

Role of Treatment of Amphotericin-B in Black Fungus Treatment:A Review Article

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ABSTRACT : The aim of this study is to review the role Amphotericin B in the treatment of black fungus . At present the world is dealing with the coronavirus pandemic which has completely changed the way of living for us . In the concealment of the current pandemic other diseases are also wreaking havoc on mankind . One such disease is Black Fungus infection which affects people with low immunity .For treating this infection Amphotericin B , an antifungal drug is given intravenously.It is one of the oldest yet most efficient antifungal drug. Amphotericin B has shown good results in treating the infection . In this study we will study about how Amphotericin B helps in curing the Black fungus infection , its mode of action , medical uses , pharmacokinetic properties , synthesis , side effects and possible drug interactions . Currently , Amphotericin B is drug of choice for treating the infection . However , its usefulness is limited because of its severe side effects. This review gives us the brief insight on Amphotericin and its effects on Black Fungus infection.

Keywords : Amphotericin B , Black Fungus , coronavirus , immunity .

INTRODUCTION

Black Fungus or Mucormycosis is a fungal infection caused by the Fungi of the Mucorales type. It usually occurs in people who have low/weak immune system or people whose body has reduced ability to fight infection . This fungi enters into the body through inhalation , contaminated food , or because of untreated wounds.

These type of fungi are commonly found in soils , decomposing matter and on animal manure but it does not affect humans directly. It is dangerous to those people who have weak immune system. It is not easily communicable means it cannot be transferred from person to person as a result of physical contact.

Black Fungus or Mucormycosis is usually a rare disease but in these times of covid it is very dangerous as people's immunity is low and it can cause greater damage to mankind. The cases of black fungus have seen a sudden spike recently. Black Fungus can infect humans of any age group including premature infants.

CLASSIFICATION

- Rhinocerebral Mucormycosis :-

It occurs mainly in the sinuses and can spread to brain. People suffering from diabetes are at a higher risk for this infection.

- Pulmonary Mucormycosis :-
It is more common with people having cancer or who have gone any organ replacement in the past.
- Gastrointestinal Mucormycosis :-
It is more common in childrens mainly in infants who are on medications that lower their immune response.
- Cutaneous Mucormycosis :-
It is mainly occurs due to open wounds. The fungi enters into the body through cut in the skin due to any injury. It is common in people having strong immune systems.
- Disseminated Mucormycosis :-
In this type of mucormycosis the infection spreads through blood and affect different parts of body. It mainly affects brain.

SPECIES OF FUNGI RESPONSIBLE FOR MUCORMYCOSIS ARE :-

- Rhizopus species
- Mucor species
- Rhizomucor Species
- Syncephalastrum species
- Cunninghamella bertholletiae

SYMPTOMS

Black Fungus infection usually begins through nose and affects Central Nervous System through our eyes.

If the infection is beginning with nose then one sided eye pain may occur accompanied with fever , loss of smell , runny nose are the common symptoms. The eye may get swollen.

In case the lungs are involved fever, chest pain , difficulty in breathing may occur.

In case the gastrointestinaltract are involved then nausea , vomiting , stomach ache may occur. In severe cases there may be an ulcer.

Infection in blood may result in thrombosis and death of surrounding tissue due to blood loss

CAUSES

Black fungus is caused by the infection of the fungi of the order Mucorales. In most cases the infection is due to the Rhizopus , Mucor and common bread molds.

These fungus can be found in the environment like in breads and bananas. Due to which they can get inside the body but can cause disease in only few. They get into the sinuses , nose and lungs. There they grow filaments and invade blood vessels which results in clot formation and subsequently death of nearby cells.

It can also enter into the body through open wounds or contaminated wound dressing.



Figure -1

DIAGNOSIS

There is no such test which can confirm the presence of infection in the body. It can be identified by performing biopsy in which the sample cells or tissues are taken out for identification of disease and then confirming it with a fungal culture. This method does not always give a result and requires an expert for identification.

But this method is not decisive. Several other tests are there for direct detection of possible infection in lung fluid, blood, plasma, urine.

IMAGING

CT Scan of lungs and sinuses can be helpful for diagnosis of black fungus infection. The presence of nodules and cavities and invasion of blood vessels show possible fungal infection. But still it does not confirm black fungus infection.

MRI can also be useful for diagnosis of Mucormycosis.

