochemical parameters such as glucose-6-phosphate dehydrogenase (G6PD) and blood glucose concentration. This study therefore investigates and compares the effects of Artesunate-Amodiaquine combination therapy and Amodiaquine monotherapy on G6PD activity, fasting blood glucose level and parasite clearance rate in malaria-infected adults in Abakaliki, Nigeria. **Methodology:** Twenty adults aged between 20 and 30 years were used for the study. The patients were divided into two groups-A and B of 10 individuals each. Group A was given Artesunate-Amodiaquine (AS-AQ) while group B was given Amodiaquine (AQ). Blood samples were collected from each individual at baseline (Day 0) and after drug treatment (Day 4) for the comparative analysis of G6PD activity, fasting blood glucose level and parasite clearance rate. **Result:** There was an increase in G6PD activity after drug treatment in the two groups but the increase was not statistically significant. Glucose levels decreased after treatment in both groups but the decrease was also insignificant. There was a significant ($P<0.001$) difference in malaria parasite density of both groups after drug administration. The percentage parasite clearance of AS-AQ treated group and the AQ treated group were 67% and 47% respectively. **Conclusion:** There were no significant differences in the AS-AQ and AQ effects on the G6PD activity and fasting glucose level. In contrast, AS-AQ therapy indicated higher parasitic clearance rate compared to the AQ therapy. This further proves that Artemisinin-based Combination Therapy (ACT) is more effective than monotherapy in the treatment of malaria.

Keywords: Artemisinin- Amodiaquine, Combination therapy, Amodiaquine, Parasite clearance, G6pd, Glucose.

1.Introduction

Malaria affects half of the world's population and is the third leading cause of death for children under five years worldwide (WHO, 2011). Nigeria is one of the countries most affected by malaria and accounts for 25 per cent of global malaria cases. It is estimated that about 97% of Nigeria's population are at risk of malaria. According to data from Carter Centre for Malaria Control Programme, over 300,000 Nigerians—mostly children—die from malaria attack each year (WHO, 2011).

Of major concern are several reports of increasing incidence of multi-drug resistant *Plasmodium falciparum* malaria, which is responsible for the increasing cases of malaria in this region (Olurishe *et al*, 2007; Roll Back Malaria

Partnership Secretariat, 2010). In an attempt to reduce the incidence of relapse and treatment failure due to large scale resistance to existing drugs, the World Health Organization has advocated the use of Artemisinin-based combination therapy (ACT) for the treatment of malaria (Olurishe *et al*, 2007). ACTs are preferred because artemisinin compounds have rapid parasite and fever clearance effects and reduce gametocyte rate with the potential to reduce transmission (Meremikwu *et al*, 2006). Studies (White, 1999; Meremikwu *et al*, 2006; Meremikwu *et al*, 2012; Marli *et al*, 2013; Mathieu *et al*, 2013; Stephan, 2013) have also proven the effectiveness of ACTs in the treatment of uncomplicated *Plasmodium falciparum* and delaying the emergence of drug resistance. However, the lack of alternative drugs to artemisinin derivatives (Dondorp, 2009; Dondorp, 2010; Phyo, 2012) and their short half-lives and susceptibility to recrudescence, when given as monotherapy (Ashton *et al*, 1998) are the major drawbacks of the artemisinin derivatives. Using ACT in areas co-endemic for *P. falciparum* and *P. vivax* has been suggested as a strategy to overcome difficulties in differential diagnosis and in cases of mixed infection (Douglas, 2010).

All artemisia species seem to have hypoglycemic effect. Treatment of rats with *Artemisia annua* aqueous extract reduced the serum glucose after 4 weeks from 110 to 70 mg/dl (Mojarad, 2005). In South Africa *Artemisia afra* is extensively used for several diseases including diabetes. Methanol extracts of *A. absinthium* have a strong hypoglycemic and hepatoprotective activity (Goud, 2011). For *A. herba alba* the ethanol-water extract produced stronger hypoglycemic effect than the hexane extract (Awad, 2012). *A. sieberi* has been studied for a similar effect in Iran. Artemisinin and its combination with amodiaquine resulted in lowered plasma glucose hence an index of suspicion should be put on possibility of hypoglycaemia with the use of ACTs (Olayemi *et al*, 2012).

