EFFICACY OF CHLOROQUINE MONOTHERAPY AGAINST PLASMODIUM VIVAX MALARIA

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ABSTRACT

Objective: To determine the in vivo efficacy of chloroquine monotherapy against Plasmodium (P.) vivax and frequency of relapse/reinfection.

Study Design: Quasi-experimental study.

Place and duration of study: Department of Medicine, Combined Military Hospital, Quetta Balochistan, from July 2006 to February 2007.

Patients and Methods: One hundred and ninety one subjects with positive plasmodium vivax slide were included in the study. Mean, median, minimum and maximum values along with standard deviation of age and parasite clearance time were calculated. Frequency of relapse/reinfection was estimated and significance was determined by applying test of significance.

Results: Of the 191, 21 developed P.vivax relapse/reinfection in the six months follow up. Mean duration of relapse/reinfection was 37.76 days while mean parasite clearance time was almost 30 hours in both initial infection and relapse.

Conclusion: Chloroquine monotherapy is still effective in the management of P.vivax malaria in our set up and antirelapse therapy is not routinely indicated.

Key words: Chloroquine, Monotherapy, Plasmodium vivax, Relapse/reinfection, Malaria

INTRODUCTION

Plasmodium (P.) vivax threatens almost 40% of the world's population, resulting in 132-391 million clinical infections each year. Most of these cases originate from Southeast Asia, Western Pacific and Africa. Although often regarded as a benign and self-limiting infection, there is increasing evidence that the overall burden, economic impact, and severity of disease from P. vivax have been underestimated. Malaria control strategies have had limited success and are confounded by varying numbers of relapses occurring at different intervals as a result of activation of dormant liver-stage hypnozoites after the initial infection[1]. Parasite or host factors that determine the number and timing of relapses are unclear[2]. The reported risk of relapse is variable in different parts of the world as it is ten times in Thailand as compared to India and twice that in Brazil[3]. The distinction between relapse and reinfection is very difficult due to non availability as well as inaccurate results of newer diagnostic methods[4-6]. In view of increasing reports of failing chloroquine efficacy and disappointing results of various anti relapse therapy and their side effects[7]. This study was designed to determine the in vivo efficacy of chloroquine monotherapy in P. vivax malaria and frequency of relapse/reinfection in this highly malaria endemic area.

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PATIENTS AND METHODS

This prospective non-interventional quasi-experimental study was conducted from July 2006 to February 2007 at a tertiary care hospital i.e. Combined Military Hospital, Quetta, Balochistan. One hundred and ninty one subjects fulfilling inclusion criteria (between 12 to 60 years of age, positive Plasmodium vivax slide) were enrolled in the study with non-probability sampling technique after taking informed consent. Subjects with either pregnancy, history of antimalarial drug intake during the current disease or other co morbid preexisting conditions were excluded.

Blood samples of all suspected cases of malaria reported in the hospital were drawn for diagnosis and species of parasite was determined by Leishman stained blood smears following WHO recommendations[8].

After establishing the diagnosis, detailed clinical evaluation was done and information was recorded in a previously designed proforma.

All subjects were hospitalized and treated with chloroquine monotherapy. (10mg/kg stat followed by 5mg/kg after 6 hrs and daily for two days). Subjects were discharged after confirming the clearance of parasitemia with Leishman stained blood smear. Subjects were followed for six months for relapse/reinfection of P. vivax infection.

Frequency of P. vivax relapse/reinfection was determined. Mean, median, range and standard deviation of age, parasite clearance time and duration of relapse/reinfection were calculated. Frequency of thrombocytopenia, anaemia and leucopenia were estimated.

RESULTS

One hundred and ninety one subjects with P. vivax malaria were enrolled in the study. Their mean age was 28.44 ± 7.63 years with the range of 12-51 years. Majority (96.9%) of subjects were male.

Mean parasite clearance time with chloroquine monotherapy was 30.48 hours. The detailed account of study outcome is mentioned in table.

Thrombocytopenia (less than 150 x 10^9/l) was observed in almost 75% of subjects but none bled despite fall of platelets upto 16 x10^9/l. Anemia and leucopenia was noted in 29% and 21% subjects respectively. Hypoglycemia (less than 2.2mmol/l) was not present in any of the enrolled subject at the time of clinical evaluation. Serum urea and creatinine were within normal limits in all individuals.

Of the 191, 21 developed P. vivax relapse/reinfection in the next six months. Mean duration of relapse/reinfection observed in this study was 37.76 days with the range of 12-86 days. Mean parasite clearance time remained unchanged with the relapse/reinfection.

DISCUSSION

This study demonstrates in vivo efficacy of chloroquine monotherapy against P. vivax malaria and frequency of relapse/reinfection over six months. Majority of subjects were male in this study as it was carried out in a military hospital, which mainly looks after soldiers[9].

The relapse/reinfection rate observed in this study was 11%. Multiple episodes of P.vivax malaria within a person may be attributable to treatment failure, reinfection or relapse. Treatment failure was excluded by confirming the clearance of parasitemia at the end of treatment. However relapse could not be differentiated from reinfection in this study due to non availability as well inaccurate results of newer molecular techniques.6 Most studies on the subject also reported a combined risk or rate of reinfection and relapse due to same

Table: Comparison of findings in subjects with and without relapse/reinfection

Parameters	Relapse n = 21(11%)	Without relapse n=170(89%)
Age (Years)	Mean 26.14 Median 29 Range 12-51 Standard deviation 5.67	Mean 28.72 Median 30 Range 14-43 Standard deviation 9.26
Gender (n)	Male 21 Female 0	Male 164 Female 6
Parasite clearance time (Hours)	Mean 29.43 Median 27 Range 6-60 Standard deviation 17.59	Mean 31.53 Median 33 Range 6-64 Standard deviation 16.04
Duration of relapse (Days)	Mean 37.76 Median 56 Range 12-86 Standard deviation 20.09	_

reasons[4,5]. Earlier studies[10-14] showed variable relapse rate in different parts of world ranging from 0.62% to 65% depending on the duration of follow up. This wide variation may also be due to difference in sample size ranging from 40 to 235 or due to possible inclusion of increased number of cases with reinfection.

Mean duration of relapse/reinfection observed in this study was 37.76 days. This outcome is highly variable in existing documented data. An Iranian study showed relapse risk of 16.8% and 24.5% in one and two years after the primary attack[15] while most of the other studies followed the patient for a shorter period ranging from three to four weeks[10,12,14]. This late relapse in our study as compared to previous studies may be an incidental finding but requires prolonged follow up for relapse from future researchers.

Parasite clearance time with chloroquine monotherapy in this study was almost unaffected (approx 30 to 31 hours) with the number of relapse/reinfection. This is close to one of the previous studies on the subject in Vietnam (24 hours) 16 but far from the others ranging from 49 to 67.2 hours[15,16]. This disparity may be due to difference in sample size as 113 subjects were included in Vietnam study while in others it was ranging from 26-39 cases.

CONCLUSION

Chloroquine monotherapy is still treatment of choice in P. vivax infection. Due to low frequency of relapse in this region antirelapse therapy is not indicated in routine however regular monitoring is needed to detect any alteration in the current status.

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