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# FALCIPARUM MALARIA;
## COMPARISON OF RESPONSE TO TREATMENT BETWEEN QUININE AND ARTEMETHER

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**ABSTRACT... Introduction:** Quinine and quinidines remain the drugs of choice for chloroquine resistant Plasmodium falciparum malaria. In 1972, Chinese scientists discovered the antimalarial properties of a group of compounds from the qinghao plant (Artemisia annua) which have activity against all malaria causing parasites including multi-drug resistant strains of Plasmodium falciparum. **Objective:** To compare response to treatment between quinine and artemether in Plasmodium falciparum malaria. **Design:** Quasi-experimental study. **Setting:** Department of Medicine Pakistan Air Force Hospital Lahore. **Period:** 1st Jun 2008 to 1st Dec 2009. **Patients:** 80 consecutive adult patients with positive MP slide for Plasmodium falciparum malaria. Methods: Patients were randomly divided into two groups for treatment either with quinine or artemether. **Results:** Out of total 80 patients, 40 were given quinine and 40 were given artemether. Out of 40, 16 patients responded to quinine while 24 did not respond. The responders were 34.8% in case of quinine while 70.6% patients did not respond. Out of 40 patients treated with artemether, 30 responded while 10 did not. The responders were 65.2%while non responders were 29.4%.0n calculating the P-value from the chi-square it was found that difference in terms of response to the two treatment regimens was statistically significant.(P=.0022).**Conclusion:** The frequency of response in case of quinine was 34.8% while it was 65.2% in case of artemether. So based upon statistically significant difference (P=.0022) it is concluded that Artemether is a satisfactory alternative to Quinine for the treatment of falciparum malaria in adults.

**Key words:** Malaria, Falciparum malaria, Cerebral malaria, Quinine, Artemether.

## INTRODUCTION

The introduction of cinchona alkaloids some 350 years ago has changed the treatment of malaria[1]. The principle component of qinghao plant are qinghaosu (artemisinin) and two derivatives - the water soluble hemisuccinate artesunate and the oil-soluble artemether which are the most rapidly acting and potent of all antimalarial drug. These compounds have activity against all malaria causing parasites. More than 20 lac people have been given antimalarial treatment with artemesin, artesunate or artemether. These drugs have proven to be rapidly effective in the treatment of severe malaria and remarkably nontoxic. Artemether has been reported to reduce the mortallity rate for cerebral malaria caused by chloroquine- resistant P. falciparum[2].

Unfortunately the incidence of Plasmodium falciparum malaria is significantly high among troops of Armed forces of Pakistan. This incidence can be attributed to the development of resistance by Plasmodium falciparum to commonly used anti malarial drugs. Keeping in view this resistance of Plasmodium falciparum, this study has been carried out to conduct a comparison between the two regimens of treatment & formulate the most effective and appropriate one to prevent fatal outcomes and disabling complications from this deadly disease.

## OBJECTIVES

To compare response to treatment between quinine and artemether in Plasmodium falciparum malaria.

## PATIENTS AND METHODS

This study was conducted at PAF Hospital Lahore which is a well-equipped state-of-the-art 100 bedded hospital draining a very large serving and retired dependent population of Central and Northern Punjab.

A total of 80 consecutive patients with MP positive slide for Plasmodium falciparum malaria presenting to Pakistan Air Force Hospital Lahore from 1st June 2008 to 1st Dec 2009 were included in the study if they gave informed consent, had asexual forms of P. falciparum on a peripheral-blood smear, were older than 12 years, were not in the first trimester of pregnancy, were not intravenous drug users. Each patient underwent a full clinical examination that included detailed neurological assessment. A complete blood count, estimation of the life-cycle stage of the parasite, biochemical analyses and measurements of plasma glucose were done. Blood was obtained by a finger -prick for hematocrit measurements and blood smears were done every 8 hours until three consecutive smears were negative for asexual stages of P. falciparum. 40 patients out of 80 got intramuscular

Quinine hydrochloride (20 mg per kilogram of body weight followed by 10 mg per kilogram every eight hour) and 40 received intramuscular artemether (4 mg per kilogram followed by 2 mg per kilogram every eight hours).Both drugs were given for a minimum of 72 hours.