There is paucity of reports on the effects of ACT on some vital biochemical parameters such as G6PD and blood glucose concentration. Few studies, which demonstrated the hypoglycemic effects of ACT, were conducted on animals (rats and mice). It is true that these animals are considered comparable genetic models to humans; however, they exhibit natural differences in susceptibility to malarial infection. The present study therefore investigated the effects of Artesunate-Amodiaquine combination therapy on G6PD activity, fasting glucose level in comparison with the effects Amodiaquine monotherapy on these biochemical parameters in adult humans. In addition, we also demonstrated if there is significant difference in the rate of parasite clearance in blood between patients treated with Amodiaquine and those treated with Artesunate-Amodiaquine (AS-AQ).

2. Research Design and Methods

2.1 Subjects

Twenty adult individuals within the ages of 20-30 years (mean age of 25years) with uncomplicated *P. falciparum* malaria were used for the study. They were divided into two groups (A and B) comprising ten individuals in each group. Individuals with any form of G6PD deficiency (G6PD value of <6 µ/gHb), diabetics and pregnant women were excluded from the study. The subjects' consents were obtained before participation and they were assured of their safety and privacy throughout the study. Participation was voluntary and withdrawal from the study at anytime was allowed.

2.2 Drug treatment

Before treatment was given, blood sample from each individual from the groups was collected for the determination of parasite density (parasitaemia), fasting blood glucose and G6PD enzyme activity at baseline.

Artemisinin-based Combination Therapy (ACT) - Artesunate-Amodiaquine (AS-AQ) supplied as Camosunate (Adams Pharmaceutical (ANHUI) co.ltd Xuancheng Economic and Technical Development Zone ANHUI, China email; export@adamspharm.com). Adult (14 years and above) formulation is Amodiaquine base-300mg +Artesunate-100mg (12 tablets per sachet). Group A was given Artesunate-100mg (2 white tablets) one for morning, one for evening daily for three days together with Amodiaquine-300mg (2 yellow tablets) one for morning, one for evening daily for three days.

Amdiaquine supplied as Camoquin (Pfizer Afrique de l'ouest-B.P 3857 Dakar R.P-Senegal). Dosage: Group B was given Amodiaquine-600mg one daily for three days (200mg per tablet x 3= 600mg).

2.3 Blood sample collection

Before the commencement of treatment (Day 0), blood samples were collected from subjects in each group for the determination of parasite density (parasitaemia), fasting blood glucose and G6PD enzyme activity at baseline. The drug treatment commenced on (Day 1) and lasted for three days. On (Day 4) another blood sample was collected from each individual in the two groups for the analysis of G6PD activity, fasting glucose level and parasite clearance

rate. About 10ml of blood was collected from each individual (before and after treatment) and shared into EDTA (ethylene di-aminotetra acetic acid) and K-O,NaF (potassium oxalate, sodium fluoride) bottles. Sample in the EDTA bottle was used for the analysis of G6PD enzyme activity and Parasite density while the sample in K-O Na-F bottle was used for the analysis of fasting blood glucose level.

2.4 Laboratory procedures

G6PD enzyme activity was determined using spectrophotometric method of Horecker and Komberg, (Randox Laboratories Ltd United Kingdom). Normal range of G6PD activity in erythrocyte as prescribed by Randox G6PD Kit (2010) is 6.97- 20.5 U/gHb. Baseline values outside this range were excluded. Fasting blood glucose level was measured using glucose oxidase method by Randox Laboratories Ltd United Kingdom 2010. Normal fasting blood glucose for adult is 60-110mg/dl. Parasitaemia assessment was done using a thick film stained with giemsa. A minimum of 200 WBC were counted per slide of a sample. Malaria parasite density was determined by dividing the number of parasites counted by the number of WBCs $\times 8000/1 =$ parasites/ml of blood. Blood films were considered negative if no parasites were seen in 100 oil-immersion fields in a thick blood film.

2.5 Statistical analysis

Data was expressed as mean and standard deviation. Comparative analysis involving two continuous variables was done using independent sample t-test. Experimental data were analysed using analysis of variance (ANOVA). A post Hoc comparison (Bonferonni) test was performed to further ascertain significant differences between means. Statistical significance was set at $P < 0.05$. All statistics were done using SPSS for Windows (version 16.0).

