47.011
A Study of Complicated Falciparum Malaria and Efficacy of Arteether in Children in Endemic Area of India

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Malaria has re-emerged as main public health problems. In tropical countries resulting in significant morbidity and mortality. Plasmodium falciparum is responsible for potentially fatal infections.

Aims and Objectives:

(1) To evaluate the efficacy of Arteether in the treatment of complicated malaria
(2) To analyze clinical spectrum of hospitalized cases of falciparum and virex malaria.

Material and Methods: The study at Urban Private Hospital Patients with pyrexia and slides positive for P. falciparum. Out of 75 patients 24 were children with complicated malaria. A dose of Arteether (2.5 mg/Kg.) once daily by intra-muscular injection for 3 consecutive days, patients remained hospitalised, the therapeutic response was assessed on clinical parameter and smears for parasites.

Results: Out of 75 smear positive 24 children of complicated malaria. 1 to 17 year age, clinical symptoms fever, hyperpyrexia 100%, vomiting 40%, headache 15%, icterus 35%, altered sensorium 25%, oligourea 10%, bleeding 5% weakness, bodyache, loss of appetite, insomnia. Splenomegaly and hepatomegaly > 2 cm in 82% and 78%. serum bilirubin > 3 mg% and elevated SGOT, SGPT > 3 times, serum creatinin > 3 mg% and blood urea > 40 mg% renal failure. Severe anaemia Hb < 5 mg%. Complicated falciparum malaria with jaundice and hepatic dysfunc- tion. 33.3%, cerebral malaria 25%, renal failure 13.3%, haemoglobiniria 0.4%, severe anemia with symptomatic involvement 33.3%.

The therapeutic response was assessed on clinical parameters and smears for parasites. Level of consciousness started improving with in 24–48 hours and full consciousness 48 to 72 hour Fever clearance 24 to 48 hours. Serum bilirubin levels start decreasing 3 days normal within 7-days. Serum creatinine normal within 7 days Anemia in children with arteether patient responded well. Splenomegaly regressed in one month, parasitic clearance with arteether within 2 days, in 22 patients four week 92% of cure rate in complicated P. falciparum malaria.

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47.012
The Effect of Cyclic Adenosine Monophosphate (cAMP) Modulators on the Activity of Selected Anti-Malarial Drugs

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Background: Malaria is a major global health problem with high mortality rates especially in children below five years of age. A severe limitation of chemotherapy is the rapid emergence of resistance to most available anti-malarials. Because of the slow development of new effective anti-malarials, an alternative strategy is therapy optimization using existing drugs. Combination therapy has been shown to delay the onset of resistance and improve the efficacy of treatment. This study’s objective was to establish the activity of several cyclic Adenosine Monophosphate (cAMP) modulators as potential components of combination therapy.

Methods: The cAMP modulators; forskolin, Sp-adenosine 3′ 5 cyclic monophosphorothiate triethylammonium salt, 9-cyclopentyladenine and 2′ 5′ dideoxyadenosine 3′ monophosphate were tested in vitro in combination with chloroquine, quinine, mefloquine, amodiaquine and doxycycline against the chloroquine sensitive strain (D6) and the chloroquine resistant strain (W2) of Plasmodium falciparum. Parasite susceptibility testing was performed using a semi-automated micro-dilution technique. The Inhibitory Concentration at 50% (IC50) was calculated for each drug and in fixed combinations. Isobolograms were plotted using the calculated Fractional Inhibitory Concentration at 50% (FIC50).

Results: One of the AC-inhibitors, in combination with quinine showed synergistic interactions at all concentration ratios for both the D6 and W2 strains (FIC50s < 0.92 at all concentrations). The other anti-malarial/cAMP modulator combinations demonstrated a range of responses but mainly exhibited antagonistic interactions.

Conclusion: These in vitro findings suggest that the AC inhibitor, 2′ 5′ dideoxyadenosine 3′ monophosphate, potentially enhanced the anti-malarial activity when combined with quinine and should be further evaluated. The other anti-malarial/cAMP Modulator combinations did not show the same potential.

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47.013
IgG Profile Against MSP3 Antigen in Asymptomatic Carriers of Plasmodium falciparum in Eastern Sudan

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Background: Malaria is an important cause of morbidity, however not everyone infected with the parasite develops clinical symptoms. Naturally acquired immunity to malaria varies considerably between geographical regions due to different parasite strains and transmission intensities which affect the selection of vaccine targets. Merozoite surface protein 3 (MSP3) is a polymorphic antigen induces immune response. This study measured the presence of antibodies to P. falciparum MSP3 recombinant antigen in plasma from asymptomatic individuals in relation to protection from malaria during the transmission season.

