IS CHLOROQUINE STILL EFFECTIVE FOR THE TREATMENT OF VIVAX MALARIA IN CHILDREN IN NORTHERN PUNJAB OF PAKISTAN?

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ABSTRACT

Introduction: Every year more than one billion persons in the world suffer from malaria. It kills about 1-3 million people in the world per year. In Pakistan estimated burden of malaria is 1.6 million cases each year. As most of people belong to poor socioeconomic group, it is essential that cost effective remedial measures must be taken. Moreover judicious use of antimalarials is required to avoid development of resistance.

Objective: To determine the frequency of types of malaria and frequency of cases responding to chloroquine as first line treatment in vivax malaria in children of Northern Punjab of Pakistan.

Study Design: Descriptive study.

Place and Duration of Study: From Jun 2011 to Sept 2012 at Combined Military Hospital Gujranwala in children reporting from surrounding areas both rural and urban with clinical suspicion of malaria.

Materials and Methods: During the study period, 175 children were admitted with clinical suspicion of malaria. Out of which 102 were smear positive for malarial parasites, 13 cases were excluded from the study as they lost to follow up, leaving a total of 89 children in the study.

Patients under study remained admitted till the fever settled and malarial parasites were negative on smear. Chloroquine was used as first line treatment in cases with vivax malaria. On discharge from hospital, parents of children were advised fortnightly follow up for 28 days.

Results: Out of 89 children approx 54% were males and 46% were females. Mean age of participants was 5.91 years. The minimum age was 1 year and maximum 11 years (SD ± 3.09) out of the 89 cases, 84 (94.3%) had vivax malaria, 2 (2.24%) had falciparum malaria and 3 (3.37%) had mixed infection. Our study showed that 79 (94%) cases of vivax malaria fully responded to chloroquine, 5 (6%) cases treated with Chloroquine reported with relapse.

Conclusion: Chloroquine is still the drug of choice in vivax malaria.

Keywords: Vivax malaria, Chloroquine, children.

INTRODUCTION

Malaria is a deadly mosquito-borne disease, which affects 300-500 million people with approx 1-3 million deaths each year[1]. Pakistan with a population burden of more than 180 million is among the countries where malaria continues to be a major public health problem. Extensive agricultural practices in the country, coupled with haphazard urbanization, poor sanitary conditions, heavy monsoon rains and floods contribute to the malariogenic potential[2]. Malaria is predominantly the disease of rural areas where more people live below the poverty line (38.65%).

Between 1966 and 2002, only 11% (47 out of 435) of published antimalarial drug trials assessed antimalarial efficacy in vivax malaria. This reflects the challenges of conducting such studies and interpreting the clinical drug efficacy for P.vivax. The delay in diagnosis of vivax malaria and the application of partially effective treatment regimens with inability to reliably cure the dormant stages of the parasite, all significantly contribute to host morbidity and socio-economic burden of the disease.

Chloroquine (CHQ) has been the ideal, time tested, miraculous drug for malaria control because it is low in cost, low in toxicity, effective

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against all forms of malaria, relatively easy to manufacture and chemically stable, and thus is readily stored and transported, even under extreme climatic conditions. CHQ remained the drug of choice for treatment and prophylaxis of malaria in endemic countries since 1940-1990[3]. It was launched in 1934 as a cheaper alternative of quinine. It is rapidly absorbed when taken orally. Its max concentration is reached within 1-2 hours and remains up to 3-4 hours after oral administration[4]. After the first report of vivax malaria resistance to chloroquine in 1989 ,multiple combination therapies have been suggested.

These new drugs and combinations are now available and being used injudiciously for treatment of vivax malaria due to fear of chloroquine resistance. This puts extra burden on health care delivery system due to high cost of treatment and exposes patients to their untoward effects. It is known that malaria is the disease of poor and underprivileged, which further emphasizes the need for less expensive drugs.

Keeping in view the sudden upsurge in malarial cases in our hospital during last summer and response to treatment, we felt the need to reappraise CHQ efficacy in our local population. This study was designed to see the effectiveness of chloroquine as first line drug in vivax malaria

MATERIALS AND METHODS

The study was approved by ethical committee of CMH Gujranwala. Written consent was taken from parents of participants. Findings were recorded on a specially designed proforma. During the study duration, 175 children were admitted with clinical suspicion of malaria. Out of which 102 were smear positive for malarial parasites, confirmed in each case by thick and thin slides[5].

Patients were admitted till the fever settled and malarial parasites were negative on smear examination. CHQ was used as first line treatment in vivax malaria. On discharge from hospital, parents of children were advised fortnightly follow up for 28 days, 13 cases were excluded from the study as they were lost to follow up; leaving a total of 89 children. Children reporting with relapse of vivax malaria were treated with weekly maintenance doses of chloroquine (5 mg base /kg).

