



**AN OBSERVATION ON EFFICACY AND SAFETY OF CHLOROQUINE VERSUS
ARTESUNATE IN TREATMENT OF VIVAX MALARIA IN PEDIATRIC PATIENTS: A
HOSPITAL BASED STUDY**

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ABSTRACT

Malaria is a major public health problem in India. India contributes about 70% of malaria in the South East Asian Region of WHO. Various trials conducting research in malaria doesn't include Children and number of new medicines arrives to market in treatment of malaria doesn't promise their efficacy in children. So this study mainly emphasizes the evaluation of efficacy and safety of oldest known drugs like chloroquine and artesunate in children. To study the comparative efficacy and safety of chloroquine and artesunate in treatment of malaria in children. The study was conducted from October 2017 to March 2018 in Paediatrics department, Government General Hospital, Guntur, a tertiary care teaching hospital. Out of 116 patients screened, 108 were enrolled in the study. Patients are randomly allocated into two groups each of 54, to receive either artesunate or chloroquine and done follow-up regularly on days 3, 7, 14, 21, 28. Out of which, 103 completed the study. The two groups were compared in terms of reduction of parasite load, resolution of fever, cure rate, relapse rate and incidence of adverse effects. 52 members in chloroquine group and 51 members in artesunate group completed follow-up of study. The mean fever clearance rate of chloroquine and artesunate groups are 2.94 ± 1.05 days, 2.51 ± 0.92 days respectively. The mean parasite clearance rate of chloroquine and artesunate groups are 2.81 ± 0.88 days, 2.22 ± 0.85 days respectively. Cure rate and relapse rate of chloroquine group was found to be 1.92% and 98.07% whereas for artesunate group it was found to be 11.76% and 88.23%. Incidence of side effects is more for chloroquine with 55.77% and artesunate with 23.53%. The current study showed that there is no significant difference in terms of Fever clearance time, Parasite clearance time but cure rate is maximum with chloroquine. In view of occurrence of Adverse Drug Reactions artesunate had lower incidence of side effects in this study. So, this study finally concludes chloroquine is effective than artesunate and artesunate is safer than chloroquine.

Keywords: Artesunate, Chloroquine, Malaria, Plasmodium vivax.

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INTRODUCTION

Malaria is a mosquito-borne disease caused by a parasite. People with malaria often experience fever, chills, and flu-like illness⁽¹⁾. It is the 6th leading cause of death in low income countries⁽²⁾. Malaria is a public health problem in several parts

of the country. About 95% population in the country resides in malaria endemic areas and 80% of malaria reported in the country is confined to areas consisting 20% of population residing in tribal, hilly, difficult and inaccessible area. Incidence of malaria is 2223 cases up to May

2018 all over India⁽³⁾. The use of antimalarial drugs in India has evolved since the introduction of quinine in the 17th century. The treatment of malaria depends on various factors like patient's age, the severity of infection, the likely pattern of susceptibility to antimalarial drugs, cost and availability of such drugs. For this reason recommendations vary according to geographic region and should be under constant review⁽⁴⁾.

Malaria control programme was established in 1953, soon after independence, chloroquine stayed as major choice and then newly introduced artemisinin derivatives had been used till now⁽⁵⁾. But resistance to chloroquine is observed at some places in India^{(6),(7)}. Various trials conducting research in malaria doesn't include Children and number of new medicines arrives to market in treatment of malaria doesn't promise their efficacy in children. So this study mainly emphasizes the evaluation of efficacy and safety of oldest known drugs like chloroquine and artesunate in children.

MATERIALS AND METHODS

Study Design: Prospective Observational Study

Study Period: The study was conducted in a period of 6 months i.e., from October 2017 to March 2018.

Inclusion Criteria

- Age (1-12 years)
- Infection with Plasmodium vivax species or Malaria PV strip test positive.
- Willing to provide written informed consent.

Exclusion Criteria

- Have contraindications for the use of either of the study medications.
- Any significant co-morbidity.
- Those who have taken antimalarials prior to admission.
- Malaria Parasite strip test negative.