3. Results

Data indicated that there were no significant differences in G6PD activity, fasting glucose level and malaria parasite density between patients in the groups at baseline (Table 1).

No significant differences were observed in G6PD activity and fasting glucose level of both groups after treatment. On the contrary, significant ($P < 0.01$) difference was observed in malaria density between patients treated with amodiaquine and those treated with artesunate/amodiaquine. Data indicated that parasite density was significantly reduced in patients treated with artesunate/amodiaquine compared to those treated with amodiaquine (Table 2).

The activity of G6PD enzyme was found to be increased after amodiaquine treatment but the increase was not significant. On the other hand, fasting blood glucose level was found to decrease but the decrease was insignificant. Significant ($P < 0.001$) decrease was observed in malaria density after treatment with amodiaquine. Data indicated that there was a significant reduction in parasite density after treatment with amodiaquine compared to the value before treatment (Table 3).

No significant difference was observed in G6PD activity after treatment with artesunate/amodiaquine. There was a decrease in fasting glucose level after artesunate/amodiaquine treatment but the decrease was insignificant ($P > 0.05$). On the contrary there was significant ($P < 0.001$) reduction in the malaria parasite density after treatment with artesunate/amodiaquine (Table 4).

Data indicated that patients treated with artesunate/amodiaquine had significantly ($P = 0.004$) higher percentage (67.49%) clearance of malaria parasites compared to those treated with amodiaquine (47.76%). This shows that artesunate/amodiaquine (artemisinin-base combination therapy) has higher efficacy than does Amodiaquine monotherapy (Table 5).

4. Discussion

The spread of multidrug-resistant *Plasmodium falciparum* malaria throughout the world has led WHO to recommend combination therapy as first-line treatment, with regimens containing an artemisinin based compound as a gold standard. The goal of Artemisinin-based Combination Therapy (ACT) is to enhance cure rates while simultaneously delaying the development of resistance to component drugs (White, 1999). The present study indicated that after 3 days of treatment, patients administered with artesunate/amodiaquine had significantly higher parasitaemia clearance of 67.49% compared to those treated with amodiaquine monotherapy who had a clearance rate of 47.76% and with no adverse effects recorded. In addition, there was lack of significant differences in fasting blood glucose level as well as G6PD activities between patients treated with artesunate/amodiaquine combination therapy and those treated with amodiaquine monotherapy.

The higher parasitemia clearance observed in the artesunate/amodiaquine combination therapy relative to amodiaquine monotherapy in the present study suggests that ACT has higher efficacy over monotherapy. Our finding

agrees with some studies which have shown that Artemisinin-based combination therapy has indeed proven to be more effective compared to the initial monotherapy (Meremikwu *et al*, 2006; Abdoulaye *et al*, 2010; Stephan *et al*, 2013). The use of artemisinin-based combination therapy (ACT) is previously associated with a rapid clearance of the parasite and a low probability of drug-resistant parasite emergence (White, 1999). ACT has also been shown to cure malaria in mice at very low dosages (Marli *et al*, 2013). The AS-AQ parasitemia clearance rate (67%) observed in the present study was lower than that observed in a study in Congo, which showed high efficacy of 94% (Mathieu *et al*, 2013). The assessment of artesunate/amodiaquine combination therapy by Meremikwu *et al* (2012) showed a therapeutic efficacy rate of 82.5% (Meremikwu *et al*, 2006; Meremikwu *et al*, 2012). However, these studies had longer treatment days (28 days) compared to the present study. The present finding therefore is an indication of high therapeutic efficacy of AS-AQ compared to Amodiaquine monotherapy in the treatment of malaria infection.

