

## Original Research Article

# Invasive fungal sinusitis-analysis of management scenario

Prishni Devi Dutta\*, B. P. Belaldvar, R. N. Patil

Department of ENT, KLE University Jawaharlal Nehru Medical College, Belagavi, Karnataka, India

**Received:** 29 April 2018

**Revised:** 31 May 2018

**Accepted:** 06 June 2018

**\*Correspondence:**

Dr. Prishni Devi Dutta,

E-mail: [drprishni87@gmail.com](mailto:drprishni87@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** The objective of the study was to analyse the outcomes after therapeutic treatment of invasive fungal sinusitis.

**Methods:** A cross-sectional study consisting of 30 patients from January 2015-December 2015 in Jawaharlal Nehru medical college, department of ENT, Belagavi. Antifungal drugs were used like Amphotericin B-both non-liposomal & liposomal variety, and analysis of various parameters like its duration, efficacy and dosage was done in determining the prognosis.

**Results:** The liposomal type of amphotericin B (AmBisone), which was used in 23 patients (76.6%) had a response rate of 65% and failure rate of 26%, with minimum dose of 50 mg/day to maximum dose of 200 mg/day. The maximum number of days used was for 46 days in 18 cases, which showed the effectiveness in controlling the infection. Amphotericin B deoxycholate (Fungizone) was used in 6 patients (20%) with response rate of 50% and failure rate of 33.3% and maximum dose given was 25 mg/day keeping a track of the renal profile. The total duration of treatment with Fungizone was for 14 days.

**Conclusions:** Along with surgical intervention, we were able to combat this fatal disease in 56% patients which was the overall survival rate and liposomal variety was preferred as majority of the patients had deranged renal parameters on presentation. But certain constraints like non-affordability by poor patients, cost-effectiveness on long term usage, were there. So further studies about the availability of more safer and affordable antifungals should be done.

**Keywords:** Invasive fungal sinusitis, Antifungals, Amphotericin B

### INTRODUCTION

With the development of medical field and invention of newer technologies and availability of better treatment and care of diseases, the life expectancy has increased in the last two decades. But the prolonged and rampant use of antibiotics in almost all diseases has led to development of resistances, and also the increasing incidence of diabetes and malignancies has led to development of immunocompromised state making prone for development of fungal infections

Mycotic diseases of nose and paranasal sinuses range from an indolent infection in an otherwise normal person to lethal infection in an immunocompromised individual.<sup>1</sup> It is typically developed by poorly controlled diabetics patients with diabetic ketoacidosis.

However, early diagnosis is possible because of endoscopic visualization, CT scan, microbiological tests like KOH mounts, culture and molecular detection. Moreover with advent of good antifungal drugs, endoscopic debridement, faster control of diabetes with infusion pump delivery system of insulin and better ICU

care, the chances of survival from such fatal disease looks better.

Presently we have the following antifungal drugs available for the therapy

- 1) Amphotericin B- Deoxycholate variety, lipid complex & liposomal variety
- 2) Triazoles group- Fluconazole, voriconazole, posaconazole
- 3) Echinocandins- Caspofungin, micafungin.<sup>2</sup>

Though amphotericin B deoxycholate has been the corner stone of treatment for this infection, because of associated nephrotoxicity, and infusion related toxicities on prolonged use, lipid formulations were introduced.<sup>3</sup>

We also have used the above regimen of both non-liposomal type and liposomal variety of amphotericin B in our hospital and hence we want to analyse the outcome of therapeutic treatment of invasive fungal sinusitis.

## METHODS

**Type of study:** Cross-sectional study.

This study was done on 30 patients from a time period of January 2015-December 2015 in Jawaharlal Nehru medical college, Department of ENT, Belagavi.

### Inclusion criteria

All cases (old and new) which were admitted and received treatment for invasive fungal sinusitis, with recorded documentation.

The study was cleared by the medical college ethics committee.

The following methods were applied

- By identifying the cases from the medical records which were managed in our hospital.
- Collecting detailed information about the patient from the case files, and about the treatment history.
- To analyse the duration, dosage, efficacy of the antifungals used.