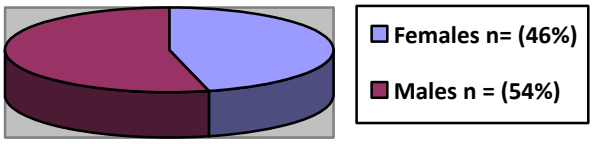

Figure-1: Percentage of male and female children in the study (n=89).

Table-1: Frequency of various types of malaria (n=89).

Species	n (%)
Vivax	84 (94.3)
Falciparum	2 (2.24)
Mixed	3 (3.37)

Table-2: Frequency of cases responding to chloroquine in cases of vivax malaria (n=84).

	n (%)
Children fully responding to Chloroquine	79 (94)
Cases reported with relapse after successful treatment	5 (6)

RESULTS

Results had been analysed using SPSS version 13. Descriptive statistics were used to describe the results. Percentages of male and female children were noted. Age of participants was expressed in mean and SD. Out of 89 children approx 54% were males and 46% were females (Figure-1). Mean age of participants was 5.91 years. The minimum age was 1 year and maximum 11 years and (SD ± 3.09).

Out of the 89 cases, 84 (94.3%) had vivax malaria, 2 (2.24%) had falciparum malaria and 3 (3.37%) had mixed infection (Table-1). Our study showed that 79 (94%) cases of vivax malaria fully responded to chloroquine and 5 (6%) cases

treated with Chloroquine reported with relapse (Table-2).

DISCUSSION

Early malariologists categorized P.vivax and P. falciparum on the basis of paroxysmal fever episodes occurring after interval of approx 48 hours and high complication rate of P. Falciparum[6] compared to P.vivax. They separated the two species into malignant and benign malaria respectively. P. vivax only rarely causes death secondary to infarct or rupture of the spleen. However some studies document more severe symptoms with vivax malaria possibly due to higher levels of inflammatory cytokines per parasitized cells[7].

Combined Military Hospital Gujranwala is a secondary care hospital taking the patient burden of not only cantonment area, but also surrounding rural population. Therefore, the sample population was representative of the whole community of this Punjab region. Majority of patients were from low income group with village background.

In this study, male to female ratio was 1.17:1 and it matched with study conducted in school children of rural areas of Bannu[8]. While some studies show high prevalence of malaria in male sex[9] possibly due to more exposure of male children to mosquito bite.

In our study, frequency of vivax malaria was higher 84 (94.3%) which correlated with study carried out in district Kharan[10] in which 88.69% cases were identified as Plasmodium vivax infection and 11.30% cases with P. Falciparum. However low incidence of vivax malaria is seen in other regions of the country[11], while mixed malarial infections in this study were 3 (3.37%) and it matched with the local study from Multan[12] which documented mixed malarial infection rate up to 2.3%, while in our study falciparum malaria cases were 2 (2.24%) which is in contradiction to most of studies conducted in other parts of the country[13,14] and it is possibly because of regional variations in prevalence of Plasmodium species .

Our study showed that 79 (94%) cases of vivax malaria fully responded to chloroquine (Table-1). While relapse occurred in 5 (6%) of vivax malaria treated cases. This finding strongly recommends the use of Chloroquine in vivax infection and correlats with studies conducted in Azerbaijan[15], Afghanistan and Pakistan[16]. Moreover surveys in Thailand[17] and India[18], showed uniform sensitivity to chloroquine.

Weekly maintenance dose of 5 mg Chloroquine base /kg was started to children who reported with relapse. This strategy was adopted due to non availability of Primaquine in the market. Although there is no such recommendation in the literature for use of Chloroquine on weekly basis but we have found excellent result of this regime as these five cases were kept under constant surveillance till the study was concluded, and not a single patient reported with fever due to vivax malaria. However this weekly maintenance dose schedule can be given a fair trial in future and further studies in a poor country like ours are required till the time a better, affordable or effective alternative is available.

No untoward reaction or side effects of CHQ were noted during our study so we support use of economical, time tested and effective medicine like CHQ in vivax malaria as first line drug. Despite widespread CHQ resistance in Plasmodium species[19], cost and availability continue to favour CHQ as the drug of choice in most poor third world countries. In these malaria-endemic regions, two major factors that contribute to the emergence of CHQ-resistance parasites are CHQ self-medication and prophylactic use of CHQ in all types of malaria. As the market is now flooded with new combinations of antimalarials which are quite expensive. These research products and their combinations should be reserved for resistant malarial cases or in life threatening situations, which are often seen with falciparum or mixed infections.

