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Antimalarial Drugs Used in the Management of Viral Infections-A Perspective

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Abstract

Antimalarial drugs are antiparasitic agents which are naturally derived from plants used in the treatment of malaria.There are various classes of antimalarial drugs seen.They are Artemisinin derivatives, aryl-amino alcohols, aminoquinolines and antimicrobial drugs.The mechanism of action of antimalarial drugs is to prevent the polymerisation of heme which results in the death of the parasite.Antimalarials are also used in the treatment and prophylaxis of viral infections which is being discussed in this review. Around 40 articles from Pubmed, Google scholar which are relevant to the topic are taken and discussed.The articles which don't fall into the criteria are excluded.The points from the article are taken and discussed.The review methods,the different classes of drugs like artemisinin derivatives, aryl-amino alcohols, aminoquinolines and antimicrobial drugs are also discussed. The antimalarial drugs are widely used in the prophylaxis and treatment of various existing and emerging viral infections.Newer viral infections have no resistance against antimalarial drugs which proves to be very useful.

Keywords: *Antimalarials, parasites, viral infections ,resistance*

Introduction

Antimalarial drugs are anti-parasitic agents which are naturally derived from plants used in the treatment of malaria.There are various class of antimalarial drugs seen.They are Artemisinin derivatives, aryl-amino alcohols, aminoquinolines and antimicrobial drugs.The mechanism of action is to prevent the polymerisation of heme which results in the death of the parasite. Artemisinin derivatives are the most effective of antimalarial drugs. Artemisinin derivatives used in vitro are proven to be effective against human cytomegalovirus.[1] Artemisinin and Artesunate have been proven to be used for the treatment of Hepatitis B and C infections. Dihydroartemisinin is effective against bovine viral diarrhoea virus.[2] Quinine sulphate tested invitro is proven to have been effective against dengue virus.

Mefloquine is also proven to be effective against Zika virus infections.Quinine which is derived from barks of Cinchona trees are proven to be effective against Swine flu. Previous research articles are taken into account.One of the studies about artemisinin used invitro against hepatitis B production is taken.The result of this study shows that the combination of artesunate and lamivudine shows synergistic effects against the infection.[3] Another study about the usage of chloroquine against influenza prevention in a randomised placebo trial is taken.The result however shows that chloroquine is not effective and alternate drugs are required for the treatment of influenza.[4]

Recently, hydroxychloroquine is being recommended for the prophylaxis and treatment of COVID-19 or coronavirus infection which is a global epidemic in recent days. SARS coronavirus which causes

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acute respiratory obstruction in the past have been treated with chloroquine with combinations of antiviral drugs.[5] The aim of this review is to study the characteristics of antimalarial drugs used in the management of various viral infections.

Materials and Methods

Review Methods

About 40 articles are chosen for this review. The articles which are taken are chosen based on the relevancy to the topic.The articles which are in other languages are excluded and the articles which are not related to the topic are excluded.The data for the review was extracted based on the characteristics of the article.[6]

Artemisinin Derivatives

Artemisinin derivatives are drugs which are derived from a plant called

Artemisia annua,a herb.These drugs are safe,well tolerated with lower potency in lower or normal dosage but high potency in larger dosages.The main derivatives discussed here are artemisinin and artesunate.[7] Artemisinin is a semisynthetic derivative which is poorly soluble. Artemisinin is proven to be effective against hepatitis B and C infections in vitro.Artemisinin is activated by iron molecules which dissolves to free radical formation.[8]

Artesunate which is another derivative has the highest activity and is effective against herpes simplex viruses.It is taken by intravenous route for the protocol treatment of malaria. Artesunate is also involved in the inhibition of human immunodeficiency virus replication and hence seen in antiretroviral therapy in the treatment of Acquired Immune Deficiency Syndrome.[9] Artesunate has a synergistic action with antiviral drugs like maribavir, lamivudine, ganciclovir, foscarnet, cidofovir, letermovir etc.[10,11]Artesunate is effective against Epstein-Barr virus infection in low micromolar ranges and acts on epithelial cells and lymphocytes.[12]

Aryl- Amino Alcohols

The important drugs in this classification are quinine sulphate and mefloquine. Quinine sulphate is the oldest drug in existence used in treating malaria.[13] Quinine sulphate in micromolar range and not in toxic doses have reduced the number of plagues formed and also in Herpes Simplex Virus-1 in vitro.[14] Quinine sulphate is also said to be effective in the treatment of dengue virus infections.