TREATMENT

Treatment of mucormycosis includes combination of antifungal drugs or removing the infected part surgically.

Medication

Once the infection is detected the patient is advised to take Amphotericin B at an initial dose of 1mg which is given slowly over 10-15 min in veins and then given as once a daily dose according to body weight for next 14 days. Isavuconazole and Posaconazole have also proved to be effective in black fungus treatment.

DRUG PROFILE

AMPHOTERICIN B

It was extracted from *Streptomyces nodosus*, a filamentous bacterium in 1955 from the cultures of an undescribed streptomycete isolated from the soil collected in the Orinoco region of Venezuela.

Amphotericin A and Amphotericin B were both isolated from this soil culture. In these two Amphotericin B had better Antifungal properties than Amphotericin A.

It was the only effective antifungal drug for many decades until the discovery of azoles in 1980.

Amphotericin B is known to cure many types of fungal infections include mucormycosis, aspergillosis, candidiasis.

It is administered into the body through IV Route.

Chemical Formula : $C_{47}H_{73}NO_{17}$

Molar Mass : 924.091 g/mol

Melting Point : $170^{\circ}C$

Pharmacokinetic Data

Bioavailability : 100% when given through IV Route.

Metabolism : Kidney

Excretion : found 40% in urine after cumulating for several days.

BIOSYNTHESIS

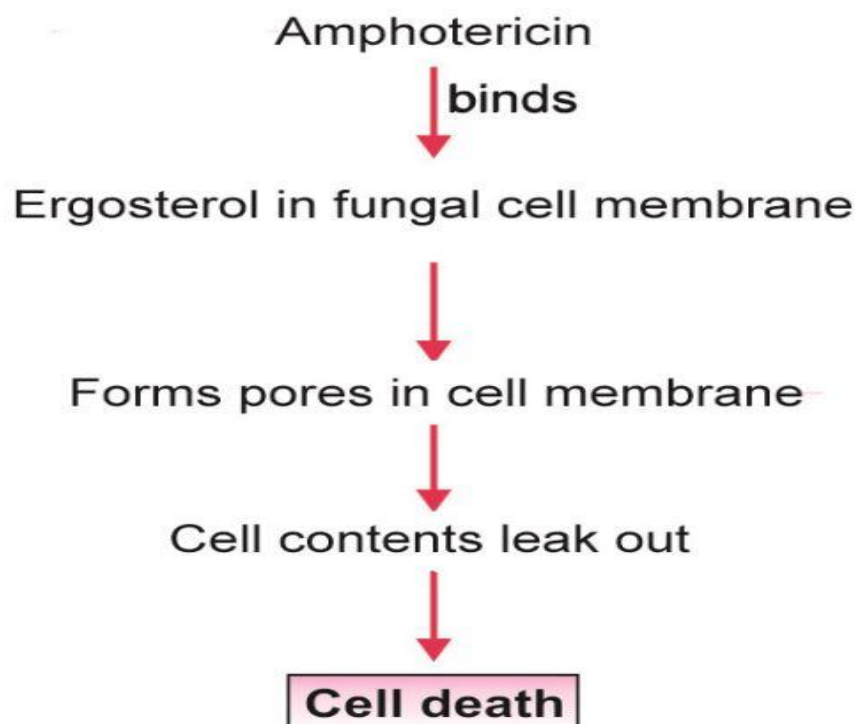
The synthesis of Amphotericin B is done by polyketide synthase components. The carbon chains of polyenes are assembled from acetate and propionate units by polyketide synthases (PKSs). Polyketide biosynthesis begins with the decarboxylative condensation of a dicarboxylic acid extender unit with a starter acyl unit to form a β -ketoacyl intermediate. With complex macrolide polyketides, the β -ketone group may be converted to an alcohol, enoyl or methylene group before another extender unit is added in the next cycle of chain extension. The final product is a unique functionalised acyl chain that may cyclise and undergo further modification by hydroxylation, methylation and glycosylation.

MODE OF ACTION

Amphotericin B binds with ergosterol, which is a component present in the fungal cell membranes, which forms pores in the membrane and causes leakage of monovalent ions (K^+ , Na^+ , H^+ , Cl^-) and results in fungal cell death. This is termed as the primary effect of Amphotericin B as an antifungal agent.

