WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

View on Pharmacovigilance of Amphotericin-B on Mucormycosis Disease

[1]Prasad Sanjay Pawar, [2]Prof. Mohini Shinde

[1]Final year B. Pharmacy, Department of Pharmacovigilance, Faculty of Pharmacy
[2]Mahavir Institute of Pharmacy, Varvandi Nashik, India

ABSTRACT-

Mucormycosis is an opportunistic fungal infection of the zygomycete family that can cause various types of infections.

The main causative agent is the mucormycete mould that occurs in soil,pile of compost, etc.

The symptoms of this disease includes fever, cough, one-sided face swelling, headache, etc.

There are many antifungal agents used to treat the mucormycosis.

Amphotericin-B is one of them used to treat Mucormycosis.

Administration of Amphotericin-B in large amounts can cause some serious adverse effects like Nephrotoxicity.

Another adverse effects of using this drugs can be hypokalemia as well as loss of calcium.

The overdose of amphotericin B can be fatal.

Highest number of cases of mucormycosis was recorded in the state of Gujarat.

Keywords:- Mucormycosis disease, zygomycete, mucormycete Moulds, Amphotericin-B, loadingdose, maintainance dose, dosage regimen, contraindications.

Mucormycosis

I. INTRODUCTION: -

- Mucormycosis is a rare fungal Infection which is caused by cluster ofmolds called Mucormycetes.
- This fungi tends to grow within the environment, specially in soil and in link with decaying matter.
- Types of fungi that most commonly cause mucormycosis are Rhizopus species, Mucor species, etc.

- People suffer from Mucormycosis by coming in contact with the Fungal spores present in the environment
- For Example, Lungs form of the infection can happen to someone after he or she inhales the spores from the air.
- Usually these forms of Mucormycosis occurs in people who have weakened immune system
- Mucormycosis can be produced on the skin as the fungus makes its way and enters the skin via. Cut, scrape, burn or other types of skin trauma.

CAUSES :-

- Mucormycosis is caused by exposure to mucormyete molds.

These organisms occur in:

- leaves
- piles of compost
- soil
- rotting wood
- Mucormycosis after causing to an individual can develop the infection in following:-
- CNS (rarer)
- eyes
- face
- lungs
- sinuses

Symptoms Of Mucormycosis Disease:-

- The symptoms of Mucormycosis rely on where in body the fungus is growing.
- One should contact the doctor, if they observe the symptoms that are similar to Mucormycosis.
- Several Symptoms of Mucormycosis includes :
- One-sided facial swelling
- Headache
- Nasal congestion
- Black leisons on upper inside of mouth
- Fever
- Cough

Treatment Of Mucormycosis Disease:-

- Mucormycosis is a severe infection and it needs to be treated with prescribed anti fungal medication generally Amphotericin-B, Posaconazole or Isavuconazole.
- All these medications are given through vein only Amphotericin-B is not administered Orally.
- Often Mucormycosis requires surgery to cut away the infected tissue.
- Usually starting dose of Amphotericin-B is 5 mg per kg per day and the doctor may increase dose upto 10 mg/kg.
- Posaconazole and isavuconazole are available in both parentral and oral formulations.
- Salvage therapy:- We use Posaconazole or Isavuconazole as salvage therapy for patients who do not respond to or cannot tolerate amphotericin B.
- Posaconazole is given as a loading dose of 300 mg every 12 hours on the first day, followed by a maintenance dose of 300 mg every 24 hours thereafter.
- Isavuconazole should be given as a loading dose of 200 mg IV or orally every 8 hours for the first six doses followed by 200 mg IV or orally every 24 hours thereafter.

DOSAGE REGIMEN:-

- A dosage regimen is a plan for drug administration over a period of time.
- An appropriate dosage regimen results in the achievement of therapeutic levels of drug in the blood, without exceeding the minimum toxic concentration.
- Loading Dose
- If it is necessary to achieve the target plasma level rapidly, a loading dose is used to “load” the volume of distribution with the drug
- Maintainance Dose
- To maintain the plasma concentration within a specified range over long periods of therapy, a schedule of maintainance doses is used.