The antifungal regimen used for the treatment was Amphotericin B– deoxycholate (Brand name- Fungizone) and liposomal variety (Ambisone), Fluconazole and Voriconazole (Vfend).

The etiological profile was 26 cases with diabetes mellitus, 10 cases with chronic kidney disease and 2 cases of hematological malignancies and in two cases no immunocompromised state was seen.

## RESULTS

On analyzing data of 30 cases, majority belonged to elderly group of 51-65 years (53.33%) i.e. 16 out of 30 cases with age range of 37-70 years.

The majority patients, 23 patients (76.6%) were treated with liposomal amphotericin B (Ambisone) with response rate of 65% and failure rate 26%. The reason why liposomal variety was preferred, in maximum patients was keeping in view of the deranged renal parameters on presentation and hence also were recommended to patients who had no renal involvement due to its nephrotoxic effect on prolonged treatment.

In 6 patients (20%), who were treated with Amphotericin B deoxycholate variety, the response rate was 50% and failure rate was 33.3%.

**Table 1: Type of antifungal regimen.**

Antifungal drugs (brand names)	No. of cases (%)	Cured (%)	Died (%)
<b>Amphotericin B liposomal (AmBisone)</b>	23 (76.6)	14 (60)	6 (26)
<b>Amphotericin B deoxycholate (Fungizone)</b>	6 (20)	3 (50)	2 (33.3)
<b>Fluconazole</b>	2 (6.66)	2 (100)	
<b>Voriconazole (Vfend)</b>	1 (3.33)		

Fluconazole was used in 2 patients who had localized sphenoid sinus disease by *Aspergillus sp.* and were not tolerating amphotericin B. Voriconazole was used after total clearance of frontal lobe abscess by craniotomy and neurosurgeon insisted on using this drug orally as disease was found to be localized.

### Dosage regimen

The dosage for liposomal variety ranged from 50-20 mg/day. Starting at 10 mg test dose we gradually

increases it to 1-3 mg/kg which primarily depend upon renal profile and continued till total clearance.

While using the deoxycholate variety, keeping in track of renal parameters, 2 patients were later switched over to liposomal type and 1 patient despite worsening renal profile refused to change over due to high cost. Dosage ranged from 1-25 mg/day.

The maximum period of days used was 46 days for liposomal type in 18 patients (78.2%), owing to aggressiveness of the disease which helped in combatting

the infection along with surgical debridement which was done for all patients.

**Table 2: Duration of Amphotericin B (liposomal and non-liposomal).**

Antifungal drugs	No. of cases	Minimum days	No. of cases	Maximum days	No. of cases
<b>Liposomal amphotericin B</b>	23	7	5	46	18
<b>Amphotericin B deoxycholate</b>	06	5	2	14	4

## DISCUSSION

In the present study we analysed the outcomes after the medical management of invasive fungal sinusitis. But it must be stressed that multiple surgical debridement was must go hand in hand in managing such a notorious disease which will help in penetration of the antifungal drugs.

Though amphotericin B has been in the market for more than 40 years, for treating mucormycosis, but unfortunately the development of immunocompromised state has also increased magnanimously, with uncontrolled diabetes mellitus occurring even in younger age and also the incidences of hematological malignancies.<sup>10</sup>

Hence, though many studies have emphasized the necessity of both medical and surgical management along with early diagnosis, but still many lapse can be seen specially in case of antifungals. This could be due limitations and side-effects associated with the medical line of management on prolonged therapy.

Chakrabarti et al have treated 33 patients with conventional amphotericin B, and 12 patients with liposomal type.<sup>4</sup> The mortality rate was 100% when only amphotericin B deoxycholate was used alone.

Whereas in our study, the response rate was 60% and failure rate was 26% for liposomal type which was similar with study done by Kasapoglu et al.<sup>5</sup>

In our study, amphotericin B deoxycholate, though cost wise effective, was not the first choice as 30% patients had deranged renal profile and on longer term it cause acute renal injury, and further deterioration of renal parameters.

We continued the antifungal therapy until we were sure of total clearance of disease from the sinuses which were assessed with repeated nasal endoscopy and negative microbiological confirmations of tissue sent for fungi.

