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Cumulative Dose Reaction of Ambisome Infusion after Small Bowel Transplantation: A Description of 3 Cases and Review of Literature

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Abstract: AmBisome [Injection] is a non-pyrogenic lyophilized product for intravenous infusion and each vial contains amphotericin B [50 mg], intercalated into a liposomal membrane. The safety of Ambisome as prophylactic antifungal has been assessed in bone marrow transplant recepients, liver transplant recepients, renal transplant recepients and combined organ trans plant recepients. AmBisome was discontinued due to side-effects in 3% of the cases. In the current study involving small bowel transplant [SBT] patients it can be noted that all SBT patients tolerated the amBisome test dose well. However when intravenous infusion of amBisome was administered especially in neutropenic patients, it was noted that 3 patients (11%) developed a severe drug reaction and the drug had to be discontinued. The small bowel transplant patients in whom ambisome was discontinued there was a drug reaction which can be considered as a cumulative dose related reaction. It can be concluded that Ambisome is generally a safe drug for antifungal prophylaxis in small bowel transplant patients. The use of ambisome in neutropenic patients may amplify the cumulative dose reaction and may contribute to the picture that we have seen.
Keywords: Ambisome, amphotericin B, small bowel transplant, drug allergy.

INTRODUCTION

Renal, liver, heart and lung transplantation are considered the standard therapeutic interventions in patients with end-stage organ failure. The transplant recipients' overall immunosuppressed status predisposes to infectious complications following transplantation. Of all the infectious complications, invasive mycoses seem to be the most dreaded. Depending on the organ transplanted, the incidence of invasive mycoses ranges from 5 to 42%. Candida and Aspergillus spp. produce most of these mycoses [1].

Mortality due to these invasive fungal infections is still high, particularly in patients with invasive aspergillosis. However, the progressive improvement achieved in diagnosis and prevention of invasive fungal infections has led to a lower mortality rate[2]. The safety and side effect profile of ambisome is well documented however its use in the neutropenic patients may bring forth peculiarities in its side effects profile.

In this report we describe 3 cases of cumulative dose reaction to the infusion of AmBisome in neutropenic patients in a total cohort of 26 patients after small bowel transplant [SBT] in a five year period.

CASE PRESENTATION

The current study describes the concept of cumulative toxicity and side-effect profile of three patients with neutropenia after small bowel transplant (SBT) treated with ambisome to prevent invasive aspergillus infection.

Case 1

The patient was a fifty two year old lady who had received a SBT, 5 years ago. She had lost her native intestine to a thrombus in the superior mesenteric vein (SMV) on the background of an Antithrombi III deficiency. She had tolerated primary antifungal prophylaxis post small bowel transplant without any complications. Her current admission was associated with neutropenia of unknown origin in addition to clinical features of high-grade fever, a dry cough and generally feeling lethargic. Her chest radiograph (CXR) was inconclusive. Viral titres for CMV did not reveal any significant rise in her CMV counts.

An antibiotic and anti-viral therapy was instituted with a broad-spectrum third generation cephalosporin intravenously (IV) and oral valgancyclovir for CMV prophylaxis. Antifungal therapy with ambisome at 3mg/kg, IV once a day was

started. The amBisome infusion was started half an hour after the test dose. Fifteen minutes after starting the intravenous infusion the patient developed lower backache that the patient described as "a knife stabbing from the lower back through to the front". The stabbing pain worsened in intensity as the infusion continued and soon became intolerable. The patient's AmBisome infusion had to be stopped and her symptoms subsided over the next few minutes.

The patients drug history at this time including medication received over the past one month included low-dose azathioprine, cotrimoxazole, prednisolone, fentanyl , aranesp, belatacept, sodium bicarbonate, warfarin, calcichew and loperamide

Case 2

The patient was a thirty eight year old man who had a small bowel and abdominal wall transplant 8 weeks back. He had received AmBisome intravenous infusions as primary antifungal prophylaxis post small bowel transplant in the immediate post operative period for nearly six weeks without any adverse reaction to the drug. He was readmitted two weeks post discharge as he was pyrexic and neutropenic. He tolerated the test dose of AmBisome without any complications. Ten minutes after the intravenous AmBisome infusion was started he developed lower back-ache that worsened in intensity as the infusion continued and the patient found it impossible to move due to excruciating pain in his lower back. The infusion was stopped. He could feel immediate improvement in his symptoms although complete relief was obtained over next few minutes. The patients drug history including medication received over the past one month included tacrolimus, prednisolone, omeprazole, paracetemol, fentanyl, quinine, loperamide, valgancyclovir, cotrimoxazole, metronidazole, aspirin, dalteparin, sodium bicarbonate

