ORIGINAL ARTICLE

COMPARISON OF EFFICACY OF CHLOROQUINE AND ARTEMETHER/LUMAFANTRINE IN TREATING *VIVAX* MALARIA IN THALL AND SURROUNDING AREA

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Background: Fever is the main complaint in patients reporting to our hospital and the most common cause of fever in our set up is malaria. The aim of this study was to know about the clinical response, efficacy and resistance of *vivax* malaria to chloroquine in patients reporting to Thall Scouts Hospital. **Methods:** All the adult male patients reporting to Thall Scouts Hospital with fever and other symptoms of malaria having slide positive *vivax* malaria were included in the study. Both thick and thin slide were used for the diagnosis and species determination of malaria. Age group of the patients was from 18–40 years old. The study was conducted for the period of two years. **Results:** Total number of patients included in the study was 518. Of the 518 patients, 374 (72.2%) responded to chloroquine and the remaining 144 (27.8%) were given Arthemether/Lumafantrine combination. Having positive symptoms of malaria total 374 patients treated with chloroquine 171 (45.72%) were asymptomatic after 24 hours, 98 (26.2%) after 48 hours, 78 (20.86%), after 72 hours of treatment while 27 (7.22%) were found to be resistant to chloroquine. Of the 144 patients having positive malaria treated with Artemether/Lumafantrine 62 (43.06%) were asymptomatic after 24 hours, 65 (45.14%) after 48 hours, 13 (9.03%) after 72 hours while 4 (2.78%) had still positive symptoms of malaria. **Conclusion:** *Vivax* malaria in our set up is sensitive to both Chloroquine and Arthemether/Lumafantrine. As Chloroquine is a cheap and easily available drug, so it can be safely given to patients with *vivax* malaria. It will also decrease the total cost of the disease.

Keywords: Malaria; *Vivax*; Chloroquine; Artemether; Plasmodium

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INTRODUCTION

According to world health organization (WHO), about 1.6 million cases of malaria are occurring in Pakistan.[1] Of these, about 67% malaria cases are caused by *vivax* species while the falciparum is responsible for the remaining third.[2] For all uncomplicated cases of malaria, chloroquine was the drug of choice for more than fifty years.[3] With the emergence of plasmodium parasites resistant strains, the efficacy of different anti-malarial drugs has been questioned. Studies conducted in most part of the Asia mainly from Indonesia have reported *P.vivax* resistance to chloroquine.[4–6] In Pakistan, *P.falciparum* resistance to chloroquine is almost established.[7,8] Reports of different studies carried out during 2006 in Pakistan showed that p.*vivax* is still sensitive to chloroquine but some resistance is also found.[9] For the treatment of *P.falciparum* malaria, chloroquine is no longer recommended. The use of Sulfadoxine Pyrimethamine+Artesunat for the treatment of uncomplicated *P.faciparum* malaria is as a first line therapy in Pakistan was started in 2008.[10] But still in some part of the world, mostly African countries, fever in children is treated with anti-pyretic, home remedies and chloroquine.[11] Studies in Sub Sarahan Africa have shown such home based treatment to be effective in children with fever.[12,13] In our study, we treated all diagnosed cases of *vivax* malaria with chloroquine and Arthemether/Lumafantrine. With clinic improvement of these patients with both group of drugs, we presumed that *vivax* malaria in this part of Pakistan is sensitive to chloroquine yet some resistance has developed.

MATERIAL AND METHODS

The study was conducted in Thall scouts hospital, frontier corps (FC), Khyber Pakhtunkhwa province of Pakistan. Thall district is located at the junction of north Wazirstan agency, Kuram Agency and Orakzai agency. This hospital is a primary health care centre where only FC soldiers and their families are treated. In this setup, we had a small laboratory, where all baseline investigations are done. This study was conducted for the duration of two years.

Only adult male with *vivax* malaria and who had positive malaria symptoms were included in the study. Actually, this is serving soldier hospital and here facilities for only male admission are available.

Exclusion criteria included children and female patients with malaria as no admission facilities are available for these patients. Malaria was confirmed by doing both thick and thin slides. The tests were performed by expert technicians who were being trained in combined military hospitals. All the patients with *vivax* malaria were admitted in the hospital and standard dosage of chloroquine was given. The patients remain admitted in the hospital till they were asymptomatic for at least 48 hours.

Treatment outcome were evaluated by modifying WHO protocol which are used for measuring anti-malarial drug efficacy. Such modified protocols have been used in some other studies also.[14] We defined treatment failure (TF) as recurrence of fever on day 3–14. In absence of fever, on day 3–14 was defined as adequate clinical response (AR), without meeting any of the criteria of treatment failure. Fever was defined as auxiliary temperature of more than or equal to 37.5 °C we also studied the malaria parasite density in blood of patients before and after treatment under microscope.