In study done by Kasapoglu et al, the optimal dosage was 1 mg/kg/day for Amphotericin B and 5-7.5 mg/kg/day for liposomal type, they stated duration of treatment is tailored to each individual and factors affecting this are, resolution of clinical signs of infection, stabilizing or resolution of radiological findings, and immune-suppression and this period is usually 6-8 weeks.<sup>5</sup>

However Shoham, Idoko and Bongiovanni found no correlation between patient outcomes and dosage.<sup>6,7,9</sup>

But from our analysis we believed, cases which were treated with liposomal variety for more than 4 weeks, with daily increment in dose definitely helped in better control of spread of infection. But still the overall mortality rate was 30%, which was due to aggressiveness of the underlying illness which leads to intracranial and orbital spread and lead to loss of those cases with complications associated with it like multiple organ failure, ventricular arrhythmia, complications of chronic kidney disease, blast crisis of chronic lymphocytic leukemia.

We implemented both medical and surgical intervention with the plan of removing all diseased tissue with multiple endoscopic assessments along with, if needed repeated debridements and aggressive measures, and also that with the use of appropriate antifungal agent we can get easy access and penetrance and substantially help in local control and prevent dissemination of disease.

## CONCLUSION

The final outcome depends on the underlying illness, site of infection and type of antifungals used. The overall mortality rate in our study was 30% and survival rate was 56.6%.

Hence we emphasize on early diagnosis and further improvement in microbiological diagnostic measures so that valuable time is not lost between identifying the exact mucorale species and initiating appropriate measures. But certain constraints were there like cost of liposomal amphotericin B, not easily afforded by patients from poor background, and refusal on the part of patient or their relatives for surgery and further treatment due to comorbidities associated with it.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Morgan J, Warnock D. Mycotic diseases of the Paranasal sinuses. Scott-Brown's Otorhinolaryngology Head and Neck surgery. 7th ed. London: Hodder Arnold; 2008: 216.

2. Fliickiger U, Marchetti O, Bille J, Eggimann P, Zimmerli S, Imboff A, et al. Treatment options of invasive fungal sinusitis in adults. *Swiss Med Weekly.* 2006;136:447-63.
3. Ferguson B. Fungal Rhinosinusitis A Spectrum of Disease. *The Otolaryngologic Clin North America.* 2000;33(2):227-454.
4. Chakrabarti A, Chatterjee S, Das A, Panda N, Shivaprakash M, Kaur A, et al. Invasive zygomycosis in India experience in a tertiary care hospital. *Postgrad Med J.* 2009;85:573-81.
5. Kasapoglu F, Coskun H, Ozmen O, Akalin H, Ener B. Acute invasive fungal rhinosinusitis: Evaluation of 26 patients treated with endonasal or open surgical procedures. *Otolaryngol Head Neck Surg.* 2010;143:614-20.
6. Shoham S, Magill S, Merz W, Gonzalez C, Seibel N, Buchanan W, et al. Primary treatment of zygomycosis with liposomal amphotericin B analysis of 28 cases. *Medical Mycol.* 2010;48:511-7.
7. Idoko K, Gomes I, Sharma P. Rhinocerebral Mucormycosis in patient with Acquired Immunodeficiency Syndrome. *Infecti Dis Clin Practice.* 2011;19(6):431-2.
8. Roden M, Zaoutis T, Buchanan W, Knudsen T, Sarkisova T, Schaufele R, et al. Epidemiology and Outcome of Zygomycosis: A review of 929 cases. *Clin Infect Dis.* 2005;41:634-53.
9. Bongiovanni M, Ranieri R, Ferrar D, Codeca C, Tartaro T, Uzie L. Prolonged survival of an HIV-infected subject with severe lymphoproliferative disease and rhinocerebral mucormycosis. *J Antimicrob Chem.* 2007;60(1):192-3.
10. Greenberg R, Scott L, Vaughn H, Ribe J. Zygomycosis (mucormycosis): emerging clinical importance and new treatments. *Current Opinion Infect Dis.* 2004;17:517-25.

**Cite this article as:** Dutta PD, Belaldvar BP, Patil RN. Invasive fungal sinusitis-analysis of management scenario. *Int J Otorhinolaryngol Head Neck Surg* 2018;4:1061-4.