Original Article

Therapeutic Efficacy of Chloroquine vs Artemether/lumefantrine Combination in Vivax Malaria in Nowshera and Surroundings

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ABSTRACT

Objective: The study's main objective is to find the therapeutic Efficacy of chloroquine vs. artemether/lumefantrine combination in vivax malaria in Nowshera and its surroundings.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at department of medicine, CMH hospital, Nowshera, from June 2019 to January 2020.

Materials and Methods: The data was collected from 121 patients with malaria. Total vivax-infected patients were divided in two groups. The Chloroquine group consisted of 62 patients, and Artemether/Lumefantrine group had 59 patients. All patients under investigation were male patients due to the non-availability of a facility for female admissions in the treatment centre. All study participants received the P. vivax infection treatment plan in accordance with national medication policy. The data was gathered and analyzed using SPSS 20.0. Each value was expressed as the mean SD.

Results: The patient's mean age was 29.39 years and range between 19 to 57 years. Both groups showed similar resolution in fever after 24 hours. Mean hemoglobin, bilirubin, ALT and ALP were 14.4 g/dl, 9.7 µmol/L, 45.2 U/L, and 168.2 IU/L respectively. After applying the chi-square test, the difference in response to treatment with Chloroquine and Lumefantrine/Artemether was insignificant (p-value=0.35). However, the mean time in resolution of symptoms was less in the Chloroquine group. No significant adverse effects were experienced with both treatments.

Conclusion: It is concluded that there is no difference in response to treatment with Chloroquine and Lumefantrine/Artemeter for Vivax Malaria in the Nowshera and suburbs.

Key Words: Malaria, Vivax, Chloroquine, Artemether/Lumefantrine

Citation of article: Khan SMD, Sheram SA, Malik MF, Shafi H, Anjum K, Afzal A. Therapeutic Efficacy of Chloroquine vs Artemether/lumefantrine Combination in Vivax Malaria in Nowshera and Surroundings. Med Forum 2022;33(10):53-56.

INTRODUCTION

Plasmodium vivax infection is a serious worldwide health problem. This particular malarial parasite type has the greatest global distribution among the five that may infect humans. Between 80 and 300 million clinical cases of P. vivax are believed to happen annually, and around 2.5 billion people are expected to be at risk for malaria.

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Received: April, 2022
Accepted: July, 2022
Printed: October, 2022

Although P. vivax is largely native to Southeast Asia and Latin America, it has recently been discovered in Ethiopia and Sudan [1]. In Sudan, malaria is a serious and widespread health issue that resulted in an estimated 9 million illness episodes and 44,000 deaths in 2002 [2].

One of the key elements of the World Health Organization's plan to lower malaria-related mortality is early diagnosis and successful treatment with the right medication. P. vivax infections need to be treated right away with efficient antimalarial drugs. Chloroquine continues to be the primary treatment for P. vivax in the majority of malaria-endemic countries, even though ACT has been accepted by the majority of these nations to lower the danger of P. falciparum strains that exhibit treatment resistance [3]. But there is growing proof that the effectiveness of chloroquine against P. vivax is declining, especially in Southeast Asia. Therefore, it is suggested to use ACT against both P. vivax and P. falciparum, particularly in a nation like Sudan where chloroquine is no longer approved or readily [4].

Chloroquine resistance against P. vivax was first reported from Papua New Guinea in 1989. Since then, a number of nations have reported treatment failures with chloroquine, including Myanmar, Turkey, Ethiopia, Vietnam, Indonesia, Korea, and Madagascar. 2011 saw the first Chloroquine-resistant P. vivax cases reported in Thailand, while the treatment with Chloroquine is still working in India [5].

The WHO recommended AS + SP to treat uncomplicated P. falciparum infections in 2007 after learning that Pakistan had developed chloroquine resistance. However, the national treatment recommendations were changed in 2017, and the recommended first-line treatment for uncomplicated P. falciparum malaria is artemether-lumefantrine (AL) administered coupled with a single low dose of primaquine. This was done in response to the most recent findings from India as well as the rapidly rising AS + SP treatment failure rates in Somalia and Sudan (varying from 12% to 22%) [6]. In a study conducted by Zubairi et al. [7], P. vivax and P. falciparum were shown to be responsible for 83% and 13% of cases, respectively; P. vivax infection affected 79.9% of patients with severe malaria. According to another study, P. vivax prevalence varied from 2.4% in Punjab Province to 10.8% in Sindh Province. P. falciparum infection rates varied from 0.1% in Islamabad to 3.8% in Balochistan. [8]

Since Vivax is prevalent in Pakistan, this study is planned. The study's primary objective is to find the therapeutic Efficacy of chloroquine vs. artemether/ lumefantrine combination in vivax malaria in Nowshera and its surroundings.

