Original Article

Efficacy of Arthemether-Lamefuntrine In Malaria

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Abstract

Objective: To determine the efficacy of Arthemether-Lamefuntrine (AL) in patients with malaria. **Study Design:** Quasi-experimental study. **Place and Duration of study:** Study was conducted in Medical Unit DHQ Hospital Sargodha and Medical Unit V, DHQ Hospital Faisalabad from 1st January 2011 to 30 June 2011. **Subjects and Methods:** 129 adult patients both male and female diagnosed to have malaria both on clinical and laboratory examination were included in the study. Patients were given AL (20/120) 2 tablets 12 hourly for three days. An adequate clinical and parasitological response (ACPR) was defined as absence of fever and parasitaemia (negative slide for Malarial parasite) by day 45 after end of treatment. **Results:** Out of 129 patients adequate response (ACPR) was seen in 122 patients with efficacy of 94.6%. **Conclusion:** AL is an important and effective treatment option for treatment of patients with malaria. **Key Words:** Malaria, Arthemether-Lamefuntrine (AL), Malarial Parasite.

INTRODUCTION

Malaria affects an estimated 300 million people and causes more than a million deaths per year World-wide.[1] According to World Health Organization (WHO, 1993) study group malaria is a major killer of mankind and is responsible for 300 to 500 million clinical cases and 1.5 to 2.7 million deaths per year.[2] More than 100 million cases occurring in sub-Saharan Africa alone and with an estimated one million deaths, mostly in infants and children.[2] Falciparum and vivax malaria are major health problems in Pakistan. In the last decade there has been a six fold increase in falciparum malaria, which now comprises 42% of all malaria cases recorded by National Malaria Control Program. Factors associated with the upsurge include chloroquine resistance across the country, warmer autumns favoring prolonged transmission and a chronic decline in vector control activities.[3] In one recent study in Pakistan the over all incidence of Plasmodium was 43.44%, Plasmodium vivax was observed to be the highest (88.69%) as compared with to *P. falciparum* (11.30%).[4] The World Health Organization (WHO) recommends that artemisinin-based combination therapies (ACTs) be used as first-line treatment for uncomplicated *Plasmodium* falciparum malaria.[5] A large evidence base is now available to demonstrate the efficacy of Artemether-Lamefuntrine (AL) in the treatment of uncomplicated malaria in a range of patient types and locations worldwide, but particularly for *P. falciparum* infections. This includes the most extensive data for any ACT in children and pregnant women the two populations most vulnerable to malaria.[6-9] AL also offers the most extensive safety data base of all ACTs.[10] Resistance to lumefantrine in field isolates has not yet been convincingly demonstrated, an important advantage attributed to the relatively short half-life of lumefantrine.[11] AL have also been found to be effective for all stages of Plasmodium vivax malaria.[12] The rationale of this study was effectiveness of AL in patients presenting with malaria in our setting, as limited data is available in Pakistan regarding the use of AL in patients with malaria.

MATERIALS AND METHODS

It was a Quasi-experimental study, conducted in Medical Unit, DHQ Hospital Sargodha, Medical Unit-V DHQ Hospital Faisalabad between 1st January 2011 to 30th June 2011. After taking Informed Consent 129 adult patients of age >15 both male and female diagnosed to have malaria in outpatient and Inpatient departments on the basis of history, clinical examination presenting with high grade fever, shivering, headache etc, and investigation showing positive slide for Malarial parasite were included in the

study. Patients having pregnancy, documented intake of AL, any other anti malarial or another sulfa-drug in the two weeks prior to recruitment, other causes of fever, evidence of underlying chronic diseases (cardiac, renal, hepatic, malnutrition), history of allergy to study drug or known allergy to other sulpha drugs such as cotrimoxazole and being non-resident in the study area were excluded from the study. Patients included in the study were given Artemether-Lamefuntrine (AL) (20/120 mg) in a dose of 2 tablets 12 hourly for 3 days. Patients were advised to record their temperature twice daily and were asked to report back to hospital after completion of treatment. An adequate clinical and parasitological response (ACPR) was defined as absence of fever and parasitaemia (negative slide for Malarial parasite) by day 45 after end of treatment. All the data was recorded on performa.

