



COMPARISON OF AMPHOTERICIN AND AMPHOTERICIN WITH POSACONAZOLE IN TREATMENT OF RHINOORBITOCEREBRAL MUCORMYCOSIS SECONDARY TO COVID 19 INFECTION.

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Abstract-

Background- Infectious hyphae can invade the blood vessels, leading to necrosis of the structures involved in rhino-orbital-cerebral mucormycosis. Large cases have been recorded from India, proving that this clinical entity is regionally variable. According to the disease's stage, the affected individuals experience different levels of clinical suffering. Treatment for rhino-orbital-cerebral mucormycosis requires a multidisciplinary strategy. This study compared the effectiveness of amphotericin and amphotericin with posaconazole in treating rhinoorbitocerebral mucormycosis caused by Covid 19 infection.

Methodology- A total of 36 subjects were included in the current investigation who were presented with Rhinoorbitocerebral mucormycosis. This was a double-blinded randomized controlled trial study conducted between May 2021 to August 2021. Patients have then divided into two groups: Group A, received Amphotericin alone in postoperative care. Group B, received Amphotericin along with posaconazole in postoperative care.

Results- Among 36 patients, majority of the patients 14 (38.9%) belonged to the age group of 50 – 60yrs and males were showing gender preponderance 27 (75%). Majority of the patients (66.7%) had not used Amphotericin alone, not used amphotericin and posaconazole. Among those patients who had used 20-30 vials of Amphotericin alone, majority of the patients (63.6%) had used Amphotericin with Posaconazole drug. This is not found to be statistically Significant (p=0.658).

Conclusion- During the COVID-19 pandemic, rhinoorbitocerebral mucormycosis was one of the most prevalent and severe fungal diseases seen. The best way to increase survival rates in these situations is through early detection, appropriate antifungal dosage, and prompt action.

As compared to amphotericin alone, posaconazole plus amphotericin resulted in better outcomes. The study reveals that even though it was not statistically significant, it was clinically important.

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INTRODUCTION:

A fungal infection of the nose that affects primarily immunocompromised individuals is sinus Mucormycosis. It is an opportunistic, potentially fatal, and rare fungal infection. Mucorales, Mucoraceae, genus Mucor and Rhizopus are the saprophytic and opportunistic fungi that are responsible for this condition [1]. **Paultauf** reported the very first case of mucormycosis in **1885**. In the past, people with diabetes along with ketoacidosis would present with sinus involvement.

The mucormycosis prevalence rate has increased over the past century and is linked to high attributable mortality as a result of assertive chemotherapies and immunosuppressive therapeutic approaches in hematological malignancies (HMs), hematopoietic stem cell transplantation (HSCT) and solid-organ transplantation (SOT). Lung infections are the

primary site of infection in HM, which is the most prevalent underlying illness.

Advances in medical technology have helped to increase life expectancy, but aside from the advancements in medicine, the population has increased its risk of developing fungal rhinosinusitis due to the prolongation of survival rates among patients with hematologic malignancies and diabetes mellitus. A rise in immunocompromised patients has resulted in an increased prevalence of acute invasive fungal sinusitis [2].

According to anatomical location, mucor can manifest in a variety of ways, including pulmonary, gastrointestinal, cutaneous, encephalic and rhinocerebral. Some of the frequently isolated species of mucor from the patients are as follows [2].

Frequently isolated species of mucor from the patients are as follows.

- *Cunninghamella (C. bertholletiae)*
- *Apophysomyces (A. variabilis), Cunninghamella (C. bertholletiae)*
- *Lichtheimia [Absidia] (L. corymbifera L.raosa)*
- *Mucor (M. circinelloides)*
- *Rhizopus (R. arrhizus (oryzae) R. microsporus)*
- *Rhizomucor (R. pusillus)*

Many instances of Covid 19 throughout the second wave in India were confirmed to present with side effects like facial thickening (swelling), facial pain, and nasal blockage; however, upon careful examination, Mucormycosis was determined to be the cause of these situations. The overuse of steroids and oxygen therapy during the course of treating Covid 19 infection was primarily blamed for the expansion of Mucormycosis in patients [6].

Objective:

1. To study the effect of Amphotericin as compared to Amphotericin with Posaconazole in the management of Rhinorbitocerebral mucormycosis .
2. To assess the sex and age pattern of Rhinorbitocerebral Mucormycosis

Materials and Methods:

In the present investigation, a total of 36 subjects were included in the study who were presented with

Rhinorbitocerebral mucormycosis. This was a double-blinded randomized controlled trial study conducted between May 2021 to August 2021.

Patients were assessed using a thorough medical history as well as ENT, ophthalmic, as well as neurological exams. Regular blood tests were performed. For three weeks, a diagnostic nasal endoscopy was performed weekly, along with serial biopsies and KOH collection. To determine the severity of the illness, a CT scan of the nose and PNS were obtained. To assess the intraorbital and intracranial extent, MRI was performed. Patients have then divided into two groups:

Group A, received Amphotericin alone in postoperative care.

Group B, received Amphotericin along with posaconazole in postoperative care.

