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KEY WORDS: "Quinine, Artesunate, Malaria"

COMPARATIVE STUDY OF ARTESUNATE VERSUS QUININE REGIME IN PEDIATRIC PATIENTS WITH SEVERE MALARIA.

Dr Aditi Lingayat* Professor, Department of Pediatrics, Govt. Medical College & Cancer Hospital, Aurangabad, Maharashtra *Corresponding Author

Dr Rakesh Chikhlonde Assistant Professor, Department of Pediatrics, Govt. Medical college & Hospital, Aurangabad, Maharashtra

ABSTRACT

Aims & Objectives:
1. To study artesunate versus quinine regime in treatment of pediatric patients with severe malaria.
2. To study adverse effects and outcome in pediatric patients with severe malaria.

Material and methods: This study is done in admitted pediatric patient at Government Medical College, Aurangabad from January 2014 to October 2015 in age group of 0 to 12 years having severe malaria.
Those who fulfilled criteria of severe malaria were enrolled in the study. History was taken in detail & general & systemic examination was done. All necessary investigations were carried out. Patients were randomized in group A (n = 42) to receive Artesunate and group B (n = 42) to receive Quinine regime alternately. This randomization made at the time of admission. Treatment regime are used as per National Guidelines 2011 for diagnosis and treatment of malaria. Efficacy of both drugs was compared.

Results: Most common age group in group A was between 0 to 1 years and in group B was 1 to 5 years. Maximum number of cases in group A was Female (61.9%) and in group B was Male (52.38%), maximum number of patients in group A (69.04%) and in group B (57.14%) had fever clearance time of 1 to 2 days in both groups. Maximum number of patients in group A (66.66%) had coma resolution of 6 to 24 hrs and in group B (71.4%) had 24 to 48 hrs. Maximum number of patients (50%) in both groups had parasite clearance time at 12 to 24 hrs in group A and 24 to 48 hrs in group B. Maximum number of patients in group A (40.47%) had duration of hospital stay to be 5 to 10 days and in group B (47.61%) to be 10 to 15 days. Maximum number of patients in group A had vomiting (38.1%) followed by nausea (33.3%) as compared to group B had nausea (29.4%) followed by vomiting (20.6%) as adverse effect. Mortality in group A is 5 (11.9%) as compared to group B 7 (16.66%).

Conclusion:
1. The different variant studied after antimalarial treatment with Artesunate and Quinine regime were comparable and no statistically significant difference was found.
2. In the present study adverse effect of both the groups were comparable and no statistically significant difference was found.
3. In the present study mortality in both groups were comparable and no statistically significant difference was found.

Introduction

Malaria is the most important parasitic disease in the world and remains of highest public health importance. It is a major communicable disease that affects approximately 149 – 274 million clinical cases and causes 0.7 to 2.7 million deaths every year worldwide. About 36% of the world population i.e. 2020 million is exposed to the risk of contracting malaria in more than 90 countries.[1]

In India about 27% population lives in malaria high transmission (> 1 case/ 1000 population) areas and about 58% in low transmission (0-1 case/1000 population) area. Malaria is curable if effective treatment is started early. Delay in treatment may lead to serious consequences including death. Prompt and effective treatment is also important for controlling the transmission of malaria.[2]

In past chloroquin was effective for treating nearly all cases of malaria. In recent studies, chloroquin resistant P. falciparum malaria has been observed with increasing frequency across the country. The continued treatment of such cases with chloroquin is probably one of the factor responsible for increased proportion of P. falciparum relative to vivax.

A revised national drug policy on malaria has been adopted by Ministry of Health and Family welfare, Govt. of India in 2010 and these guidelines have been prepared for healthcare personnel including clinicians involved in the treatment of malaria.

There is belief that Artesunate should be preferred over quinine in treatment of malaria. According to national guidelines both drugs are equally effective in case of severe malaria. This study is being done to throw a light about this present issue.[3]

Materials and methods

All pediatric patients below 12 yrs of age having severe malaria as per national malaria guidelines 2011 admitted and treated in pediatric ward in Govt. Medical College and Hospital, Aurangabad from January 2014 to October 2015 are included in this study.

