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RESEARCH ARTICLE

A BRIEF REVIEW ON TAFENOQUINE IN RELAPSE MALARIA

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Abstract

Malarial relapse is the reactivation of the hypnozoite form of parasite in the liver cells. It is the reappearance of the symptoms after elimination of the parasite from the blood where the parasite still persists as the dormant hypnozoites in the liver cells. It usually occurs between 8-24 weeks after the elimination of parasite from the blood and is most common among the individuals with P.vivax and P.ovale infections. Drugs having both hypnozoiticidal and schizonticidal effects are used in the treatment of relapse malaria. Primaquine is the only drug which shows both schizonticidal and hypnozoiticidal effect in treating the relapse malaria. Primaquine has a long term chemoprophylaxis with adverse effect profile hence, there is a requirement for a drug with long acting hypnozoiticidal action in a single dose where, tafenoquine serves the need in providing a short-course treatment regimen for the radical cure instead of prescribing a 14-day course of primaquine. In this article, we mainly reviewed the approval, adverse effects profile, contraindications and precautions to be taken during the usage of Tafenoquine. In India, clinical trials are still under progress and yet to be approved to replace the current 14 day treatment regimen of primaquine. In order to cope up with the challenge in the treatment of relapse malaria, tafenoquine offers a ray of hope in dealing the relapse malaria effectively.

Introduction:-

Malaria is a life threatening disease caused by parasites that are transmitted to the people through the bite of infected female anopheles mosquito. It usually occurs due to Plasmodium species that include P.vivax, P.falciparum, P.malariae & P.ovale and among these species, P.falciparum & P.ovale are predominant. About 99.7% of malaria cases in African region, 62.8% in South-East Asia, 69% in Eastern Mediterranean and 71.9% in Western Pacific were caused due to Plasmodium falciparum. Plasmodium vivax is the most prominent parasite in America causing 74% of the total malaria cases. In the year 2017, it was estimated that there were about 219 million malarial cases and 4,35,000 deaths occurred due to malaria among 87 countries.[1]

The parasite which enters into the blood stream of a healthy individual attacks the liver cells and the red blood cells. The signs & symptoms usually may appear after 10-15 days of the bite of the infected mosquito. The most common signs & symptoms of malaria are headache, fever, chills, muscle pain, fatigue, nausea, vomiting, cough, abdominal

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pain, bloody stools, hepatomegaly and splenomegaly.[2-5] Various tests used for the diagnosis of malaria include microscopic diagnosis, antigen detection, serology, drug resistance tests and molecular diagnosis. [6,7] The drugs used in the treatment must have both schizonticidal and gametocidal effects. Various approaches in the treatment of malarial infections include prophylaxis, clinical cure, radical cure and the inhibition of the malarial transmission. The prophylactic therapy includes causal prophylaxis (primaquine, proguanil) which mainly targets the pre-erythrocytic phase and suppressive prophylaxis (mefloquine, doxycycline) that inhibits the erythrocytic phase of the parasite. Clinical cure involves elimination of the malarial parasite from the body and the available treatment options are classified into low efficacy drugs (proguanil, pyremethamine, sulfonamides, tetracyclines & clindamycin) and high efficacy drugs (artemisinin, chloroquine, amodiaquine, quinine, mefloquine, halofantrine & lumefantrine). Radical cure can be considered as the treatment for malarial relapse (primaquine).

Relapse Malaria:

Even after treating this disease with effective anti-malarial drugs, we may often observe the relapse of malaria in some patients. Malarial relapse is the reactivation of the hypnozoites form of parasite in the liver cells. It is the reappearance of the symptoms after elimination of the parasite from the blood where the parasite still persists as the dormant hypnozoites in the liver cells. It usually occurs between 8-24 weeks after the elimination of parasite from the blood and is most common among the individuals with P.vivax and P.ovale infections. In temperate areas, relapse of P.vivax malaria cases usually begins a year after the bite of mosquito.

Drugs having both hypnozoiticidal and schizonticidal effects are used in the treatment of relapse malaria. Chloroquine and primaquine are the available options in treating relapse malaria. In several geographical regions, chloroquine has attained a wide spread resistance to P.falciparum malaria thus resulting in reduced efficacy. Therefore, primaquine is the only drug which shows both schizonticidal and hypnozoiticidal effect in treating relapse malaria.[8-10] World Health Organization (WHO) recommends a 14 day primaquine therapy after the completion of standard malarial treatment for the prevention of relapse. It is the only drug recommended in treating the hypnozoites in liver up to now. But it is contraindicated in individuals with glucose 6 phosphate dehydrogenase (G6PD) deficiency, pregnant and lactating women. In G6PD deficient individuals, primaquine destroys the red blood cells causing oxidative stress in the erythrocytes which results in haemolysis thereby, the short term course of primaquine might help in reducing the risk of anemia.[6]