Study Method: The study was conducted in Paediatrics Department, Government General

Hospital, Guntur, and a tertiary care teaching hospital. Patients are screened for their eligibility to fit in the study. Then patients are randomly allocated into two groups for their treatment and followed up to Day 28 as per WHO standard protocol⁽⁸⁾.

Group-I: Total no. of patients in this group is 54. They received oral chloroquine 10 mg/kg on day 1 and 5mg/kg for next 2 days.

Group-II: Total no. of patients in this group is 54. They received Intravenous artesunate 2.4mg/kg for 5 days.

Then the efficacy is evaluated using following parameters.

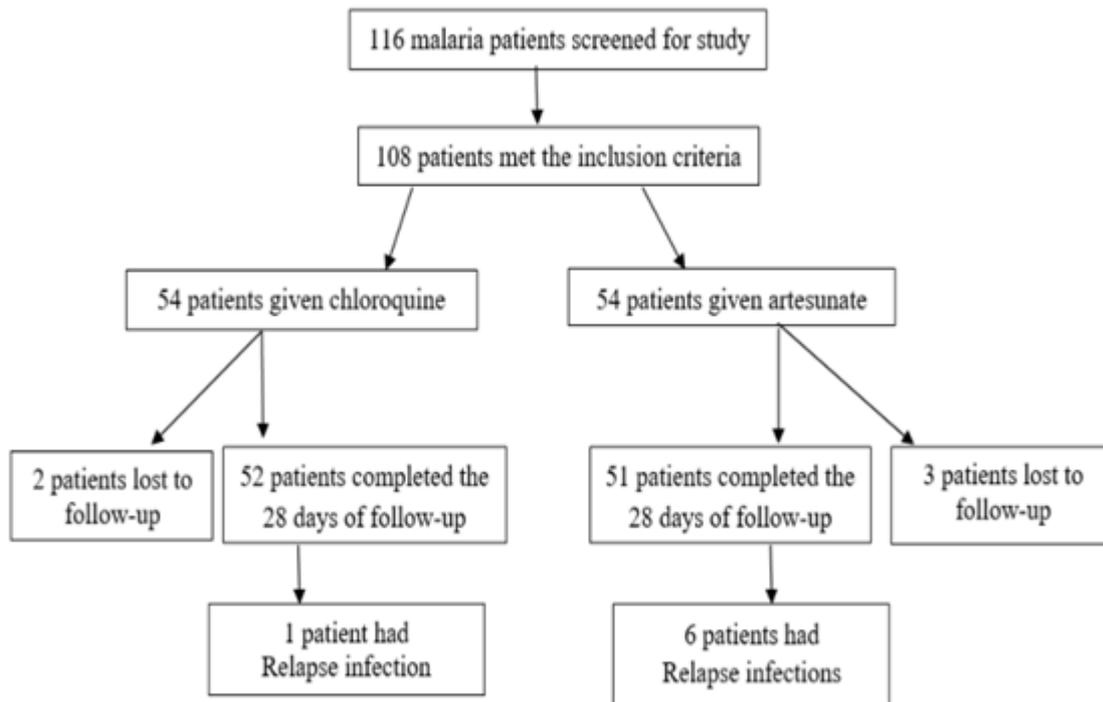
1. **Fever clearance time:** It was the period from the administration of the first dose till the buccal temperature reached 37° C and did not rise above 37° C for 48 hours.
2. **Parasite clearance time:** It was defined as the interval between the start of treatment and the time of the first of two sequential negative thick films.
3. **Cure Rate:** Defined as the proportion of the patients who responded to treatment and remained symptomatically relieved (i.e. no fever and other symptoms) till the 28th day of follow up.
4. **Relapse Rate:** Defined as the proportion of the patients affected with malaria till 28th day of follow up.