DATA ANALYSIS PROCEDURE

All data were entered and analyzed through SPSS version 15. Categorical variables like Gender, Symptoms, Malaria Parasites etc were presented as frequencies and percentages. Numeric variables like Age were expressed as Mean ± S.D. Chi-square test was used to see the significant difference between Gender and Symptoms. P value < 0.05 was considered as statistically significant.

RESULTS

In our study a total of 129 patients were included in the study. 83 patients were male and 46 were female. (Table1) Table 2 shows the frequency of different symptoms of patients. 128 patients were having High grade fever, 122 were having shivering, 95 were having vomiting, 120 had severe headache and 31 had other complaints. Table 3 shows the follow up response of patients. It shows that at the end of treatment, 122 patients were improved both clinically as well as by absence of Malarial parasite on thick and thin slide for Malarial parasite at day 45 (ACPR achieved). 7 patients did not show improvement on both clinical examination and laboratory investigations and did not achieve ACPR. Table 4 shows Mean± Standard Deviation for Quantitative Variables such as Age. Table 5 shows Chi-square test used to see the significant difference between Gender and Symptoms.

Table-1
Gender of Patients

Variables	n=129	n%
Male	83	64.3%
Female	46	35.7%

Table-2
Symptoms of Patients

Symptoms	n=129
High fever	128
Shivering	122
Vomiting	95
Severe Headache	120
Others	31

Table-3
Follow up Response

Response	n=129	%n
Improved (achieved ACPR)	122	94.6%
Not Improved (not achieved ACPR)	07	5.4%

Table-4
Age of Patients

Variables	N	Minimum	Maximum	Mean ± S.D
Age (years)	128	15	72	30.5 ± 14.3

Table-5
Relation between Gender and Symptoms

	Gender		P-Value
	Male (n=46)	Female (n=83)	
Symptoms			
High fever	46 (100%)	82 (98.8%)	***< 0.001****
Shivering	42 (91.3%)	80 (96.4%)	***< 0.001****
Vomiting	30 (65.2%)	65 (78.3%)	***0.065****
Severe Headache	44 (95.7%)	76 (91.6%)	***< 0.001****
Others	11 (23.9%)	20 (24.1%)	0.803

DISCUSSION

Falciparum malaria has high mortality as it causes complications like cerebral malaria, renal failure and algid malaria.[1] Different medications and different combinations are available worldwide for the treatment of malaria. AL combination has been widely used worldwide. AL also offers the most extensive safety data base of all ACTs, being the most widely used ACT for falciparum malaria worldwide, with over 400 million treatments having already been distributed.[10] AL is highly effective against the blood stages of P. *vivax infection,* consistent with results from trials of

AL in falciparum malaria.[13,14] It is important to note that fever resolution is rapid following AL therapy.[15,16,17] Parasite clearance is rapidly achived in vivax infected patients.[15,16,17] The rate of parasite clearance was markedly faster with artemether and artesunate than with the other non-ACT antimalarials. Randomized, multicenter trials during 2005–2009 in Africa [18-26] and Asia [27-29] have each demonstrated a PCR-corrected cure rate greater than 95% after AL treatment in a variety of populations and settings. Factors associated with the upsurge include chloroquine resistance across the country, warmer autumns favoring prolonged transmission and a chronic decline in vector control activities.[3,30] In our study, response to treatment with AL was 94.6% which is almost equal to different studies conducted worldwide. This study showed no unexpected safety concerns in almost all patients treated with AL. These results are consistent with those of other studies that demonstrated excellent safety and tolerability of AL.[31,32] High grade fever and headache are the most important and common complaints of patients presenting in present study with malaria. Recently a pooled analysis regarding the effectiveness of AL in malaria especially falciparum malaria was published in 2011. It showed that in almost 2,000 patients, the PCR-corrected cure rate for AL treatment of uncomplicated *P. falciparum* malaria exceeded 95% in adults and children, and showed a good safety and tolerability profile and rapid reduction in gametocytemia, and recommended that AL should be used as first-line treatment of uncomplicated *P. falciparum* malaria in patients of all ages.[5]

CONCLUSION

This study confirmed the excellent efficacy and safety of the AL in adult patients with malaria. AL offers an important treatment option in treatment of Malaria in Pakistan where Quinine resistance and other factors are making Malaria one of the most common and life threatening infectious disease in the country.

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