Mefloquine combined with mirtazapine acts on the 5-HT2A serotonin receptor. It inhibits the entry of JCPyV into glial cells preventing the diffusion and the infection of oligodendrocytes.[15–18] Mefloquine is widely used in the prophylaxis of mild to moderate malaria.[19] Lumefantrine with combination with artemether is called CoArtem commercially. It is used in treatment of non severe malaria.

Aminoquinolines

The important drugs in this classification are chloroquine and hydroxychloroquine. Chloroquine has low toxicity and high tolerance and is used as an antiviral drug. Chloroquine is used in combination with antiviral drugs to produce synergistic effects.[20] Chloroquine is also used in the treatment of amoebiasis, systemic and discoid lupus erythematosus, sarcoidosis,porphyria cutanea tarda and in decreasing the symptoms for rheumatoid arthritis.[21] Hydroxychloroquine is used in the treatment of RNA virus infections.It is also used in the treatment of lupus erythematosus and rheumatoid arthritis.[22] Hydroxychloroquine goes by the commercial name Planequil.

Anti- Microbial Drugs

The drugs seen here are atovaquone, doxycycline and sulfonamides. Atovaquone is an antimalarial drug used in pregnant women.Atovaquone is an analogue of ubiquinone and is used to treat a very serious lung infection called Pneumocystis pneumonia.[23] Doxycycline is a semisynthetic tetracycline used in the combination treatment of malaria along with quinine.[24] Sulfonamides are a group of drugs that are prescribed to treat urinary tract infections,bacterial meningitis,bronchitis, eye and ear infections etc.[25,26] Recent studies have demonstrated the activity of sulfonamides as they act on latent herpes viruses, Epstein-Barr virus and Kaposi sarcoma virus.[27,28]

Discussion

In this review, we discussed the previous articles related to antimalarial drugs used in the management

of viral infections. We have evaluated the drug actions of artemisinin derivatives, aryl- amino alcohols, aminoquinolines and other antimicrobial drugs.

Artemisinin derivatives such as artemisinin and artesunate are taken into account.They produce synergistic actions when combined with other antiviral drugs and are effective against hepatitis B and C and also inhibit the replication of human immunodeficiency virus.Aryl- amino alcohols such as quinine sulphate and mefloquine are earlier derived drugs which are effective in treatment of Herpes simplex virus-1 and Zika virus infections.[29,30] Quinine sulphate might cause a condition that affects the heart rhythm by QT prolongation in the electrocardiogram readings.[31] Mefloquine should not be taken with hydroxychloroquine as it increases the risk for occurence of seizures.[32–34]

Aminoquinolines such as chloroquine and hydroxychloroquine has low toxicity, high tolerance and hence used in the anti- retroviral regimen therapy. Hydroxychloroquine and diabetes drugs taken together will cause hypoglycemia.[35] Hydroxychloroquine should not be taken with other cardiac drugs as it causes dangerous cardiac arrhythmias.[36] Other antimicrobial drugs like atovaquone, doxycycline and sulfonamides are used in the treatment of Epstein-Barr virus and Kaposi sarcoma virus infections.[37] The complications like hepatic inflammation and fibrosis are caused due to chronic viral deposition.[38] Sulfonamides antimicrobials can be combined with trimethoprim to make them bactericidal.[39,40] Other natural agents like Acacia species have less toxicity and good efficacy.[41,42] The main drawback of antimalarial drugs is their efficacy.The efficacy of these drugs are declined due to the emergence of drug resistant organisms.It can be corrected by usage of nanoparticles for targeted drug delivery and thus rendering excellent efficacy.[43]

The limiting factors of usage of antimalarials are the usage of older drugs.Different dosages given for each infection, ongoing trials on the usage of drugs are also considered to be a drawback. The uncertainty of the adverse effects of the drugs on healthy individuals should be considered.Recently, hydroxychloroquine is recommended in the prophylaxis and treatment of COVID-19 or coronavirus infections. SARS coronavirus in the early 2000's was treated back then with a combination of chloroquine with antiviral drugs.[44]

Conclusion

The antimalarial drugs are widely used in the prophylaxis and treatment of various existing and emerging viral infections.Newer viral infections have almost no resistance against antimalarial drugs which proves to be very useful.Newer antimalarial drugs with a wide spectrum against viral infections might bring favourable results.

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