Mechanism Of Action Of Amphotericin-B:-

- Amphotericin B acts by binding to ergo sterol in the cell membrane of the fungus
- After binding with ergosterol, it causes the formation of ion channels leading to loss of protons, which results in depolarization and concentration-dependent cell killing.
- Additionally, Amphotericin B also produces oxidative damage to the cells with the formation of free radicals and increased membrane permeability.
- Additionally, Amphotericin B has a stimulatory effect on phagocytic cells, which assists in fungal infection clearance.
- The half life of amphotericin B is from 24 hours to 15 days.

ADMINISTRATION OF AMPHOTERICIN-B:-

- Amphotericin-B is an amphoteric i.e. can act as an acid as well as base.

- It is not absorbable via oral administration.
- Its IV infusion administration is over 2 to 6 hours.
- The risk of nephrotoxicity increases at doses greater than 1mg/kg.
- Pre-treating the patient with 1 ltr of normal saline can attenuate nephrotoxicity.
- Topical amphotericin B is irritating to the skin; therefore the decision to use topical amphotericin B should be made based on expert consultation.
- Amphotericin B achieves high concentrations in tissue such as the liver, spleen, bone marrow, kidney and lungs.
- The concentrations in the cerebrospinal fluid are low(5% of serum), it is effective in the treatment of fungal infections of the central nervous system when given intrathecally(higher risk of toxicity)
- If we compare the rate of drug clearance from plasma between children and adults, children seems to clear the drug from plasma more rapidly than the adults.

Amphotericin-B For Iv Route Of administration:-

Adverse Effects Of Amphotericin-B:-

- About 80% of the patients will develop either infusion-related or renal toxicity.
- Amphotericin B also reacts with cholesterol in human cell membranes, which is responsible for its toxicity.
- The most common side effects of amphotericin B includes:
  - Loss of potassium
  - Loss of magnesium
  - Anaphylaxis
  - Fevers
- Nephrotoxicity: renal toxicity correlates with conventional amphotericin B use and can lead to renal failure and requirement of dialysis.
- But the renal damage is reversible after discontinuation of amphotericin B.
- Another potential uncommon side effect includes demyelinating encephalopathy in which it affects the white matter of the brain and spinal cord.
- The long term administration is associated with the normocytic anaemia in which the patient have fewer red blood cells than normal, and those red blood cells do not have the normal amount of haemoglobin present in them.

Contraindications Of Amphotericin-B:-

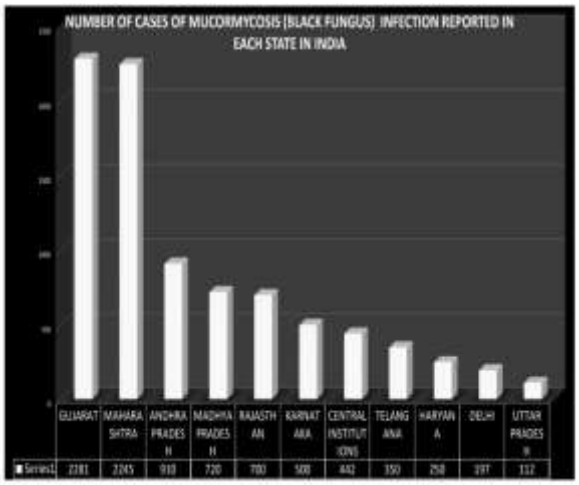
- Absolute contraindications includes a history of anaphylactic reactions to amphotericin B.
- Before the administration, drug-drug interactions require a thorough review.

- Concomitant use of steroids should be reconsidered to reduce the risk of hypokalemia.
- Hypokalemia can also potentiate digoxin toxicity.
- Simultaneous infusion of amphotericin B and granulocytes(mast cells,basophils,eosinophils) has seen some acute pulmonary reactions and the clinicians should avoid the combination.

TOXICITY OF AMPHOTERICIN-B:-

- Amphotericin B exhibits infusion-related toxicity.
- It should be infused slowly over 3 hours.
- The rapid infusion might lead to cardiotoxicity.
- Due to the similarity of mammalian and fungal membranes,which both contain sterols,(the therapeutic target for amphotericin B),amphotericin B can exhibit cellular toxicity.