Case 3

The patient was a thirty four year old man who had small bowel and abdominal wall transplant twenty-one months ago. He had developed fever, abdominal pain, nausea and neutropenia on several occassions over the past one and a half years that required numerous hospital admissions. He had received AmBisome intravenous infusions without any complications six times during these admissions. His current admission also involved fever, abdominal pain, nausea and neutropenia. Following the test dose, intravenous infusion of AmBisome was started. The patient developed increasing stiffness and pain in his neck soon after the infusion was started. As the infusion continued he felt the pain and stiffness radiating from his neck towards his upper limbs and it became increasingly difficult for him to move his hands/fingers also. Within the next few minutes he developed blurring of vision and his ribs seemed stiff to him. He felt it was getting difficult to breathe as his chest wall also seemed to stiffen. The AmBisome infusion was stopped. Patient was also given 100 mg hydrocortisone IV. His symptoms settled immediately. The medication including the past one month that he was receiving included tacrolimus, fentanyl, omeprazole, paracetemol, amitryptyline, dalteparin, and domperidon

DISCUSSION

AmBisome [Injection] is a non-pyrogenic lyophilized product for intravenous infusion and each vial contains amphotericin B [50 mg], intercalatedinto a liposomal membrane. Amphotericin B is a macrocyclic, polyene, antifungal antibiotic that is produced from a strain of *Streptomyces nodosus* [3]. Walsh et al reported that liposomal amphotericin B was associated with fewer breakthrough fungal infections than conventional amphotericin B [4]. The safety of Ambisome as prophylactic antifungal has been assessed in bone marrow transplant recepients, liver transplant recepients, renal transplant recepients and combined organ trans plant recepients. AmBisome was discontinued due to side-effects in 3% of the cases. Side-effects definitely attributed to AmBisome therapy included low potassium (n = 3), low back pain (n = 3), dyspnoea (n = 2), allergic rash (n = 1), nausea and vomiting (n = 1), confusion (n = 1), rise in alkaline phosphatase (n = 1) and cholecystitis (n = 1) with an overall incidence 7% [5].

In the current study it can be noted that the small bowel transplant patients (in whom ambisome was discontinued) there was a drug reaction which can be considered as a cumulative dose related reaction. In case one the lady developed the adverse reaction after the test dose. In case two the patient developed adverse reaction after having received ambisome for 6 weeks previously during which time there was no adverse reaction to the drug. In case 3 the patient developed the reaction to ambisome when it was administered in the seventh episode of neutropenia.

CONCLUSION

Ambisome is generally a safe drug for antifungal prophylaxis in small bowel transplant patients. The use of ambisome in neutropenic patients may amplify the cumulative dose reaction and may contribute to the picture that we have seen.

All SBT patients tolerated the amBisome test dose well. However when intravenous infusion of amBisome was administered especially in neutropenic patients, it was noted that 3 patients (11%) developed a severe drug reaction and the drug had to be discontinued. However at the same time the rest of the patients tolerated AmBisome intravenous infusions very well both as primary prophylaxis as well as emperical antifungal therapy during episodes of persistent fever and neutropenia.

REFERENCES

1. Marik PE. Fungal infections in solid organ

transplantation. Expert Opin Pharmacother. 2006 Feb;7(3):297-305.
2. Montego M. Epidemiology of invasive fungal infection in solid organ transplant Rev Iberoam Micol. 2011 Jul-Sep;28(3):120-3.
3. Ringdén O, Andström E, Remberger M, Svahn BM, Tollemar J. Safety of liposomal amphotericin B (AmBisome) in 187 transplant recipients treated with cyclosporin. Bone Marrow Transplantation. 1994; 14 Suppl 5:S10-4.
4. Walsh TJ, Finberg RW, Arndt C. Liposomal amphotericin B for emperical therapy in patients with persistent fever and neutropenia. N engl J Med. 1999:340:764-71.
5. www.rxlist.com/ambisome-drug.htm