## RESULTS

Total 80 patients were enrolled in the study. On calculating the gender distribution in our study population we noted that the no of females were 21 out of total 80 patients while the no of males were 59. Same is shown in the following table.

On comparing the gender distribution in the two treatment regimens in our study population, we observed that in Quinine treatment regimen, 54.2%were males while 38.1% were females. While in case of Artemether 45.8%were males while 61.9% were females. The gender distribution in the two treatment regimens is shown in the following table.

**Table-I. Gender distribution in the study population (n=80)**

| Gender | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Male | 59 | 73.8% | 73.8% | 73.8% |
| Female | 21 | 26.3% | 26.3% | 26.3% |
| Total | 80 | 100% | 100% | 100% |

We calculated the no of responders and non-responders in female population. The no of female responders in artemether regimen was 10 while it was 3 in case of quinine. The same is shown in the following table.

**Fig-1. Gender distribution shown on Pie-chart (n=80)**

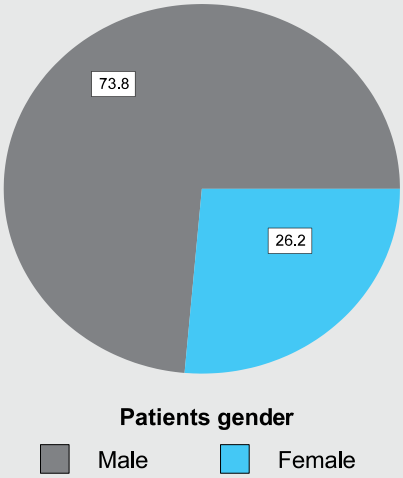



**Fig-2. Bar chart showing the gender distribution in the two treatment regimens (n=80)**

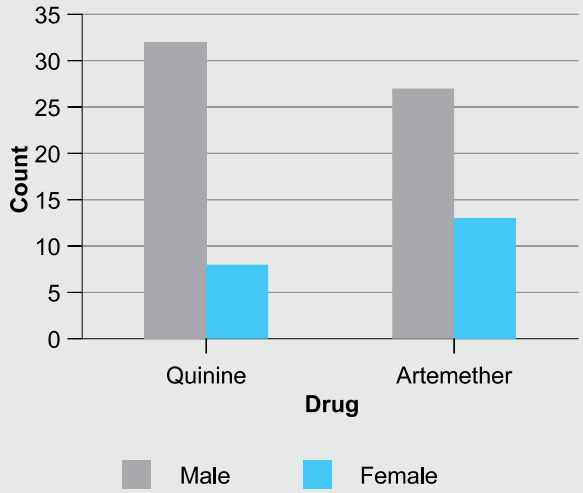



**Table-II. Gender distribution in the two treatment regimens (n=80)**

| | | | Patients | | Total |
|---|---|---|---|---|---|
| | | | Male | Female | |
| Drug | Quinine | Count % with in patients gender | 32 (54.2%) | 8 (38.1%) | 40 (50.0%) |
| | Artemether | Count % with in patients gender | 27 (45.8%) | 13 (61.9%) | 40 (50.0%) |
| Total | | Count % with in patients gender | 59 (100%) | 21 (100%) | 80 (100%) |

**Table-III. Frequency of responders and non responders in female population (n=21)**

| Gender Female | Drug | |
|---|---|---|
| | Quinine | Artemether |
| | Response | Response |
| Responders | 3 | 10 |
| Non responders | 5 | 3 |