Methods: The study was conducted in an area of seasonal transmission on a cohort of 114 asymptomatic sub-patent P. falciparum carriers who were examined for the presence of IgG, IgG1 and IgG3 by ELISA. The cohort was treated
in the pre-transmission season (August 2004) with Artemether + Sulphadoxine/Pyrimethamine and followed for 14 days. They were screened for malaria in the following transmission season (October 2004). Further samples were collected in October 2006.

Results: Detected anti-MSP3 antibodies on Day0 of treatment were 41%, 20% and 12% for IgG, IgG1 and IgG3 respectively. Positive percentage on Day14 after treatment were 25%, 12% and 9% for IgG, IgG1 and IgG3 respectively and in 2006 were 33.3%, 21% and 6% for IgG, IgG1 and IgG3 respectively. Twenty six and 16 individuals had IgG1 or IgG3 or both on Day0 and Day14 respectively, all of them were slide negative in the next transmission season. In October 2006, 24 had IgG1 or IgG3 or both, 19 were slide negative.

Conclusion: Pre-season treatment has no significant effect on the number of reactive antibodies (p > 0.05). There was no significant association between IgG presence and malaria infection in 2006 (p > 0.05), despite approximately same IgGs positivity in 2004. Anti-MSP3 IgG1 and IgG3 could contribute to the persistence of asymptomatic low parasitaemia during the dry season. Different epitopes between recombinant and natural MSP3 antigen stimulate different IgGs response. That should be considered when assessing vaccine trails.

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47.014

Determination of Parasite Clearance Time in Antimalarial Drug Trials Using Real-Time Quantitative PCR (PCR)

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Microscopy is generally relied upon for malaria diagnosis and determination of parasite density. However in drug efficacy trials where high throughput screening is required, microscopy is slow, labour intensive and unable to detect low-grade infections reliably. Estimation of parasite density in antimalarial drug trials is important as endpoints such as time to parasite clearance or percentage reduction in the initial parasitaemia level allows comparison of the efficacy of different drug combinations. In this study, Real-time Quantitative PCR (qPCR) was used to determine parasite clearance time in an efficacy trial of two antimalarial drugs, Artemether-Lumefantrine combination (Coartem®) and Pyronaridine-Artesunate combination (Pyramax®). Blood samples were collected at 8-hourly intervals following treatment from each of the 106 patients enrolled in the study. The resulting 10 samples per patient collected over a 3-day period were analyzed by qPCR amplification of the 18SrDNA gene to determine the time to parasite clearance. The results indicate that low-grade parasitaemia (<20 parasites/μL) was still detectable by qPCR in 20% of the patients up to 24 hours after they were negative by microscopy. Our results indicate that the application of a more sensitive parasite detection method such as qPCR, could lead to more precise determination of the relative efficacy of antimalarial drugs.

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47.015

Peritoneal Dialysis: A Life Saving Intervention for Acute Renal Failure from Falciparum Malaria in a Secondary Care Setting

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Background: The mortality associated with severe malaria remains high in malaria endemic regions due to the non availability of sophisticated intensive care facilities and limited resources. Acute renal failure from falciparum malaria requiring renal replacement therapy portends a grave prognosis in rural India. In a low resource country like ours hemodialysis facilities are found only in tertiary care centres which are inaccessible to the majority of people who suffer from this disease.

Objective: To describe peritoneal dialysis as a relevant alternative to hemodialysis in a secondary care setting in rural India. Materials and methods: Case series of 13 patients admitted to the Baptist Christian hospital with severe malaria requiring dialysis.

Results: Thirteen patients underwent peritoneal dialysis for acute renal failure resulting from falciparum malaria. 10 were between 18–45 years of age and three were below 12 years of age. 11 had falciparum malaria while 2 had mixed falciparum and vivax malaria. 10 were oliguric. Serum creatinine levels ranged between 2.8 mg% to 23.4 mg%. 9 had cerebral involvement and 9 had jaundice. Seven patients had elevated transaminases of which five had levels more than 200. All but one had AST more than ALT. 8 patients had Hb less than 7 gms of which four were less than 5 gms. 10 patients had respiratory distress. All adult patients were treated with artesunate and doxycycline, artesunate and clindamycin were used in the pediatric age group. Continuous peritoneal dialysis was carried out for an average of 4.7 days. One peritoneal dialysis was complicated by peritonitis which resolved with antibiotics. 11 patients recovered completely while two succumbed to the disease within 24 and 48 hours of admission.

Conclusion: Peritoneal dialysis can be a life saving intervention for patients with severe malaria in a secondary care centre in rural India.

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47.016

Production and Modification of Human Monoclonal Antibody Fab Fragments to the 19-Kilodalton C-Terminal Merozoite Surface Protein 1 of Plasmodium falciparum

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An effective vaccine for malaria has not yet been developed. Passive immunotherapy with human monoclonal antibodies may provide a valuable therapeutic alternative. A combinatorial immunoglobulin gene library was

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