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Short Communication

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INTRAVENOUS ANTIBIOTIC SALVAGE THERAPY IN SEVERE FALCIPARUM MALARIA: ROLE OF TIGECYCLINE?

***Arash Eatemadi[1], Mohammed Abbas Bokhari [2], Elham Mohammed Abdalla[2], Khalafellah Ali Osman[2], Heytham Adam Mustafa[2], Musaab Mohmed Zaroug[2], Islam TajelsirrAwad[2]**

[1]Division of Infectious Diseases, General medicine Department, Suhar hospital, Suhar, Sultanate of Oman
[2]Division of acute Medicine, General medicine Department, Suhar hospital, Suhar, Sultanate of Oman

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ABSTRACT

Malaria chemotherapy remain a major area of research, and new drug molecules are constantly being developed before drug-resistant plasmodium strains emerge. Some antibiotics that have shown potential effects on malaria parasite have been recently studied in vitro or in vivo intensively. Antibiotics with anti-malarial activity, in combination with traditional anti-malarial drugs, are potentially useful options for drug-resistant, uncomplicated as well as complicated cases of malaria. As an exclusively parent rally administered antibiotic, tigecycline may represent an alternative drug for treating patients with severe and complicated Plasmodium falciparum malaria.

Keywords: Drug-resistant plasmodium strains, Complicated Plasmodium falciparum malaria, Tigecycline.

INTRODUCTION

Malaria is still a serious health problem in some parts of the world. Improper treatment, delays in diagnosis or treatment, infections with drug-resistant Plasmodium falciparum and non-immunity of the infected individuals have been contributed to malaria-related mortality. On the other hand, the use of anti-malarial drugs is a complex process due to contra-indications, drug-resistant Plasmodium falciparum, drug tolerability and cost. Universally, patients with severe and complicated malaria are treated with intravenous artemis in in derivates. However, regarding the spreading of drug-resistant P. falciparum to available drugs, even artemisinin derivates, there is a need to develop new anti-malarial agents. (Klein, 2013; Rosenthal, 2013; Wongsrichanalai and Sibley, 2013) Antibiotics with antimalarial activity, such as azithromycin, doxycycline, and clindamycin, in combination with commonly used intravenous antimalarial drugs (quinine or artesunate) are chosen for treatment of multidrug-resistant falciparum malaria. (Noedl *et al.,* 2007; Ramharter *et al.,* 2003; Sponer *et al.,* 2002; Tiphaine Gaillard *et al.,* 2016; Obonyo and Juma, 2012; Pradel and Schlitzer, 2010; van Eijk and Terlouw, 2011; Sponer *et al.,* 2010) Among them, doxycycline has been included in the World Health Organization (WHO) list of Essential Medicines for the prevention and treatment of malaria. (World Health Organization) Tigecycline is the first member of a new class of antimicrobials, the Glycylcyclines, is a semisynthetic derivate of minocyclineand was firstly approved for treatment of skin and soft tissue infections, as well as intra-abdominal infections. For the first time, tigecycline was tested by P. Starzengruber et al. on 66 clinical isolates of Plasmodium falciparum from Bangladesh using the histidine-rich protein 2 in vitro drug susceptibility assay. Their data with 24- and 72-h incubations suggested that tigecycline developed a delayed-death response and suggested tigecycline as a potential candidate in combination with faster-acting antimalarials (e.g., artesunate or quinine) in the intravenous treatment of multidrug-resistant falciparum malaria in critical patients (Starzengruber *et al.,* 2009). Subsequently, Held et al. determined the geometric mean 50% inhibitory concentrations of tigecycline in culture-adapted strains as well as in 23 clinical P. falciparum isolates from Lambaréné, Gabon and saw that tigecycline was found to act faster against plasmodia than clindamycin and doxycycline with the highest activity at day 3. Their study also defined the substantial in vitro effect of tigecycline on P. falciparum. (Held *et al.,* 2010) Later on, Ribatski-Silva et al. evaluated the in vitro antimalarial activity of tigecycline against chloroquine-sensitive and chloroquine-resistant reference strains of P. falciparum and clinical isolates from the Brazilian Amazon. A histidine-rich protein in vitro assay was used to evaluate antimalarial activity and they concluded that tigecycline may represent an alternative drug for the treatment of patients with severe malaria. (Ribatski-Silva *et al.,* 2014) Finally, Sahu et al. evaluated tigecycline in vitro against Chloroquine-susceptible and -resistant strains of P. falciparum in combination with Chloroquine. Tigecycline was found to be significantly more active against the resistant P. falciparum strain than the susceptible. Further, low concentrations of tigecycline markedly and selectively sensitized the Chloroquine -resistant strains to Chloroquine effect. The anti-malarial activity of tigecycline was significantly higher against Chloroquine-resistant than against – susceptible P. falciparum strains. (Sahu *et al.,* 2014)

CONCLUSION

with increasing resistance to artemisinin derivates, tigecycline could be a accompany drug to artesunate in complicated falciparum malaria, however, its use - only as combination therapy- should be reserved for critically ill patients.

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***Corresponding Author: ArashEatemadi,**
[1]Division of Infectious Diseases, General medicine Department, Suhar hospital, Suhar, Sultanate of Oman

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