5. Statistical Methods

6. All the collected data were analyzed using the Statistical Package for the Social Science (SPSS) version 16 in Windows 10 and Microsoft Excel. Student t test (two tailed, independent) was used to calculate the significance of study parameters on continuous scale between two groups. Chi-square and Fisher Exact test were used to find the significance of study parameters on categorical scale between two groups. Results on continuous measurements were presented on mean \pm SD and results on categorical measurements were presented

in percentage. P value less than 0.05 was considered as significant.

Fig 1: Flowchart of Study Procedure



RESULTS

Table 1: Demographics and Baseline disease characteristics of patients according to treatment group

PARAMETER	GROUP-I CHLOROQUINE	GROUP-II ARTESUNATE	P Value
No. of Patients	52	51	-
Age in Years	6.73 (2.8)	5.04 (3.0)	0.004 ¹
Body weight in Kgs	18.67 (7.2)	14.20 (7.8)	0.003 ¹
Male: Female	1:1	1: 0.8	-
Axillary Body temperature at time of admission (°C)	38.2 (0.76)	38.5 (0.70)	0.039 ¹

¹ student t test

Total no. of patients involved in the study is 103. Of 103, 52 members belongs to chloroquine group and 51 members belongs to artesunate group. The demographics and other characteristics of patients is shown in Table 1. Average age and body weight

of children in chloroquine group is greater than artesunate group. The Males: Female’s ratio is not equal in both groups. The axillary body temperature at the time of admission is greater in artesunate group.

Table 2: Response parameters of patients in both groups

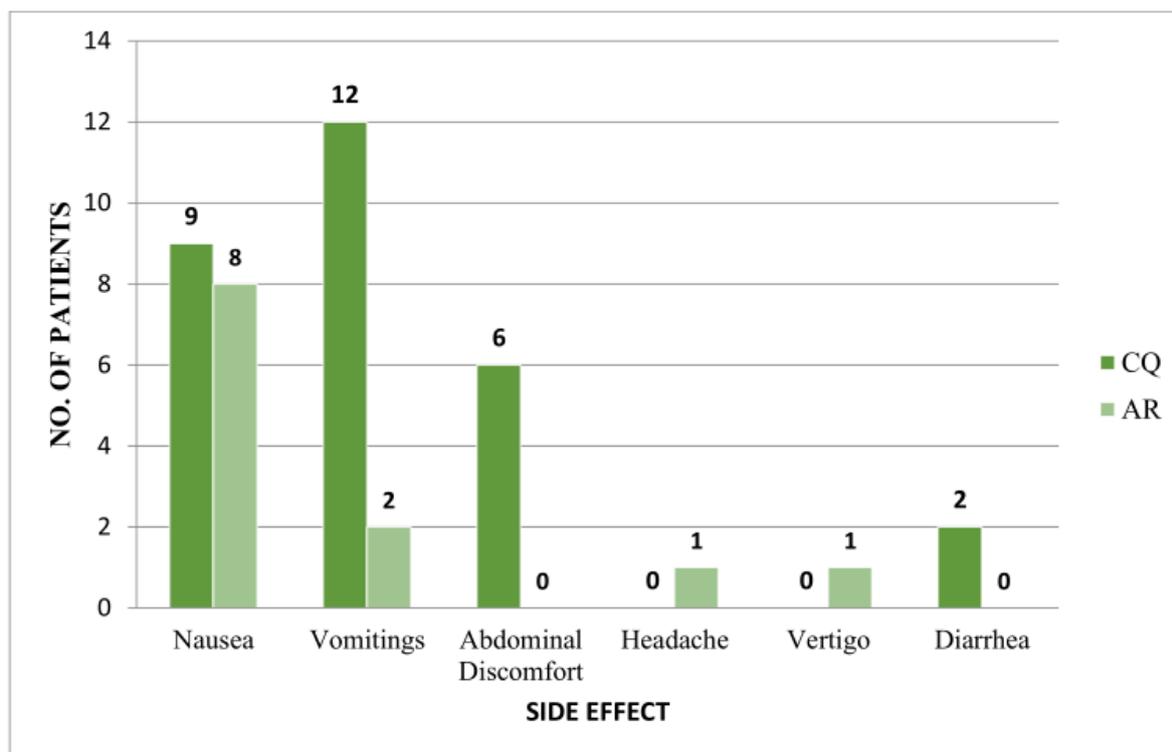
PARAMETER	GROUP-I CHLOROQUINE	GROUP-II ARTESUNATE	P Value
Fever clearance time in days (Mean ± SD)	2.94 ± 1.05	2.51 ± 0.92	0.029 ¹
parasite clearance time in days (Mean ± SD)	2.81±0.88	2.22±0.85	0.001 ¹
Positive Cure rate (%)	98.07	88.23	0.047 ²
Positive Relapse rate (%)	1.92	11.96	0.047 ²