The pharmacological hallmark of the artemisinin derivatives is that they clear parasitaemia more rapidly than other drugs (White, 2011), however, not much is known about the adverse effect (if any) this ACT might have on some vital biochemical parameters. The present data indicated that there was insignificant decrease in fasting blood glucose level in both groups treated with artesunate-amodiaquine and amodiaquine monotherapy after the third day. The present finding is suggestive of slight hypoglycaemic effect of both antimalarial drugs. However, previous studies have reported significant reductions in glucose levels after artemisinin based therapy. For example, treatment of rats with *Artemisia annua* aqueous extract significantly reduced the serum glucose from 110 to 70 mg/dl after 4 weeks (Mojarad, 2005). *Artemisia afra*, *Artemisia absinthium*, *Artemisia sieberi* and *Artemisia herba alba* have also been shown to have hypoglycaemic effects (Awad, 2012). This shows that the hypoglycaemic activity of ACT anti-malarial is deposited in the Artemisinin group derived from artemisia. Treatment with artesunate, amodiaquine, artesunate-amodiaquine combination and quinine on mice infected with *plasmodium berghei* also indicated significantly lower plasma glucose compared to the control group, thus suggesting the possibility of hypoglycaemia with the use of ACTs (Olayemi *et al*, 2012). It is of noteworthy that the slight decrease (though not significant) in blood glucose observed in both ACT and amodiaquine treated patients is an indication that both drugs may exhibit hypoglycaemic effect. However, no literature supports the glucose lowering ability of amodiaquine or its derivative-quinoline. We recommend further studies to establish the hypoglycaemic effect of ACT and Amodiaquine monotherapy by extending the study to longer days.

The glucose VI phosphate dehydrogenase is an enzyme that protects the red cells from oxidative injury caused by oxidants and drugs (Luzzatto *et al*, 2001; Beutler *et al*, 2002; Abdoulaye *et al*, 2010). Our data indicated lack of significant differences in G6PD activities before and after treatment with both drug regimens. This indicates lack of adverse/hemolytic effects of both drug regimens on red blood cells and consequently related hematological indices in G6PD normal/sufficient individuals. To the best of our knowledge, there is lack of scientific literatures on the effects of ACTs and monotherapies on G6PD activities in G6PD sufficient individuals treated for malaria infection. The present findings therefore call for further research to confirm our findings and elucidate more facts on this subject matter.

5. Conclusion

There were no significant differences in the G6PD activity and fasting blood glucose after artesunate-amodiaquine and amodiaquine monotherapy treatments. In contrast, AS-AQ therapy indicated higher parasitic clearance rate compared to the AQ therapy. This further proves that Artemisinin-based Combination Therapy (ACT) is more effective than monotherapy in the treatment of malaria. Further studies on hypoglycaemic effect of ACT and Amodiaquine monotherapy and the effects of ACTs and monotherapies on G6PD activities in G6PD sufficient individuals treated for malaria infection are needed and the research should be extended to 28 days or more.

References

- Abdoulaye, K.K., Issaka Sagara, Mahamadou, A. T., Alassane Dicko, Aldiouma Guindo, Seidina Diakite, Joseph Kurantsin-Mills, Abdoulaye Djimde, Asikiya Walcourt & Ogabara Doumbo (2010), “*falciparum* clearance with artemisinin-based combination therapy (ACT) in patients with glucose-6-phosphate dehydrogenase deficiency in Mali”, *Malaria Journal*, 9, 332.
- Ashton, M., Hai, T.N., Sy, N.D., Huang, D.X., Van Huong, N., Niêu, N.T. & Công, L.D. (1998), “Artemisinin pharmacokinetics is time-dependent during repeated oral administration in healthy male adults”, *Drug Metab Dispos*, 26, 25-27.