Patients with severe malaria with chronic illness like CRF, Chronic liver disease and known case of G6PD deficiency and known case of cardiac disease are excluded.

Institutional ethics committee approval and informed consent were obtained. After fulfilment of criteria of severe malaria children were randomly divided alternately in to two groups.

Group A – 42 patients of severe malaria receiving Artesunate regime.

Group B - 42 patients of severe malaria receiving Quinine regime.

After admission detailed history was taken. General examination and systemic examination carried out for all patients. Laboratory investigations done like peripheral smear for malarial parasite on admission and then repeated every 12 hrly until two successive blood films were negative. Other investigations like TLC, DLC, Hb, RDT, LFT, KFT, Chest X rays, ECG, Plasma glucose level, CSF Examination & Blood culture were also done. Coagulation studies and other necessary investigations are done whenever indicated.

Patient assigned to the Artesunate group received Artesunate 2.4 mg/ kg IV given on admission (time = 0), then at 12 hrs and 24 hrs, then once a day for 7 days (along with either clindamycin or doxycycline) shifted to oral therapy once child is able to swallow.

And those assigned to Quinine group received Quinine 20mg/kg on admission (IV infusion in 5% dextrose / dextrose saline over 4 hrs) followed by maintenance dose of 10mg/kg 8 hrly. Once patient can take oral therapy patient is shifted on oral therapy and complete course of 7 days is given along with doxycycline.

(Doxycycline is contraindicated in children below 8 yrs so instead clindamycin is used.)

Supportive treatment was given in all patients as needed like antibiotics, antipyretics, anticonvulsant, IV fluids, blood and blood component, transfusion therapy.

The data was compiled, analyzed and tabulated. For comparing quantitative data 'unpaired t' test was applied. For qualitative assessment chi square test and fisher extract test were done. Statistical analysis was performed with the help of software 'Graph Pad Prism 5'.

Results,

Efficacy of both drugs was compared in relevance to clinical improvement, Glossgow coma scale score, Fever clearance time, Parasite clearance time, Mortality, Morbidity, Total duration of hospital stay and adverse effect of drugs.

Table 1 showing clinical profile

Sr. no.	Parameter	Group A	Group B	P value
1	Age	3.35 ± 3.17	3.45 ± 3.20	0.06
2	Sex			
	Male	16 (38.1%)	22 (52.4%)	0.19
	Female	26 (61.9%)	20 (47.6%)	
3	Symptoms			
	Pallor	40 (34.2%)	35 (32.1%)	0.08
4	Clinical presentation			
	Impaired consciousness	21 (26.3%)	15 (17.4 %)	0.19

The mean age and sex in both groups were comparable and no statistically significant difference was found of different symptoms studied like chills and rigors, pallor, jaundice, altered sensorium, multiple convulsion etc. Pallor was commonest in both groups. In study of different clinical presentation like hyperpyrexia, severe anemia, impaired consciousness, hypoglycemia, renal failure etc. Impaired consciousness / coma was found to be the commonest clinical presentation in both groups.

Table 2 showing different variables after the antimalarial treatment in patients of severe malaria

	GROUP A (MEAN ± SD)	GROUP B (MEAN ± SD)	P VALUE
Fever clearance time (Days)	2.13 ± 1.32	2.13 ± 1.32	0.06
Coma clearance time (hours)	26.00 ± 21.07	30.20 ± 22.09	0.62
Parasite clearance time (hours)	28.00 ± 4.38	34.60 ± 14.53	0.52
Total duration of hospital stay (Days)	9.84 ± 4.69	9.77 ± 4.61	0.63

The different variable studied after antimalarial treatment with Artesunate and Quinine regime were comparable and no statistically significant difference as found.

Table 3 showing adverse effects of drugs

ADVERSE EFFECTS OF DRUGS	GROUP A	GROUP B
Vomiting	8 (38.1%)	7 (20.6%)
Nausea	7 (33.3%)	10 (29.4%)
Headache	6 (28.6%)	5 (14.7 %)
Tinnitus	0 (0.00%)	3 (8.8%)
Vertigo	0 (0.00%)	2 (5.9%)
Slurring of speech	0 (0.00%)	2 (5.9%)
Hypoglycemia	0 (0.00%)	5 (14.7 %)
TOTAL	21 (100%)	34 (100%)

Maximum number of patients in Group A had vomiting (38.1%) as compared to Group B had nausea (29.4%) as adverse effect.

