

# **A STUDY ON THE EFFICACY OF TRANSCUTANEOUS RETROBULBAR INJECTION OF AMPHOTERICIN B ON THE OCULAR MANIFESTATIONS OF STAGE – III MUCORMYCOSIS (ROCM)**

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# INTRODUCTION

- Mucormycosis (Black fungus- which is a misnomer) is a potentially lethal, angioinvasive fungal infection predisposed by diabetes mellitus, corticosteroids and immunosuppressive drugs, primary or secondary immunodeficiency, hematological malignancies and hematological stem cell transplantation, solid organ malignancies and solid organ transplantation, iron overload, etc. It is an aggressive opportunistic fungal infection, also known as Phycomycosis and Zygomycosis. It is caused by organisms of the family Mucoraceae (including the genera Mucor, Absidia, Rhizopus).
- The fungus that causes the disease is ubiquitous in nature and is found in soil and on decaying vegetation. Because the fungus is so widespread, humans are exposed to it on regular basis. The spores of the fungus are inhaled through the mouth and nose, but infection rarely occurs in a person with an intact immune system, because macrophages phagocytize the spores. However, an immunocompromised individual is unable to mount an effective immune response against the inhaled spores; thus, germination and hyphae formation occur and infection develops, most commonly in the paranasal sinuses and lungs.
- The increasing incidence of Rhino-orbito-cerebral Mucormycosis (ROCM) in the setting of COVID-19 in India and elsewhere has become a matter of immediate concern. Since February 2021, there has been an exponential increase in incidence in India, in sync with the soaring second wave of COVID19. New corona virus SARS COV 2 itself is a risk factor - chronic respiratory disease, prolonged corticosteroid therapy, intubation /mechanical ventilation, deranged glucose metabolism, which may lead to secondary fungal infection



## **MATERIALS AND METHODS:**

Out of about 300 cases of mucormycosis attended GGH, Guntur ,150 cases of Post COVID Rhino-orbito-cerebral Mucormycosis stage-3 were taken in this study,during the period of May to July 2021.

Patients in stage-3 ROCM were admitted ,stopped steroid ,monitored daily blood sugar levels titration with oral hypoglycemic agents and injection insulin in some patients, systemic iv antifungals – amphotericin-B ,in some cases posaconazole were given and FESS was done for almost all cases along with other supportive treatment .

Transcutaneous Retrobulbar Liposomal-Amphotericin-B injection(TRAMB)3.5 mg/ml given as 3 doses on alternative days

## **INCLUSION CRITERIA**

1.All the cases with proven fungal elements on biopsy or proven fungal invasion of Orbits/Orbital apex/Extraocular muscles/Retrobulbar fat on MRI

## **EXCLUSION CRITERIA:**

- 1.Patients who are not willing to give consent
- 2.Patients with age less than 18 years
- 3.Patients who are negative for fungal biopsy
- 4.Patients with stage 4ROCM

## **DIAGNOSIS: Symptoms + Investigations**

- H/o COVID infection (Immunosuppressive drugs/ Ventilatory care, etc.)
- Co morbid conditions: Diabetes mellitus/ Malignancy/ HIV/ Chronic kidney disease / Obesity/ Other systemic illness

## **Investigations include:**

- 1) Lab parameters: CBC, ESR, FBS, PPBS, HbA1C, LFT, RFT with electrolytes, Viral markers (HIV/HBV/HCV)
- 2) Diagnostic nasal endoscopy: crusting, debris, scabbing, granulation, discoloured mucosa (either darkened or pale), decreased bleeding and insensate mucosa



3)CECT Nose and PNS: Erosion and thinning of bones, Enlargement of masticatory muscle, Mucosal thickening of sinuses Changes in Fat Planes

CEMRI Brain Orbit and PNS: Optic neuritis, Intracranial involvement, Cavernous sinus thrombosis, extraocular muscle thickening, Infratemporal fossa involvement

4) KOH staining & microscopy - Direct microscopy using fluorescent brightener and histopathology with special stains (e.g. PAS and GMS) Typical findings: non-septate/pauci-septate, ribbon-like hyphae (at least 6–16µm wide), Vessel occlusion

5) Histopathology- haemorrhagic infarction, coagulation necrosis, angioinvasion, infiltration by neutrophils (in non-neutropenic hosts), and perineural invasion.

