



Case Report

Artesunate Resistant *Plasmodium Falciparum*

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Abstract

Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female *Anopheles* mosquitoes. WHO recommends artemisinin-based combination therapies (ACTs) for the treatment of uncomplicated malaria caused by *P. falciparum*. ACTs have been integral to the remarkable recent successes in global malaria control. However, *P. falciparum* resistance is now emerging to artemisinin having detected in five countries of the Greater Mekong Subregion: Cambodia, Laos, Myanmar, Thailand and Viet Nam. In India, it is also reported artesunate resistant *Plasmodium falciparum*. We described a 22year male patient admitted with cerebral malaria caused by *p. falciparum* and found artesunate resistance case.

Keywords: Malaria; *Plasmodium falciparum*; Artesunate resistant.

Introduction

Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female *Anopheles* mosquitoes. In 2015, 91 countries and areas had ongoing malaria transmission.⁽¹⁾ In 2015, nearly half of the world's population was at risk of malaria.⁽¹⁾ According to the latest WHO estimates, released in December 2016, there were 212 million cases of malaria in 2015 and 429 000 deaths.⁽²⁾ Malaria is preventable and curable, and increased efforts are dramatically reducing the malaria burden in many places. Malaria is caused by *Plasmodium* parasites. The parasites are spread to people through the bites of infected female *Anopheles* mosquitoes, called

"malaria vectors." There are 5 parasite species that cause malaria in humans, and 2 of these species *P. falciparum* and *P. vivax* – pose the greatest threat. Malaria is an acute febrile illness. In a non-immune individual, symptoms appear 7 days or more (usually 10–15 days) after the infective mosquito bite. The first symptoms – fever, headache, chills and vomiting – may be mild and difficult to recognize as malaria. If not treated within 24 hours, *P. falciparum* malaria can progress to severe illness, often leading to death. In 2008, artesunate resistance *P. falciparum* was found in Cambodia. *P.falciparum* resistance is now emerging to artemisinin having detected in five countries of the Greater Mekong Subregion:

Cambodia, the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam.⁽³⁾ Artesunate resistance *P. falciparum* also reported in Kolkata, India.⁽⁴⁾ Artemisinin-resistant strains of malaria means the artemisinin compound does not clear all parasites by the third day of treatment.⁽⁵⁾ Artemisinin is a very fast acting drug which means that within 12 hours of starting treatment around half of the parasites in the body are removed.⁽⁶⁾ Artemisinin is combined with a partner drug that usually works more slowly, hammering the remaining malaria parasites until they are all dead.

A molecular marker of artemisinin resistance was identified as Kelch 13 (K13) and associated with delayed parasite clearance in vitro and in vivo.⁽⁷⁾

Case Report

We reported an artesunate resistant *Plasmodium falciparum* in the the city of Kolkata, West Bengal, India. A 22 year old male, resident Kolkata, has been admitted in the tertiary centre for infection "*Infectious Disease & Beliaghata General Hospital, Kolkata -10; West Bengal, India*" The patient was admitted with high fever with chill and rigor followed by unconscious for last few hours. We have tested dual antigen (MPDA) test and found *P. falciparum* positive. On next day, both thick (Giemsa stained) and thin (Leishman stained) films of the patient were prepared and ring of *P. falciparum* was detected.

We started with artesunate injection alone, 120 mg i.m. on the first day followed by 120mg after 12 hours then 120mg i.m. daily for the next 3 days. But patient was febrile and his GCS was improved from 8/15 to 13/15. His peripheral blood was reexamined after 3 days but ring of *P. falciparum* was persisting. So, we continued the Injection Artesunate for another 4 days but ring of *P. falciparum* was persisting after 7 days of artesunate course. Same time patient was not clinically improving eg fever is persisting and patient was in confusional state. We have done CT scan of brain and there was no structural brain damage. His Hb was 11gm/dl and WBC count

was 5400/cmm and metabolic panel was normal limit. Then we started injection Quinine 600mg with DNS 8 hourly along with injection Clindamycin 600mg thrice daily. After 2 days of Quinine + Clindamycin injection patient became afebrile and became fully conscious and oriented. His peripheral blood was examined for *P. falciparum* and not detected. He had no history of travel to neighboring countries in recent years.

Discussion

This is the 2nd clinical case report of only artesunate resistant *P. falciparum* malaria from Kolkata. Though the present national drug policy is ACT (artemisinin and SP) that has not been followed in this particular case.⁽⁷⁾ A significant failure rate of artesunate and SP (9.5%) has recently been observed in the district Jalpaiguri, West Bengal, though no specific mutation has been observed in *pfATPase6* gene.⁽⁸⁾ In view of the above findings to get a clear picture of artemisinin resistance in *P. falciparum* Ration-ality of inclusion of SP in ACT also raises a serious question as among isolates from Kolkata most common mutations in DHFR gene (responsible for pyrimethamine resistance) are at positions 108 and 51. Again, in Kolkata 36.67% of isolates contains quadruple dhps AGEAT mutation (436+437+540+613), responsible for sulphadoxine resistance.⁽⁹⁾ This case suggests that inj. Quinine with inj. Clindamycin combination will be the treatment of Artesunate resistance *P. falciparum* malaria. In Cambodia, A consensus meeting on the national treatment policy for *P. falciparum* was held in January 2014, Artesunate-mefloquine was reintroduced as first-line treatment and Quinine plus doxycycline over 7 days has been adopted as rescue therapy.⁽⁶⁾ A molecular marker of artemisinin resistance was not identified as Kelch 13 in this case. So, this is a clinical case report of only artesunate resistant *P. falciparum* malaria.

Conclusion

Our report demonstrate that artisunte resistance *P. falciparum* is found in Kolkata, West Bengal. The parasite was not cleared after 7 days of artisunate therapy. Atisunte resistance *P. falciparum* to be treated with quinine with combination of clindamycin.

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Conflict of Interest: No conflict of interest is declared

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