Malarial prevention in the travelers to endemic areas depends on chemoprophylaxis which is of two types that includes primary prophylaxis and terminal prophylaxis. Primary prophylaxis involves the administration of the drug at a lower dose to prevent the infections in asymptomatic individuals within an endemic area while the terminal prophylaxis involves the administration of a drug with hypnozoiticidal effect to a temporary asymptomatic individual leaving an endemic area. Primaquine has a long term chemoprophylaxis with adverse effect profile and hence, there is a requirement for a drug with long acting hypnozoiticidal action in a single dose where, tafenoquine which is a new 8-aminoquinoline serves the need in providing a short-course treatment regimen for the radical cure instead of prescribing a 14-day course of Primaquine.[8,11]

Tafenoquine in Relapse Malaria:

Tafenoquine is an analogue of primaquine and is effective against all stages of plasmodium vivax life cycle. It acts against the pre-erythrocyte stage of the parasite and prevents the development of the erythrocytic form which is responsible for the relapse. It was first synthesized by the scientists of Walter reed army institute of research in the year 1978. From the last two decades, GlaxoSmithKline (gsk) started developing it as an anti-malarial drug in the prevention and treatment of relapse malaria.

United States Food and Drug Administration (USFDA) and Australian Therapeutic Goods Administration (TGA) are the two stringent regulatory authorities that approved the tafenoquine recently. In USA, tafenoquine was approved in July 2018 for the radical cure of P.vivax malaria in the patients aged ≥16 years. Subsequently, in the month of august 2018, it was approved for the prophylaxis of malaria in patients aged ≥18 years. According to the data reviewed by USFDA, tafenoquine is the first single dose therapy available in treating relapse malaria. Though, the exact mechanism of action is not known, it is assumed to exert its effect by inhibiting the haemetin polymerization and mitochondrial dysfunction leading to apoptosis of the parasite.

The serious adverse effects like, hematological (hemolytic anemia & methemoglobinemia), immunological (hypersensitivity reaction) & ophthalmic (vortex keratopathy) and the common adverse effects like gastrointestinal

(diarrhea, nausea, vomitings) & neurological (dizzines, headache & motion sickness) can be observed with tafenoquine. Tafenoquine is contraindicated in individuals with G6PD deficiency, history of psychotic disorders or psychotic symptoms (hallucinations, delusions and grossly disorganized behavior), hypersensitivity to tafenoquine or to any other 8 aminoquinolines and lactating women. A close monitoring is required when tafenoquine is prescribed in diabetic patients receiving metformin and dofetilide as it might result in the increased plasma concentrations. It is recommended to test the G6PD status of the individual prior to the initiation of the therapy as this drug may cause hemolytic anemia and hemolysis in patients with G6PD deficiency.[12-14]

Conclusion:-

Tafenoquine is a long-acting hypnozoiticidal effect in a single dose regimen that bypasses the barrier of prescribing a 14-day regimen of primaquine. In India, clinical trials are still under progress and yet to be approved to replace the current 14 day treatment regimen of primaquine. In order to cope up with the challenge in the treatment of relapse malaria, tafenoquine offers a ray of hope in dealing the relapse malaria effectively.

References:-

1. Definition and epidemiology of malaria available at: https://www.who.int/news-room/fact-sheets/detail/malaria
2. Rita c, David C, O. John, Michael F, Scott Joing, Vincent W. Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 8th Ed. McGraw-Hill Education 2016
3. Breman JG. Clinical manifestations of malaria in nonpregnant adults and children 2018.
4. Jameson, Fauci, Kasper, Hauser, Longo, Loscalzo. Harrison's Principles of Internal Medicine. 20th Ed. The McGraw-Hill Companies 2018
5. Clinical manifestations of malaria available at: https://www.healthline.com/health/malaria#symptoms
6. Diagnosis of malaria available at: https://www.who.int/malaria/areas/diagnosis/en/
7. Diagnosis of malaria available at: https://www.cdc.gov/malaria/diagnosis_treatment/diagnosis.html
8. KD Tripathi. Essentials of medical pharmacology.7th Ed. Jaypee Brothers Medical Publishers 2013
9. White N.J. Determinants of relapse periodicity in Plasmodium Vivax malaria. Malar J 2011; 10:297.
10. Price RN, Tjitra E, Guerra CA, Yeung S, White N.J, Anstey N.M. Vivax malaria: neglected and not benign. Am J Trop Med Hyg 2007; 77(6):79-87.
11. Peters W. The evolution of tafenoquine-antimalarial for a new millennium. JR Soc Med1999; 92(7):345-52.
12. Rajapakse S, Rodrigo C, Fernando SD. Taffenoquine for preventing relapse in people with Plasmodium vivax malaria. Cochrane Database Syst Rev 2015.
13. Ebstie YA, Abay SM, Tadesse WT, Ejigu DA. Tafenoquine and its potential in the treatment and relapse prevention of plasmodium vivax malaria: the evidence to date. Drug Des Devel Ther 2016; 10:2387-99.
14. Drug approval information available at: https://www.who.int/malaria/news/2019/new-opportunities-to-prevent-vivax-malaria-relapse/en.