Abstract

Introduction: Chemotherapy still is the most effective way to control malaria, a major public health problem in sub-Saharan Africa. The large-scale use of the combination therapy artemether-lumefantrine for malaria treatment in Africa predisposes lumefantrine to emergence of resistance. There is need to identify drugs that can be used as substitutes to lumefantrine for use in combination therapy. Methylene blue, a synthetic anti-methemoglobinemia drug, has been shown to contain antimalarial properties, making it a candidate for drug repurposing. The present study sought to determine antiplasmodial effects of methylene blue against lumefantrine- and pyrimethamine-resistant strains of *P. berghei*.

Methodology: Activity of methylene blue was assessed using the classical four-day test on mice infected with lumefantrine-resistant and pyrimethamine-resistant *P. berghei*. A dose of 45 mg/kg/day was effective for testing ED90. Parasitemia and mice survival was determined.

Results: At 45 mg/kg/day, methylene blue sustained significant parasite inhibition, over 99%, for at least 6 days post-treatment against lumefantrine-resistant and pyrimethamine-resistant *P. berghei* ($p = 0.0086$ and $p = 0.0191$, respectively). No serious adverse effects were observed.

Conclusions: Our results indicate that methylene blue at a concentration of 45 mg/kg/day confers over 99% inhibition against lumefantrine- and pyrimethamine-resistant *P. berghei* for six days. This shows the potential use methylene blue in the development of antimalarials against lumefantrine- and pyrimethamine-resistant parasites.