RESULTS

Total no of patients with *vivax* positive in this study were 518. Only male patients with age group from 18–40 years were included in the study as most of the serving soldiers lie in this age group. All of them were given chloroquine, of which 374 (72.2%) patients responded to chloroquine with the mean recovery days of 1.90±0.973 and rest of 144 (27.8%) were given Artemether/ Lumafantrine and all of them responded to it with the mean recovery days of 1.72±0.745 as given in the table. Of the 374 patients responded to chloroquine 171 (45.72%) were asymptomatic after 24 hours, 98 (26.2%) after 48 hours, 78 (20.86%) after 72 hours while 27 (7.22%) shows resistance to Chloroquine even after 72 hours, although these 27 patient's symptoms were not as so much worse after three days of treatment as was on the time of admission to hospital on first day, however these malaria patients were still having positive malaria sign and symptoms which were put on alternative medication to get quick recovery. Of the total 144 patients treated with Artemether/Lumafantrine, 62 (43.06%) were asymptomatic after 24 hours, 65 (45.14%) after 48 hours and 13 (9.03%) 72 hours and 4 (2.78%) had still positive symptoms of malaria which were treated with alternative medicine to get quick recovery. Independent t test was applied to see the fever resolution with both treatment with equal variance assumed and equal variance not assumed. The p value in both cases was less than 0.05 which show statistically significant response as shown in table-1.

Table-1: Comparison fever resolution in malaria patients with chloroquine and Arthemether/Aumafantrine

Medicine Given	Total Patients	Mean Days of Recovery	*p*-value
Chloroquine	374	1.90±0.973	0.00
Arthemether/Lumafantrine	144	1.72±0.745	

DISCUSSION

In many parts of the world, chloroquine has been used in both prophylaxis and treatment of malaria. It is the cheap and easily available drug. P. *vivax* resistance to chloroquine has been reported in the pacific[4], part of Asia[15,16] and Latin America[17] but very little observed in Afghanistan and Pakistan[18] and p. *vivax* remains sensitive to chloroquine in India[19,20]. Incidence of *vivax* malaria has increased in some part of the world. The ratio of p. falciparum to *vivax* has changed from 1.1:1 in 1999 to 0.8:1 in 2001. This increase in p. *vivax* emergence can be attributed to: change in anopheles fauna, effective treatment response of p. falciparum to new drugs and emergence of *vivax* malaria resistance to chloroquine.[21] Emergence of chloroquine resistance strains is not the only cause of treatment failure.[22] Treatment failure could also be due to poor drug quality, malabsorption of drug, relapse of malaria, recrudesce of parasitemia and low drug level of drug.[23]

Our study showed 92.78% sensitivity and 7.22% resistance of *vivax* malaria to chloroquine. Other studies done on *vivax* sensitivity to chloroquine in different parts of Pakistan[9,18], India and Afghanistan[19,20] also showed little resistance of *vivax* to chloroquine. Although their results show very little resistance as compared to our study, indicated the increasing trend of chloroquine drug resistance in Pakistan.

In our study, we studied various symptoms of malaria which were noted during therapy and the patients were consider relieve of malaria when these symptoms disappear which was further confirmed by analysing patient's blood under microscope with decrease in parasitic density. Symptoms like body aches, headache, nausea and vomiting were all included in our study. All of the patients were treated with both chloroquine or Lumafantrine/Artemeter, along with anti-pyretic and in some cases these patients were hydrated with intravenous fluids. All the patients responded to this treatment without any complication. The total cost of this treatment was less than 200 rupees as compared to those who were treated in private clinics where the cost was more than thousands of rupees. Most of those patients were treated with parental chloroquine, intravenous fluids and multi vitamins.

We observed during the study that incidence of vomiting with chloroquine could be reduced by first settling down fever and once the fever is settled then to start oral chloroquine. In addition, some patients could not tolerate taking four tablets of chloroquine at a time. So, giving patients two tablets of chloroquine and then to wait for 4–5 minutes and then to give the two tablets were well tolerated by the patients. The most common adverse effects observed with chloroquine therapy were itching and gastritis, which responded well to chlorpheneramine and H2 blocker drugs. Though we observed excellent clinical response of *vivax* malaria to chloroquine, it resulted in significant loss of working days, which is of great concern in military, and Para military set up.

CONCLUSION

Vivax malaria in our set up is sensitive to both Chloroquine and Arthemether/Lumafantrine. As Chloroquine is a cheap and easily available drug, so it can be safely given to patients with *vivax* malaria. It will also decrease the total cost of the disease.

AUTHORS' CONTRIBUTION

SMA: Statistical analysis and manuscript writing. SAS: Data collection. RJA: Concept review. SR: critical Analysis. FM: Proof Reading

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