- Awad, N.E. (2012), "Ethanol-water extract of *A. herba alba* produced stronger hypoglycemic effect than the hexane extract", *J Appl Pharm Sc.*, 2(3), 30-39.
- Beutler, E. & Vulliamy, T.J. (2002), "Hematologically important mutations: glucose-6-phosphate dehydrogenase", *Blood Cells Mol Dis*, 28, 93-103.
- Dondorp, A.M., Nosten, F., Yi, P., Das, D., Phyto, A.P., Tarning, J., Lwin, K.M., Ariey, F., Hanpithakpong. W., Lee, S.J., Ringwald, P., Silamut, K., Imwong, M., Chotivanich, K., Lim, P., Herdman, T. & An, S.S. (2009), "Artemisinin resistance in *Plasmodium falciparum* malaria", *N Engl J Med*, 361, 455-467.
- Dondorp, A.M., Yeung, S., White, L., Nguon, C., Day, N.P.J., Socheat, D. & Von Seidlein, L. (2010), "Artemisinin resistance: current status and scenarios for containment", *Nat Rev Micro*, 8, 272-280.
- Douglas, N.M., Anstey, N.M., Angus, B.J., Nosten, F. & Price, R.N. (2010), "Artemisinin combination therapy for vivax malaria", *Lancet Infect Dis*, 10, 405-416.
- Goud, B.J. (2011), "Methanol extracts of *A. absinthium* have a strong hypoglycemic and hepatoprotective activity", *Int J Adv Pharm Res*, 2, 7.
- Luzzatto, L., Mehta, A. & Vulliamy, T. (2001), "Glucose-6-phosphate dehydrogenase deficiency", In: *The Metabolic & Molecular Bases of Inherited Disease*. Volume 3. Edited by Scriver C, Beaudet A, Sly W, Valle D. New York. McGraw Hill, 4517-4553.
- Marli, C.L., David D. N'Da, Christophe Tran Van Ba, Sharon Wein, Jennifer Norman, Lubbe Wiesner & Henri Vial (2013), "Potent *in vivo* anti-malarial activity and representative snapshot pharmacokinetic evaluation of artemisinin-quinoline hybrids", *Malaria Journal*, 12, 71.
- Mathieu Ndounga, Pembe Issamou Mayengue, Prisca Nadine Casimiro, Dieudonné Loumouamou, Leonardo K. Basco, Francine Ntoui & Philippe Brasseur (2013), "Artesunate-amodiaquine efficacy in Congolese children with acute uncomplicated falciparum malaria in Brazzaville", *Malaria Journal*, 12, 53.
- Meremikwu, M., Alaribe, A., Ejemot, R., Oyo-Ita, A., Ekenjoku, J., Nwachukwu, C., Ordu, D. & Ezedinachi, E. (2006), "Artemether-lumefantrine versus artesunate plus amodiaquine for treating uncomplicated childhood malaria in Nigeria: randomized controlled trial", *Malaria Journal*, 5, 43.
- Meremikwu, M.M., Friday Odey, Chioma Oringanje, Angela Oyo-ita, Emmanuel Effa, Ekpereonne B. Esu, Eyam Eyam, Olabisi Oduwole, Vivian Asiegbu, Ambrose Alaribe & Emmanuel N. Ezedinachi (2012), "Open-label trial of three dosage regimens of fixed-dose combination of artemisinin and naphthoquine for treating uncomplicated falciparum malaria in calabar, Nigeria", *Malaria Journal*, 11, 413.
- Mojarad, T.B. (2005), "Effect of *Artemisia annua* extract on serum glucose", *Iranian Biomedical Journal*, 9(2), 57-62.
- Olayemi, S.O., Arikawe, A.P., Akinyede, A., Oreagba, A.I. & Awodele, O. (2012), "Effect of Malarial Treatments on Biochemical Parameters and Plasma pH of Mice Infected with *Plasmodium berghei*", *International Journal of Pharmacology*, 8, 549-554.
- Olurische, T.O., Maiha, B.B., Olurische, C.O. & Abdullahi (2007), "Short term pre-intervention evaluation of artemisinin combination therapy usage in a tertiary health facility in northern Nigeria", *Nigerian journal of pharmaceutical sciences*, 6(2), 93 – 98.
- Phyo, A.P., Nkhoma, S., Stepniewska, K., Ashley, E.A., Nair, S., McGready, R., Ler Moo, C., Al-Saai, S., Dondorp, A.M., Lwin, K.M., Singhasivanon, P., Day, N.P., White, N.J., Anderson, T.J. & Nosten, F. (2012), "Emergence of artemisinin-resistant malaria on the Western border of Thailand: a longitudinal study", *Lancet*, 379, 1960-1966.
- Roll Back Malaria Partnership Secretariat (2010), World Malaria Day. *Africa Update* <http://www.rollbackmalaria.org/ProgressImpactSeries/docs/wmd2010report-en.pdf>. [Date accessed: March 4 2013]
- Stephan Duparc, Isabelle Borghini-Fuhrer, Carl J. Craft, Sarah Arbe-Barnes, Robert M Miller, Chang-Sik Shin & Lawrence Fleckenstein (2013), "Safety and efficacy of pyronaridine-artesunate in uncomplicated acute malaria: an integrated analysis of individual patient data from six randomized clinical trials", *Malaria Journal*, 12, 70.
- White, N.J. (1999), "Delaying anti-malarial drug resistance with combination chemotherapy", *Parasitologia*, 41, 301-308.
- White, N.J. (2011), "Parasite clearance curve", *Malaria Journal*, 10, 278.
- World Health Organization (2011), "World Malaria Report", http://www.who.int/malaria/world_malaria_report_2011/9789241564403_eng.pdf website [Date accessed: March 4 2013]

Table 1. Baseline mean values of G6PD enzyme activity, fasting blood glucose level and malaria parasite density in subjects before treatment with anti-malaria drugs.