6) Fungal culture- sabourad's dextrose agar at 30°C and 37°C. Typical findings: cotton white or greyish black colony

## OBSERVATION

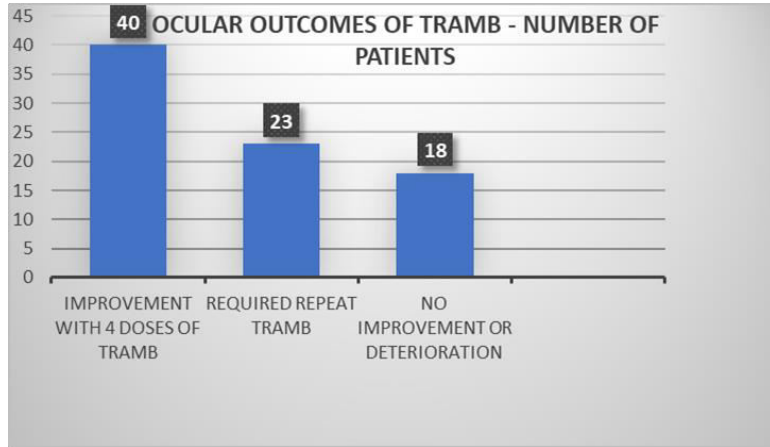
- Patients in stage-3 ROCM who were administered with Transcutaneous Retrobulbar Liposomal-Amphotericin-B injection(TRAMB)3.5 mg/ml given as 3 doses on alternative days and followed for a period of 1 week and depending on the clinical improvement, one more dose is repeated after one week.150 cases were followed closely, and ocular findings were recorded.

## RESULTS

Ocular presenting features	Number of patients
Periorbital edema and discoloration	94
Ptosis	55
Proptosis	39
Chemosis	56



# RESULTS



- 103 patients(69%) had improvement in symptoms like decrease in edema, pain, improvement of vision and no further deterioration of vision, resolution of proptosis and chemosis.
- Of the 103 cases, 41 cases had improvement with 4 doses, and 62 cases required repetition of doses after 1 week.
- 18 cases (31%) had neither improvement nor deterioration in ocular complaints.



Before treatment



After treatment

## DISCUSSION

- Proposed staging of ROCM(Dr.Santhosh G Honavar IJO 18/06/2021)

STAGE	CLINICAL FEATURES
Stage 1	Involvement of Nasal mucosa
Stage 2	Involvement of Paranasal sinuses
Stage 3	Involvement of Orbit
Stage 4	Involvement of CNS



- **Patients with COVID-19 illness (active/recovered) presenting with the following symptoms:**
- Sinusitis: Fever, nasal stuffiness, facial pain and numbness, retro-orbital headache, hyposmia, blood-tinged/brownish black nasal discharge, Nasal mucosal erythema, inflammation, purple or blue discoloration, white ulcer, ischemia, or eschar
- Maxillary: Toothache, loosening of maxillary teeth, jaw involvement
- Eye symptoms: Redness and swelling of eye, diplopia (double vision), visual loss, Eyelid swelling, periocular, facial discoloration, Sudden loss of vision, Sudden ptosis, Ocular motility restriction
- Regional pain – orbit, paranasal sinus or dental pain
- Facial paresthesias, anesthesia
- Facial palsy
- Fever, altered sensorium, paralysis, focal seizures
- Management of mucormycosis essentially involves control of hyperglycemia, other risk factors, optimal surgical debridement & medical management with SYSTEMIC anti fungal agents.

- Amphotericin-B is the antifungal drug of choice for mucormycosis. Posaconazole & Isavuconazole have also found to be effective.
- Prolonged step down oral antifungal therapy is warranted for 3-6 months.

## CONCLUSION

- In patients with early diagnosis and administration of TRAMB, vision could be saved and other ocular complaints were resolved. Delay in presentation or diagnosis led to Intracranial extension, leading in poor general condition as well as loss of vision.
- Initially Retrobulbar administration on consecutive days was done, which later was shifted towards alternate days to prevent the dreaded complication of Orbital Compartment Syndrome,
- **REFERENCES** Honavar SG. Code Mucor: Guidelines for the Diagnosis, Staging and Management of RhinoOrbito-Cerebral Mucormycosis in the Setting of COVID-19. Indian J Ophthalmol 2021;69:1361-5.
- Harrison's Principles of Internal Medicine –20<sup>th</sup> edition.