In cases of relapse of vivax infection, we found weekly maintenance dose of Chloroquine, an effective remedy. However to prevent CHQ resistance we strongly recommend to treat blood smear positive vivax malaria cases.

CONCLUSION

This study supports use of chloroquine as the first line treatment in cases of vivax malaria .It is therefore strongly recommended that an examination of MP smear is mandatory in diagnosing type of malarial infection before starting antimalarials. More work is needed to be done to look for an easily available, less expensive and safe alternative to Primaquine to completely cure relapse of vivax infection.

REFERENCES

1. Guerin PJ, Olliaro P, Nosten F, Druilha P, Larminarayan R, Binka F, et al. Manson's Tropical Diseases. Philadelphia, PA: WB Saunders; 2003; 1205-95.
2. WHO, 2000. The World Health Report 2000. Fighting disease, fostering development. Report of the Director-General, WHO.
3. Patel KN, Patel JK. A Review - Qualitative and quantitative analysis of antimalarial drugs and their metabolites in body fluids. J Curr Pharm Res 2010; 2: 5–14.
4. Cooper R.G and Magwere T. Chloroquine: novel uses and manifestations. Indian J Med Res 2008; 127: 305-16.
5. Microscopic procedures for diagnosing malaria. Appendix. MMWR Surveill Summ 2003; 52: 15.
6. Khan SJ, Shah N, Ali M. Efficacy of loading versus standard doses of quinine in cerebral malaria. RMJ 2011; 36: 86-8.
7. Baird JK. Resistance to therapies for infection by Plasmodium vivax. Clin. Microbiol. Rev. 2009; 22: 508-34.
8. Awan ZUR, Khan AK, Shah AH, Suleman M and Khan MA. Assessment of malaria prevalence among school children in rural areas of Bannu District Khyber Pakhtunkhwa, Pakistan. Pakistan J. Zool. 2012; 44: 321-6.
9. Ud din J, Khan SA, Ally SH. Malaria in children: study of 160 cases at a private clinic in Manshera. J Ayub Med Coll Abbottabad 2006; 18: 44-5.
10. Yasinzai MI and Kakarsulemankhel JK. Incidence of human malaria infection in desert area of Pakistan: District Kharan. J Agri. Soc. Sci. 2008; 4: 39–41.
11. Yasinzai MI, Kakarsulemankhel JK. A study of prevalence of malaria infection in urban areas of district Quetta, Pakistan. Pak J Zool 2004; 36: 75-9.
12. Yar HM, Masood K, Maqbool A and Malik GQ. Prevalence of malarial parasite species in Multan district. The Professional 1998; 5: 183–7.
13. Ejaz A, Haqnawaz K, Hussain Z , Butt R, Awan Z I, Bux H. Treatment of uncomplicated plasmodium falciparum malaria with quinine doxycycline combination therapy. J Pak Med Assoc 2007; 57:502-5.
14. Yasinzai MI, Kakarsulemankhel JK: Prevalence of human malaria infection in bordering areas of East Balochistan, adjoining with Punjab: Loralai and Musakhel. J Pak Med Assoc 2009, 59: 132-135.
15. Valibayov A, Abdullayev F, Mammadov S, Gasimov E, Sabatinelli G, Kondrachine AV, et al. Clinical efficacy of chloroquine followed by primaquine for Plasmodium vivax treatment in Azerbaijan. ActaTropica 2003; 88:99–102.
16. Kolaczinski K, Durrani N, Rahim S, Rowland M. Sulfadoxine-pyrimethamine plus artesunate compared with chloroquine for the treatment of vivax malaria in areas co-endemic for Plasmodium falciparum and P. vivax: a randomised non inferiority trial in eastern Afghanistan. Trans R Soc Trop Med Hyg 2007; 101:1081–7.
17. Tasanor O, Ruengweerayut R, Sirichaisinthop J, Congpuong K,Werndorfer WH, Na-Bangchang K. Clinical-parasitological response and in-vitro sensitivity of Plasmodium vivax to chloroquine and quinine on the western border of Thailand. Trans R Soc Trop Med Hyg 2006; 100: 410–8.
18. Valecha N, Joshi H, Eapen A , Ravinderan J, Kumar A, Prajapati KS, et al. Therapeutic efficacy of chloroquine in Plasmodium vivax from areas with different epidemiological patterns in India and their Pvdhfr gene mutation pattern. Trans R Soc Trop Med Hyg 2006; 100: 831–7.
19. Farooq U and Mahajan RC. Drug resistance in malaria. Vect Borne Dis 2004; 41:45-53.