Thesis Title Involvement of Rosette Formation in Severe Falciparum Malaria.

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ABSTRACT

Rosette formation of Plasmodium falciparum-infected red blood cells (RBC) was studied with RBC from healthy or malaria infected donors. Rosetting, characterized by two or more uninfected RBC bound to an infected RBC, occurs when the parasites mature to trophozoite/schizont stages, and is believed to be a critical factor in the development of cerebral malaria. Rosette forming ability of RBC from healthy donors was greater in group A and B than group O RBC (A=B>O). Decreased rosetting ability of these RBC was observed during storage under blood bank conditions, showing significant reduction on day 14 (group A,B and O) of storage. In addition, rosetting of RBC from healthy donors

was inhibited by antimalarial drugs. Normal RBC exposed for 30 minutes to quinine or artemether *in vitro* showed significantly decreased rosetting. These inhibitory effects could not be reversed by extensive washing and 24 hours further incubation under the *in vitro* culture conditions.

Rosetting ability of uninfected RBC from uncomplicated and complicated malaria donors was similar to those of normal RBC (A=B>O). Regardless of blood group, rosetting of uninfected RBC from uncomplicated malaria donors was decreased significantly within 8 hours after treatment with quinine. (1.46 vs 0.70), p=0.001 or qinghaosu derivatives (artesunate or artemether) (1.29 vs 0.63), p=0.001. Similarly, rosetting of the uninfected RBC from complicated malaria donors was decreased significantly within 4 hours after treatment with artesunate (1.22 vs 0.54) p=0.04. There was no significant reduction in the rosetting of uninfected RBC from complicated malaria donors after 2-24 hours treatment with quinine. Neither uninfected RBC from uncomplicated or from complicated malaria donors exhibited a greater rosetting ability than that of RBC from healthy donors.

These observations may be useful for developing a standard practice of blood transfusion in anaemic malaria patients. Moreover, the results showed that besides the killing effects, antimalarial drugs can interfere with the rosetting mechanisms of P. falciparum-infected RBC, and might therefore rapidly reduce the pathophysiology and severity of the disease.