MATERIALS AND METHODS

This cross-sectional study was conducted at CMH hospital Nowshera from June 2019 till Jan2020. The data was collected retrospectively from 121 malarial patients who confirmed *P. vivax* infection. The information was collected from male patients. According to the national drug policy, all study participants were treated with the treatment regimen used for P. vivax infections. Based on this, the patients were divided into two groups. They received a six-dose regimen of artemether-lumefantrine twice daily for three days, followed by an extra 0.25 mg/kg/d for 14 days. If patients vomited 30 minutes after taking the medication, the dose was again given. After receiving the trial drug's initial dose, patients who frequently vomited were removed from the research. While the ingestion of primaquine was not directly seen, On-site personnel oversaw the three-day artemether-lumefantrine therapy. Because it is believed that hospitals have a low prevalence of this ailment, research subjects were not tested for glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to receiving primaquine; nonetheless, trustworthy data on this deficiency in hospitals are difficult to come by. Primaquine therapy had to be stopped, and participants had to be removed from the trial if they showed signs of haemolytic anaemia (jaundice, black urine, abdominal discomfort, back pain, low haemoglobin level, etc.) during the follow-up appointments. Clinical examination was conducted on days 0, 1, 2, 3, 7, 14, 21, and 28. It included taking the axillary temperature and Giemsa staining of thick and thin blood films. Finger sticks produced thick and thin blood stains. In the thick patch, there were several asexual parasites found per 200 white blood cells, indicating parasitemia. After 100 high-power fields, the thick film was judged negative when no parasite was found. On days 0, 7, 14, 21, and 28, blood was wiped onto filter paper for follow-up and stored for DNA analysis. The data was gathered and analyzed using SPSS 20.0. Each value was expressed as the mean SD.

RESULTS

The study consisted of 121 patients. The Chloroquine group consisted of 62 patients, and Artemether/Lumefantrine group had 59 patients. All patients under investigation were male patients due to the non-availability of facilities for female admissions in the treatment centre. The patient's mean age was 29.39 years and range between 19 to 57 years. On lab investigations, the following was evident: Mean hemoglobin, bilirubin, ALT and ALP levels were 14.4 g/dl, 9.7 µmol/L, 45.2 U/L, and 168.2 IU/L respectively.

Out of the 62 patients in the Chloroquine group, 57 (91.9%) responded with a resolution of fever and parasitemia within 24 hrs. And there was no recurrence of fever till 28 days. The remaining 5 (8%) patients were afebrile within 48 hours. All patients (100%) responded to treatment. In the Lumefantrine/Artemether group, also all patients responded to treatment. Out of the 59 patients, 50 (87.4%) were afebrile within the first 24 hours. 8 (13.6%) patients responded within 48 hours with a resolution of fever. One patient, however, responded in even more than 48 hours.

Table No.1: Stratification with the Efficacy of both drugs

Treated groups	Afebrile in			Total
	24Hrs	24-48 Hrs	>48 Hrs	
Chloroquine	57	5	0	62
Lumefantrine/ Artemether	50	8	1	59
Total	107	13	1	121

P-value = 0.354 which is not significant

After applying the chi-square test, the difference in response to treatment with Chloroquine and

Lumefantrine/Artemether was insignificant (p value=0.35). However, the mean time in resolution of symptoms was less in the Chloroquine group. No significant adverse effects were experienced with both treatments.

DISCUSSION

In Pakistan, malaria is a serious public health issue. P. vivax malaria is currently gaining increasing attention [7] in addition to the Plasmodium falciparum parasite, which is resistant to almost all antimalarial medications. Rarely, P. vivax can result in serious consequences that are even fatal, but it accounts for around 50% of all malaria cases, which is a significant burden for Pakistan. Vivax malaria is becoming more common. All age groups are affected by the majority of vivax malaria, which is common in regions with limited immunity and low endemicity. During a 2-month follow-up after falciparum malaria treatment, 20-40% of cases will have detectable vivax parasitemia [8]. Primaquine must occasionally be administered at a high dose (30 mg/day) for a lengthy period of time (14 days) in order to completely eradicate the hypnozoite stage of the parasite in vivax malaria, which has a return incidence between 20 and 40% in the first 1-2 months following an acute attack [9–10].

The cumulative risk of P. vivax and incidence of recurrence over a 12-mo period could be quantified due to the lengthy research duration and repeated administration of the same treatment regimen for each episode of malaria [11]. The rate of infection represents the effect that the related policy change will probably have. Patients who only received CQ or AL experienced four to five recurrences overall, with an incidence rate of about two episodes each PYO. The incidence rate was reduced by four times, from two to one attack per PYO, with the inclusion of a supervised 14-day PQ regimen. The total mg/kg dose given affects the radical cure with PQ [6]. By 2020, Pakistan has set goals to lower the burden of malaria by 75% in areas with high endemicity and to eradicate it entirely in areas with low endemicity [12]. However, efforts to further control and eradicate malaria will be severely impeded if artemisinin resistance spreads westward from nearby South East Asian regions [8]. Achieving these goals requires early detection of antimalarial drug resistance through molecular epidemiology research.

Our study shows that the mean age of the patients was found to be 29.39 years. All the patients were males because the hospital didn't have any facility to admit female patients. This was due to social and cultural restrictions that were to be followed. In this study, the results we obtained were quite obvious, in the chloroquine group out of 62 patients, 57 (91.93%) were afebrile in the first 24 hours, whereas in the lumefantrine group, 50 (84.7%) patients out of 59 patients were afebrile in the first 24 hours. The p-value was less than 0.05; hence, this difference in the results is insignificant. This result shows that there are no differences in the effects of both the drugs as far as the number of patients concerned that were afebrile in the first 24 hours of the administration. The results of this study also showed that no adverse reactions were reported in either of the groups. The cost of the treatment in both groups was also comparable, and there were no significant differences between the two groups. Our results are similar to the studies conducted by krudsood et al. [14] and Eibach et al [10].

CONCLUSION

We conclude that the treatment of P. Vivax can be done effectively with either Chloroquine or the combination drug Lumefantrine/Artemether. The cost of the treatment is almost similar. However, the combination of two drugs, i.e lumefantrine /artemether, is easier to manage regarding the dosing schedule, and the patient's compliance is also good.

Author's Contribution:

Concept & Design of Study:	Sardar Muhammad Daud Khan
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Revisiting Critically:	Sardar Muhammad Daud Khan
Final Approval of version:	Sardar Muhammad Daud Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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