VARIABLES	AMODIAQUINE Baseline GROUP B	ARTES/AMODIAQUINE Baseline GROUP A	t-STAT	P
G6PD(μ /gHb)	8.9 \pm 1.52	9.06 \pm 1.67	-0.15	0.88
Glucose(mg/dl)	77.40 \pm 21.52	77.0 \pm 16.73	0.04	0.97
Parasite Density(count/ml)	5906.2 \pm 852.23	5322.6 \pm 1103.32	1.30	0.23

Table 2. G6PD activity, fasting glucose level and malaria parasite density in subjects after treatment with anti-malaria drugs.

VARIABLES	AMODIAQUINE TREATED GROUP B	ARTES/AMODIAQUINE TREATED GROUP A	t-STAT	P
G6PD(μ /gHb)	9.1 \pm 1.66	9.2 \pm 1.74	-0.10	0.92
Glucose (mg/dl)	70.8 \pm 14.57	72.6 \pm 14.96	-0.28	0.78
MALARIA DENSITY(count/ml)	3086.1 \pm 739.26	1720.8 \pm 553.09	4.16	0.002

Table 3. G6PD activity, fasting glucose level and malaria parasite density before and after treatment in subjects treated with amodiaquine

VARIABLES	BEFORE TREATMENT	AFTER TREATMENT	t-STAT	P
G6PD(μ /gHb)	8.94 \pm 1.52	9.1 \pm 1.66	-0.19	0.85
Glucose (mg/dl)	77.4 \pm 21.52	70.8 \pm 14.57	0.80	0.43
Parasite Density(count/ml)	5906.2 \pm 852.23	3086.1 \pm 739.27	7.90	0.000

Table 4. G6PD activity, fasting glucose level and malaria parasite density before and after treatment in subjects treated with artesunate/amodiaquine drug.

VARIABLES	BEFORE TREATMENT	AFTER TREATMENT	t-STAT	P
G6PD(μ /gHb)	9.1 \pm 1.67	9.2 \pm 1.74	-0.14	0.89
Glucose (mg/dl)	77.0 \pm 16.73	72.6 \pm 14.96	0.62	0.54
Parasite Density(count/ml)	5322.6 \pm 1103.3	1720.8 \pm 553.09	9.23	0.000

Table 5. The percentage malaria parasite clearance in patients treated with amodiaquine and artesunate/amodiaquine drugs.

DRUGS	BEFORE TREATMENT	AFTER TREATMENT	DIFFERENCE	% CLEARANCE
Amodiaquine	5906.2 \pm 852.23	3086.1 \pm 739.27	2820.1 \pm 778.92	47.76 \pm 10.62
Artes/Amodiaquine	5322.6 \pm 1103.3	1720.8 \pm 553.09	3601.8 \pm 936.18	67.49 \pm 7.96

This academic article was published by The International Institute for Science, Technology and Education (IISTE). The IISTE is a pioneer in the Open Access Publishing service based in the U.S. and Europe. The aim of the institute is Accelerating Global Knowledge Sharing.

More information about the publisher can be found in the IISTE's homepage:

<http://www.iiste.org>

CALL FOR PAPERS

The IISTE is currently hosting more than 30 peer-reviewed academic journals and collaborating with academic institutions around the world. There's no deadline for submission. **Prospective authors of IISTE journals can find the submission instruction on the following page:** <http://www.iiste.org/Journals/>

The IISTE editorial team promises to review and publish all the qualified submissions in a **fast** manner. All the journals articles are available online to the readers all over the world without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. Printed version of the journals is also available upon request of readers and authors.

IISTE Knowledge Sharing Partners

EBSCO, Index Copernicus, Ulrich's Periodicals Directory, JournalTOCS, PKP Open Archives Harvester, Bielefeld Academic Search Engine, Elektronische Zeitschriftenbibliothek EZB, Open J-Gate, OCLC WorldCat, Universe Digital Library, NewJour, Google Scholar