The Amphotericin B/ergosterol complex which forms the pores on fungal cell membranes are regulated by Van der Waals interactions. Researches have also shown that Amphotericin B causes oxidative stress in the fungal cell, but it is not clear upto which extent it causes oxidative stress.

There are two amphotericins, Amphotericin A and Amphotericin B but only B is used because it shows better anti-fungal properties. Amphotericin A is almost similar to Amphotericin B but shows very low antifungal activity.



AVAILABLE FORMULATIONS

INTRAVENOUS

When given intravenously the bioavailability is 100% , there are several formulations which are given to patients including Lipid based formulations which is believed to have low adverse effect and better tolerated by patients .

BY MOUTH

An oral preparation of amphotericin B exists but it is not widely available. Oral preparations have very low availability and also low solubility.

MEDICAL USES

Antifungal

Amphotericin B is used to treat a wide range of Antifungal infections. It has very vast side effects due to which it is used in severe cases. It is mainly used to treat mucormycosis infections , cryptococcosis and candidal infections . It has been used as an highly efficient drug for over approx. 50 years now. Amphotericin B exposes the pathogen to host environment makes it weak to cause infection.

CRYPTOCOCCOSIS

It is a fungal disease caused by *Cryptococcus neoformans*, it mainly affects the lungs and brain and can be fatal if not treated properly. Usually for the treatment Amphotericin B is given along with flucytosine but due to lack of flucytosine, it is given along with fluconazole. Amphotericin B is given intravenously whereas fluconazole is given orally.

CANDIDIASIS

It is a type of fungal infection which is caused by *Candida* which is a type of yeast. It mainly affects the mouth of infected person. It is treated by administering patient with antifungal medications such as Clotrimazole, Amphotericin B and voriconazole. Amphotericin B is mainly given intravenously when the infection is in the blood.

SIDE EFFECTS OF AMPHOTERICIN B

Amphotericin B is known for its severe side effects and sometimes can be lethal. Therefore, proper administration of the medication must be taken care of and under the guidance of a Doctor. It can cause very mild to severe side effects which include fever and chills up to kidney damage in some cases.

COMMON SIDE EFFECTS

- Fever And Chills
- Headache
- Increased or Decreased Urination
- Irregular Heartbeat
- Muscle Cramps
- Nausea
- Pain At The Place Of Administration
- Weakness
- Vomiting

RARE SIDE EFFECTS OR LESS COMMON SIDE EFFECTS

- Blurred Or Doubled Vision
- Convulsions
- Numbness
- Shortness Of Breath
- Tightness In Chest
- Skin Rash
- Itching
- Sore Throat And Fever
- Unusual Bleeding And Bruising

SURGERY

Black Fungus infection can also be treated with the help of surgery but it is a complicated process and used in severe cases. It involves removal of the affected tissue from the body.

In Surgery , more than one operation may be required. In severe cases sometimes there is removal of nasal cavity and eyes which can be very distorting.

CONCLUSION

From this article it can be concluded that the cases of black fungus infection are increasing day by day. Amphotericin B is the drug of choice for the treatment of black fungus infection. Black fungus infection is caused due to the weak immune system of presently ill patients. People should more focus on enhancing the immunity and follow a balanced routine for a fit mind and fit routine . Black Fungus cases rise in times of natural calamities or pandemic when people's immunity is at there weakest.

Black fungus can affect different parts of the body but most commonly it affects eyes of the patient or sinuses.it spreads through soil , eating contaminated food or through formation of spores on open or untreated wounds.

Amphotericin B has proved to be a useful drug for treatment of Black Fungus but it has some severe side effects which in worse cases can lead to kidney failure. Better understanding and study of these side effects is necessary in order to reduce these side effects . Also, the availability is one major factor for the rise in black fungus patients , if available they are way too costly for poor people to purchase it .

Greater emphasis should be put on to make it available so anyone can buy it.Oral formulations are only available in few countries

Currently in the aftermath of covid19 the black fungus cases are one the rise , the situation should be dealt accordingly . Availability of suitable drugs in minimizing the infection and its spread should be stocked because if not treated earlier the black fungus infection can cause permanent blindness and in severe cases can cause death.

Greater emphasis should be put on to building people's immunity . People having past history of covid contractions or with major diseases such as diabetes are on a greater risk on contracting with coronavirus.

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