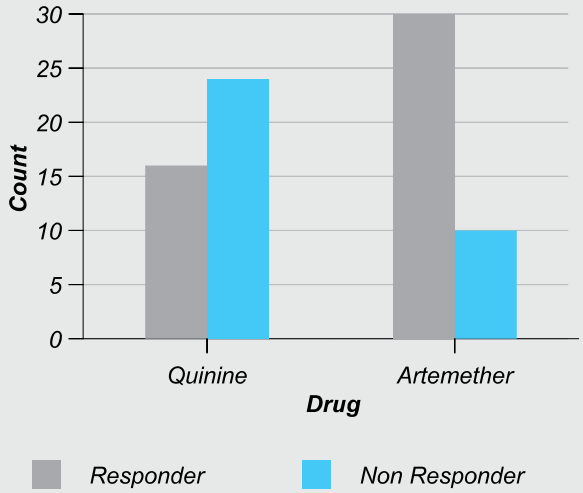
Out of total 80 patients,40 were given artemether and 40 were given quinine. The response in terms of clearance of MP slide was compared between the two regimen groups. Out of 40, 16 patients responded to quinine while 24 did not respond. Out of 40 patients treated with artemether, 30 responded while 10 did not. On calculating the frequency of responders in the two drug regimens, it was observed that the responders in case of Quinine were 34.8% while in case of Artemether the frequency of responders was 65.2%.The frequency of non-responders in Artemether was 29.4% while it was 70.6% in Quinine. Same distribution is shown in the following table.

For calculating the p value and the statistically significant or insignificant difference between the two treatment regimens.

Chi-square test was used to test the significance, if the P-value is less than or equal to 0.05, considered significant. As the P- value is less than .01, so we can say that there is very strong evidence.

So there is statistical difference in the response to the two treatment regimens.(P=.0022).

**Fig-3. Bar chart showing the frequency of responders and non-responders in two treatment regimens (n=40 in each group)**




## DISCUSSION

Malaria is the world's most important parasitic infection[3]. Although it has been eradicated from temperate zones, increasing number of travelers from temperate areas each year visit tropical countries, where the disease remains a major cause of morbidity and death[4]. The treatment of malaria has changed over the past two decades in response to declining drug sensitivity in Plasmodium falciparum and a resurgence of the disease in tropical areas.

Unfortunately the incidence of plasmodium falciparum malaria is significantly high among troops of Armed Forces. This incidence can be attributed to the development of resistance by plasmodium falciparum to commonly used anti- malarial drugs. Keeping in view this resistance of plasmodium falciparum, this study has been carried out to conduct a comparison between the

**Table-IV. Frequency of responders and non responders in the two treatment regimens (n=40 in each group)**

| | | | Response to drug | | Total |
|---|---|---|---|---|---|
| | | | Responder | Non responder | |
| Drug | Quinine | Count % with in response to drug | 16 (34.8%) | 24 (70.6%) | 40 (50.0%) |
| | Artemether | Count % with in response to drug | 30 (65.2%) | 10 (29.4%) | 40 (50.0%) |
| Total | | Count % with in response to drug | 46 (100%) | 34 (100%) | 80 (100%) |

two regimens of treatment & formulate the most effective and appropriate one to prevent fatal outcomes and disabling complications from this deadly disease. It was a comparative study, which was carried out at the Medical Unit of Pakistan Air Force Hospital Lahore which is a sole tributary of a large area of central and Northern Punjab. This hospital is equipped with an advanced and well-equipped Laboratory and Radiology dept.

In my study a total of 80 patients were included from all socioeconomic strata. They were more than 12 years old, had positive MP slides for P. falciparum malaria, were not in the first trimester of pregnancy, not infected with other plasmodia and were not IV drug abusers. They were divided into two treatment groups; 40 patients out of 80 got intramuscular Quinine hydrochloride (20 mg per kilogram of body weight followed by 10 mg per kilogram every eight hour) and 40 received intramuscular artemether (4mg per kilogram followed by 2mg per kilogram every eight hours). Both drugs were given for a minimum of 72 hours.