RESULTS:

Table 1. shows the age and gender of the Rhinorbitocerebral mucormycosis patient. Among 36 patients, majority of the patients 14 (38.9%) belonged to the age group of 50 – 60yrs, followed by 10 patients (27.8%) belonged to the age group of 40 -50yrs, 8 patients (22.2%)

belonged to age group of <40yrs and remaining 4 patients (11.1%) belonged to 60-70yrs respectively.

Among 36 patients, males were 27 (75%) and remaining were females 9 (25%) respectively.

Table 1. Socio-demographic details

SI.No	Socio-demographic details	Frequency (n)	Percentage (%)
1	Age -	8	22.2
	<40	10	27.8
	40-50yrs	14	38.9
	50-60yrs	4	11.1
	60-70yrs		
2	Gender -	27	75
	Males	9	25
	Females		
	Total	36	100

Figure 1. Distribution of patients according to Age

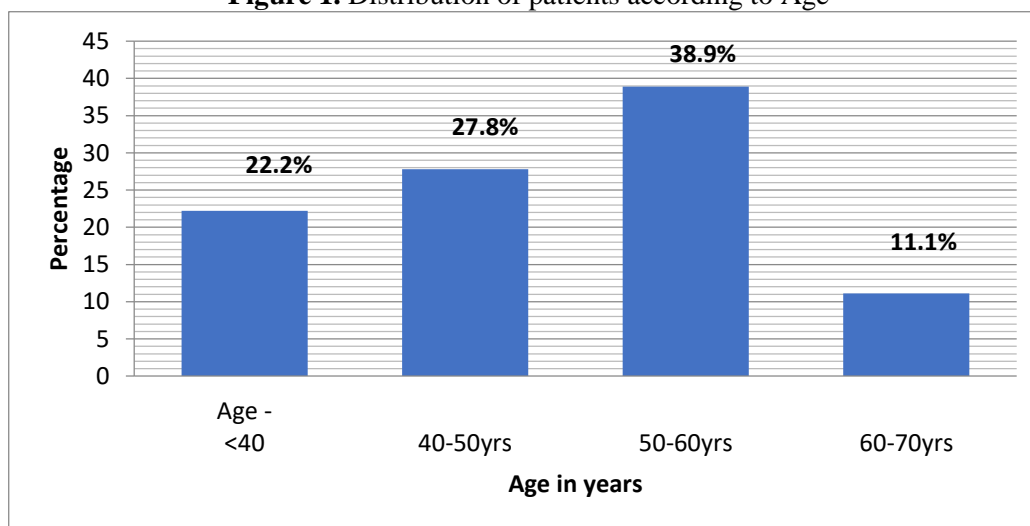


Figure 2. Distribution of patients according to Gender

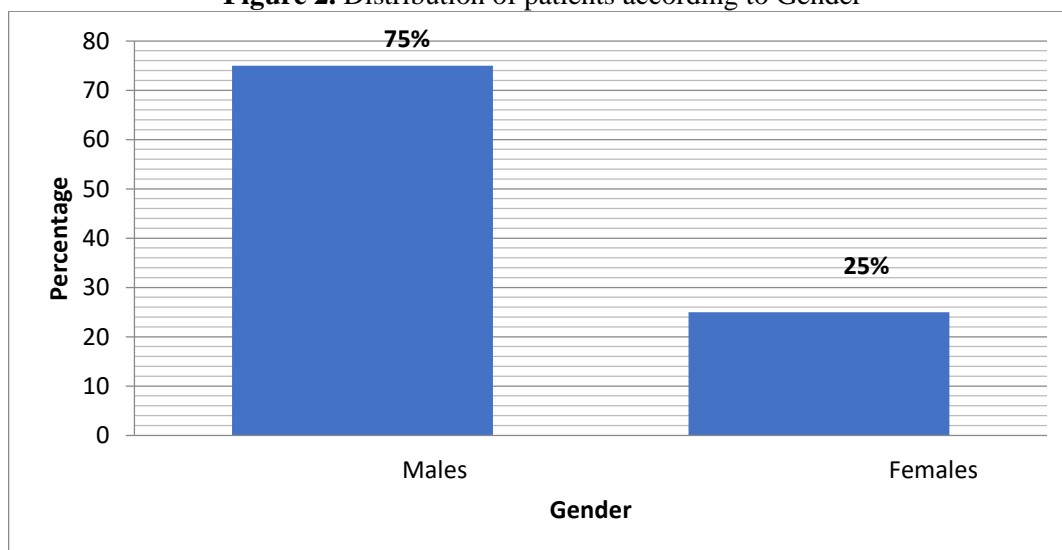


Table 2 shows the drugs used for the Rhinorbitocerebral mucormycosis. Among 36 patients, majority of the patients 22(66.7%) had not given with the ampho-lypholyophilic drug. Among those who had given with the ampho-lypholyophilic drug, majority of the patients were given >5vials i.e, 7 (19.4%) remaining patients were given <5 vials i.e, 5(13.9%) respectively. The patients who had given with the Ampho-liposomal drug, majority of the patients (11, 30.6%) were given with 20-30 vials, followed by 40- 50 vials were given in the 8 patients (22.2%), 10-20vials have been used in the 7patients (19.4%),

50-60 vials have been used in the 4patients (11.1%), 30-40vials have been used in the 2patients (5.6%) and remaining 1 (2.8%) patient had been used with the amphotericin-liposomal drug. In the other 3 patients, the amphotericin-liposomal drug was not been used.