NUMBER OF CASES OF MUCORMYCOSIS:-



II. CONCLUSION: -

Mucormycosis is a fungal infectious disease which is caused by cluster of molds called Mucormycetes and can be treated by the administration of amphotericin B. The serious adverse effects of the administration of this drug is the impaired kidney function as well as hypokalemia and the loss of magnesium.The prescribed limited use of amphotericin B can lead to the minimization of the above side effects.All these side effects are registered in WHO for that particular drug.

BIBLIOGRAPHY: -

[1]. Skiada A, Lanternier F, Groll AH, Pagano L, Zimmerli S, Herbrecht R, et al. Diagnosis and treatment of mucormycosis in patients with hematological malignancies: Guidelines from the 3rd European Conference on Infections in Leukemia (ECIL 3) Haematologica. 2013; 98(4):492–504.

[2]. Blyth CC, Gilroy NM, Guy SD, Chambers ST, Cheong EY, Gottlieb T, et al. Consensus guidelines for the treatment of invasive mould infections in haematological malignancy and haemopoietic stem cell transplantation, 2014. Intern Med J. 2014; 44(12):1333–49.

[3]. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SC, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. Lancet Infect Dis. 2019; 19(12):e405–21. [PMC free article] [PubMed] [Google Scholar]

[4]. Farmakiotis D, Kontoyiannis DP. Mucormycoses. Infect Dis Clin North Am. 2016; 30(1):143–63. [PubMed] [Google Scholar]

[5]. Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kong DC, et al. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect. 2019; 25(1):26–34. [PubMed] [Google Scholar]

[6]. Cornely OA, Arikan-Akdagli S, Dannaoui E, Groll AH, Lagrou K, Chakrabarti A, et al. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013. Clin Microbiol Infect. 2014; 20(Suppl 3):5–26.

[7]. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi. 2019; 5(1):26.

[8]. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an update. J Fungi. 2020; 6(4):265.

[9]. Stemler J, Hamed K, Salmanton-García J, Rezaei-Matehkolaei A, Gräfe SK, Sal E, et al. Mucormycosis in the Middle East and North Africa: analysis of the FungiScope® registry and cases from the literature. Mycoses. 2020; 63(10)

[10]. Skiada A, Pagano L, Groll A, Zimmerli S, Dupont B, Lagrou K, et al. Zygomycosis in Europe: analysis of 230 cases accrued by the registry of the European Confederation of Medical Mycology (ECMM) working group on Zygomycosis between 2005 and 2007.

[11]. Mignogna MD, Fortuna G, Leuci S, Adamo D, Ruoppo E, Siano M, et al. Mucormycosis in immunocompetent patients: a case-series of patients with maxillary sinus involvement and a critical review of the literature.

[12]. Lamoth F, Kontoyiannis DP. Therapeutic challenges of non-Aspergillus invasive mold infections in immunosuppressed patients.

[13]. Ruhnke M, Cornely OA, Schmidt-Hieber M, Alakel N, Boell B, Buchheidt D, et al. Treatment of invasive fungal diseases in cancer patients-Revised 2019 Recommendations of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO) Mycoses.

[14]. Peter Donnelly J, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and update of the consensus definitions of invasive fungal disease from the european organization for research and treatment of cancer and the mycoses study group education and research consortium. Clin Infect Dis. 2020

[15]. Lewis RE, Kontoyiannis DP. Epidemiology and treatment of mucormycosis. Future Microbiol. 2013; 8(9):1163–75.

[16]. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis. 2012; 54(Suppl 1):23–34.

[17]. Petrikkos G, Skiada A, Drogari-Apiranthitou M. Epidemiology of mucormycosis in Europe. Clin Microbiol Infect. 2014; 20(Suppl 6):67–73.

[18]. Bulent Ertugrul M, Arikan-Akdagli S. Mucormycosis. Emerging infectious diseases. Massachusetts : Academic Press; 2014. pp. 309–21.