In a similar study performed by Singh NB at Manipur proved that the parasites were cleared more quickly from the blood in artemether group when compared to quinine group, but resolution of fever was comparable in both artemether and quinine groups. In another similar study performed by Michael Boele van Hensbrook, MD proved that the time for complete clearance of the P. falciparum malaria was shorter in artemether group as compared to quinine group. In another similar study, a large no of patients were included. This was performed by Tran Tinh Hien MD in Vietnamese Adults. This study proved that artemether treatment was associated with quicker clearance of parasite from peripheral blood but slower resolution of fever, and longer hospitalization.

Similar studies were conducted in our country too[5-12]. In one study conducted at Jinnah Post Graduate Medical Institute demonstrated that artemether had better recovery rate than quinine[13]. Similar study conducted at DI Khan showed similar results[14]. In my study there were statistically significant difference between the two treatment groups(p=.0022). So the response to artemether is better than quinine in P. falciparum malaria. This response of artemether may be better because of the better efficacy of the drug. But we cannot rule out the possibility of change in environmental conditions or development of resistance to frequently used quinine in P. falciparum malaria though no such report is documented in the literature.

## CONCLUSIONS

Artemether is an effective alternative to Quinine for falciparum malaria. Its response in P.falciparum malaria is better than Quinine. The sample size of the study was not large enough to predict that such results represent the true picture of the whole population. Being a developing country; malaria will remain the most common infectious disease in Pakistan, so it is recommended that a study should be conducted at a larger level to compare the response to these two regimens in P. falciparum malaria.



## REFERENCES

1. Seaton RA. Trevett AJ. Wembri JP. **Randomized comparison of intramuscular artemether and intravenous quinine in adult, Melanesian patients with severe or complicated, Plasmodium falciparum malaria in Papua New Guinea.** Ann Trop Med Parasitol 1998; 92:133-6.

2. Haided G ,Caudhry MA, Shah MA, Munir SM. **Quinine compared to Artemether in adults with cerebral malaria.**! Surg Pakistan 2002;7:34-5.

3. Edstein MD, Walsh DS, Eamsila C. **Malaria prophylaxis/radical cure: recent experiences of the Australian Defence Force.** Med Trop (Mars) 2001;61:56-9.

4. Nosten F, Vincenti M, Simpson J. **The effects of mefloquine treatment in pregnancy.** Clin Infect Dis 1999; 28:380.

5. Irshad M. Imran L. Suleman M. **A study of cerebral malaria in Multan.** Pakistan Ped J Decl998;20:175-80.

6. Bhalli A, Samiullah. **Falciparum malaria — A review of 120 cases.** J Coll Physicians Surg Pak May 2001 ;11:300-3.

7. Memon I, Kanth N, Murtaza G. **Chloroquinine resistance in Children.**! Pak Med Assoc Apr 1998;48:98-100.

8. Durrani A, Durrani I, Abbas N, Jabeen M. **Epidemiology of cerebral malaria and its mortality.**! Pak Med Assoc Aug 1997;48:213-5.

9. Aslam M, Raymond A, Smego, Raza S, Beg A, **Emerging drug - resistance and Guidelines for treatment of malaria** J Coll Physicians Surg Pak May 2004; 14(5): 319-24.

10. Waseem T, Haider T, Bhatti N, Hafiz A. **Cerebral Malaria – clinical presentations in adults at Mayo Hospital, Lahore Pakistan.** Biomedica Dec 1996;12(2):143-5.

11. Khan S A, Anwar M, Hussain S, Qureshi A H, Ahmad M. **Comparison of optimal malarial test with light microscopy for the diagnosis of malaria.** J Pak Med Assoc Aug 2004; 54(8):404-7.

12. Murtaza G, Iqbal A. **Clinical update antimalarial drugs in plasmodium falciparum malaria.** J Coll Physicians Surg Pak Dec 2000; 10(12):484-8.

13. Haided G, Caudhry MA, Shah MA, Munir SM. **Quinine compared to artemether in adults with cerebral malaria.** J Surg Pakistan 2002; 7:34-5.

14. Sheraz JK, Munib S. **A comparative clinical trial of artemether and quinine in cerebral malaria.** Rawal Med J Dec 2005; 30:62-4.

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