Table 4 showing complications in patients of severe malaria

Complications	GROUP A	GROUP B
Neurological Sequelae	9 (50%)	10 (35.7%)
CCF	1 (5.5%)	3 (10.7%)
Renal failure	2 (11.1%)	3 (10.7%)
DIC	1 (5.5%)	2 (7.1%)
Respiratory Failure	3 (16.6%)	3 (10.7%)
Hepatic Impairment	2 (11.1%)	7 (25%)
TOTAL	18 (100%)	28 (100%)

Maximum number of patients in Group A had complications in the form of neurological sequelae (50%) followed by respiratory failure (16.6%). In Group B it was neurological sequelae (35.7%) followed by hepatic impairment (25%).

Table 5 showing mortality in patients of severe malaria.

MORTALITY	GROUP A (N=42)	GROUP B (N=42)	P VALUE
Dead	5 (11.9%)	7 (16.7%)	0.53
Alive	37 (88.1%)	35 (83.3%)	
Total	42 (100%)	42 (100%)	

Chi square Test for Trend; p value >0.05 not significant (@ 95% CL)

In the present study mortality in both the groups were comparable and no statistically significant difference was found.

Discussion

All pediatric patient below 12 yrs having severe malaria as per the national malaria guideline 2011 admitted in pediatric ward in government medical college and hospital Aurangabad from January 2014 to the October 2015 were enrolled in study, 42 cases in each group.

Aim of the study was comparison of Artesunate versus Quinine regime in treatment of severe malaria in pediatric patients along with to study clinical profile and outcome in severe malaria and to study adverse effects of Artesunate and Quinine regime in treatment of severe malaria. We found following observations.

In our study commonest symptom is pallor. This similar to study done by Adedapo A. D. etal (2007)[4] and this might be due to pediatric age group and had cerebral malaria as a common manifestation.

In the present study impaired consciousness or coma is commonest clinical presentation in both groups. Similar findings is in the study done by Al-Taiar A etal (2006)[5]. While Tripathy R etal[6] found respiratory distress (22%) and Mocken F.P etal[7] found circulatory collapse (21%) as commonest presentation in their studies. This variation in presentation might be because of varied presentation of cerebral malaria and late arrival of patients to the hospital in these cases.

In the present study fever clearance time in both the groups were comparable and no statistically significant difference were found. In contrast Nayak etal (2011)[8] and Adam etal (2002)[9] reported the fever clearance time to be significant less in Artesunate group than Quinine this might be due to studies done in adult population.

Nayak etal[8] reported significantly shorter coma resolution time in Artesunate group (31 hrs) than in Quinine group (64 hrs) and might be due to adult age of study population. In contrast Hien etal (1993) and Hensbroek etal (1996)[10] reported a significantly shorter parasite clearance time with Artesunate than Quinine (72 versus 90 hrs) and might be due to studies done adult age and Artesunate given by intramuscular route.

In the present study duration of hospital stay in both the group were comparable and no statistically significant difference was found. While study done by Rolling etal (2013)[11] reported the

duration to be 11 days in Artesunate and 19 days with Quinine, this variation might be because of small sample size in above study.

In our study neurological sequelae is the commonest complication in both groups and the findings are similar to the studies done by Price R etal (1999)[12] in the study of 86 patients of severe malaria. The adverse effect of both the groups were comparable and no significant statistical difference were found. Some studies have reported nausea, vomiting, headache, tinnitus, vertigo with Quinine treated group, and this might be because of Quinine given by intramuscular route or given in any isotonic fluid instead of 5% dextrose or 10% dextrose. Mortality in our study in both Artesunate and quinine group is comparable and not statistically significant. Some of studies that reported Quinine had a reduced mortality compared to Artesunate is not statistically significant and sample size used was small[13,14].

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