The patients who had been given with posaconazole drug, the majority (50%) of the patients had been used, followed by 100-200mg of Posoconazole drug had been given in patients (22.2%), <100mg and 200-300mg were given in the 5 patients each respectively.

Table 2. Distribution of patients according to the usage of drugs

Sl.No	Drugs usage	Frequency (n)	Percentage (%)
1	Ampho-lypholyophilic	24	66.7
	Not used	5	13.9
	<5 vials	7	19.4
	>5 vials		
2	Ampho - liposomal	3	8.3
	Not used	1	2.8
	<10 vials	7	19.4
	10-20 vials	11	30.6
	20-30 vials	2	5.6
	30-40vials	8	22.2
	40-50 vials	4	11.1
3	Posaconazole		
	Not used	18	50
	<100mg	5	13.9
	100 – 200mg	8	22.2
	200 – 300mg	5	13.9
	Total	36	100

Table 3 shows the comparison of Amphoterecin alone with Amphoterecin and Posaconazole drugs. Majority of the patients (66.7%) had not used Amphoterecin alone, not used amphoterecin and posoconazole. Among those patients who had used

20-30 vials of Amphoterecin alone, majority of the patients (63.6%) had used Amphoterecin with Posaconazole drug. This is not found to be statistically significant (p=0.658).

Table 3. Comparison of Amphoterecin with Posaconazole

Amphoterecin	Amphoterecin and Posaconazole				Total	P value
	Not used	<100mg	100 to 200mg	>200mg		
Not used	2 (66.7%)	0 (0%)	1 (33.3%)	0 (0%)	3 (100%)	0.658
<10 vials	1 (50%)	0 (0%)	0 (0%)	1 (50%)	2 (100%)	
10 – 20 vials	3 (42.9%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	7 (100%)	
20 – 30 vials	7 (63.6%)	3 (27.3%)	1 (9.1%)	0 (0%)	11 (100%)	
30 – 40 vials	1 (50%)	0 (0%)	0 (0%)	1 (50%)	2 (100%)	
40 – 50 vials	2 (25%)	1 (12.5%)	4 (50%)	1 (12.5%)	8 (100%)	
50 – 60 vials	2 (50%)	0 (0%)	1 (25%)	1 (25%)	4 (100%)	

DISCUSSION:

In the current investigation, we have compared the outcomes of treatment of Rhinorbitocerebral mucormycosis using Inj Amphotericin alone and Inj. Amphotericin with oral Posaconazole in the Eur. Chem. Bull. 2023, 12(Special Issue 10), 3702 –3707

postoperative period. It was observed that the disease was more common in males and in the age group of 50-60 years.

The study done by **Andrew Blitzer et al**, opted a total of 9 subjects presented with fungal infection

of the nose along with PNS. Patients included in their study had a mean age of 46 years which was similar to the present investigation. However, the predominance of fungal infection was more likely to be noted in males.

The male-to-female ratio in the study published by **Folker et al**, was observed to be 1.5:1. For the medical management of Rhinorbitocerebral Mucormycosis, we used Inj Amphotericin alone in 18 patients while the other 18 patients received Amphotericin along with Posaconazole for three weeks. The patients also underwent Nasal Endoscopy every week for 3 consecutive weeks and HPR and KOH were sent. It was observed that the patients who received Liposomal Amphotericin along with Posaconazole had a negative KOH and HPR on their second endoscopy while patients who received Inj. Amphotericin alone had a negative KOH and HPR on their third endoscopy. The dose of Liposomal Amphotericin B was 5-10mg/kg body weight from day one for sinonasal infection, while in the case of cerebral involvement, it's dose was 10mg/kg/day from day one.

Lyophilic Amphotericin B was given at a dose of 1-1.5 mg/kg each day, and Posaconazole had been given in a tablet form at a dose of 300 mg once every day for at least two weeks. Even though Amphotericin B does seem to have side effects that may restrict its administration. According to **Weber et al**. despite having systemic side effects that might restrict its administration, Amphotericin B should be the cornerstone of treatment for invasive and widely distributed fungal infections. In the current investigation, a 100% life expectancy was seen, compared to **Blitzer et al**. 79% survival rate.

CONCLUSION:

Rhinorbitocerebral mucormycosis was one of the most common and aggressive fungal infections which were observed during the COVID-19 pandemic. This was mainly attributed to the use of steroids, oxygen therapy, immunocompromised states and immunosuppressed patients. Early detection, the adequate dosage of antifungal agents and timely intervention are the keys to improving survival rates in these cases.

Overall, the results in patients who received a combination of Amphotericin and Posaconazole were better in patients as compared to Amphotericin alone. Although not statistically significant, the study shows that it was clinically significant.

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