1 Independent t test; 2 Chi-square test

After allocation of treatment, Mean fever and parasite clearance time is less in artesunate group compared to chloroquine group. Cure rate is higher in chloroquine group with 98.07% (n=

51/52) compared to artesunate group i.e., 88.23% (n= 45/51). Relapse rate is higher in artesunate group with 11.76% (n= 6/51) compared to artesunate group i.e., 1.92% (n= 1/52).

Figure II: Details of adverse drug reaction profiles of the patients in both the groups



Incidence of side effects is more for chloroquine with n=29(55.77%) and artesunate with n=12(23.53%). Among all, Vomitings is experienced by majority of patients in the chloroquine group i.e., 29.26% (n=12). Other side effects include Nausea, abdominal discomfort, and

diarrhea. In artesunate group, Nausea is the major effect experienced by most of the patients i.e., 19.51% (n=8). Other side effects include Vomitings, headache and vertigo.

DISCUSSION

On reviewing the demographic data, it was found that children of age group 5-8 years of age are more prone to this disease. Out of 103 patients, 57 were female and 46 were male which reveals that more number of females are present in this study. According to study conducted by Muhammad Aqeel Khan *et al.*, there are more no. of males in their study population⁽⁹⁾.

The efficacy of both drugs is compared by fever clearance time, parasite clearance time, cure rate, relapse rate. 69.23% of patients are afebrile by day 3 and 88.23% of patients are afebrile by day 3 in chloroquine and artesunate groups respectively. According to study conducted by Bamenla quarum goka *et al.*, there is no difference between both groups with respect to fever clearance time but our study proved that artesunate is rapid in clearing fever compared to chloroquine. These results corresponds with the study conducted by Tajeldin M Abdallah *et al.*, in which artesunate has shorter fever clearance rate^{(10),(11)}. The mean parasite clearance time is shorter in artesunate group. 80.76% of patients were parasite negative by day 3 and 92.16% of patients were parasite negative by day 3 in chloroquine and artesunate groups respectively. This results were similar to study conducted by Giovanfrancesco Ferrari *et al.*, in which artesunate group has shorter parasite clearance time. Perhaps, according to study conducted by Bamenlaquarumgoka *et al.*, there is no difference between both groups with respect to parasite clearance time^{(10),(12)}. This study revealed that higher cure rate and less relapse rate for chloroquine group. According to study conducted by A S Kerketta *et al.*, there is very less percentage of cure rate in chloroquine group but our study showed that the maximum cure rate is achieved with chloroquine group compared to artesunate group⁽¹³⁾.

Toxicity and side effects of drugs where much less in patients taking artesunate than those taking chloroquine. This corresponds to the work of Kumar Shambhu Nath *et al* 2005. In Artesunate treated group side effects is very less and nausea is the major side effect suffered by patients in their study⁽¹⁴⁾.

CONCLUSION

The Findings of this study revealed that there is no significant difference in terms of Fever clearance time, Parasite clearance time but cure rate is maximum with chloroquine. In view of occurrence of Adverse Drug Reactions artesunate had lower incidence of side effects in this study. So, this study finally concludes chloroquine is effective than artesunate and artesunate is safer than chloroquine.

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