



ABSTRACT

Mucormycosis diseases – Treatment protocol for patients with Mucormycosis infection – Approved – Orders – Issued.

HEALTH AND FAMILY WELFARE (P1) DEPARTMENT

G.O.(Ms).No.262

Dated: 02.06.2021

Pilava, Vaikasi – 19

Thiruvalluvar Aandu – 2052

Read :

1. G.O.(Ms).No.249, Health and Family Welfare (P1) Department, dated 20.05.2021.
2. G.O.(Ms).No.255, Health and Family Welfare (P1) Department, dated 26.05.2021.
3. From the Director of Medical Education, letter Ref.No.38348/H&D/2/3/2020, dated 31.05.2020.

ORDER:

In the Government Order first read above, the MUCORMYCOSIS has been declared as a notified disease in the State of Tamil Nadu. In Government order second read above, orders have been issued to constitute a Task Force Committee with medical experts to advise the Government on issues related to Mucormycosis, its prevention, treatment and also update Government with the latest on translational research on the subject and any other connected issues.

2. The Director of Medical Education has now stated that the Task Force Committee have recommended the draft treatment protocol according to the latest Guidelines and requested the Government to issue an order on the same.

3. The Government have examined the request of the Director of Medical Education and approve Treatment protocol according to the latest Guidelines for Mucormycosis.

4. The Treatment protocol for Mucormycosis disease patients with the latest Guidelines is annexed with this order.

(BY ORDER OF THE GOVERNOR)

**J.RADHAKRISHNAN
PRINCIPAL SECRETARY TO GOVERNMENT**

To

The Director of Medical Education, Chennai – 600 010.

The Director of Medical and Rural Health Services, Chennai- 600 006.

The Director of Medical and Rural Health Services (ESI), Chennai- 600 006.

The Director of Public Health and Preventive Medicine, Chennai- 600 006.

The Mission Director, National Health Mission, Chennai – 600 006.
The Commissioner, Greater Chennai Corporation, Chennai – 600 003.
The Project Director, Tamil Nadu Health System Project, Chennai – 600 006.
All District Collectors.

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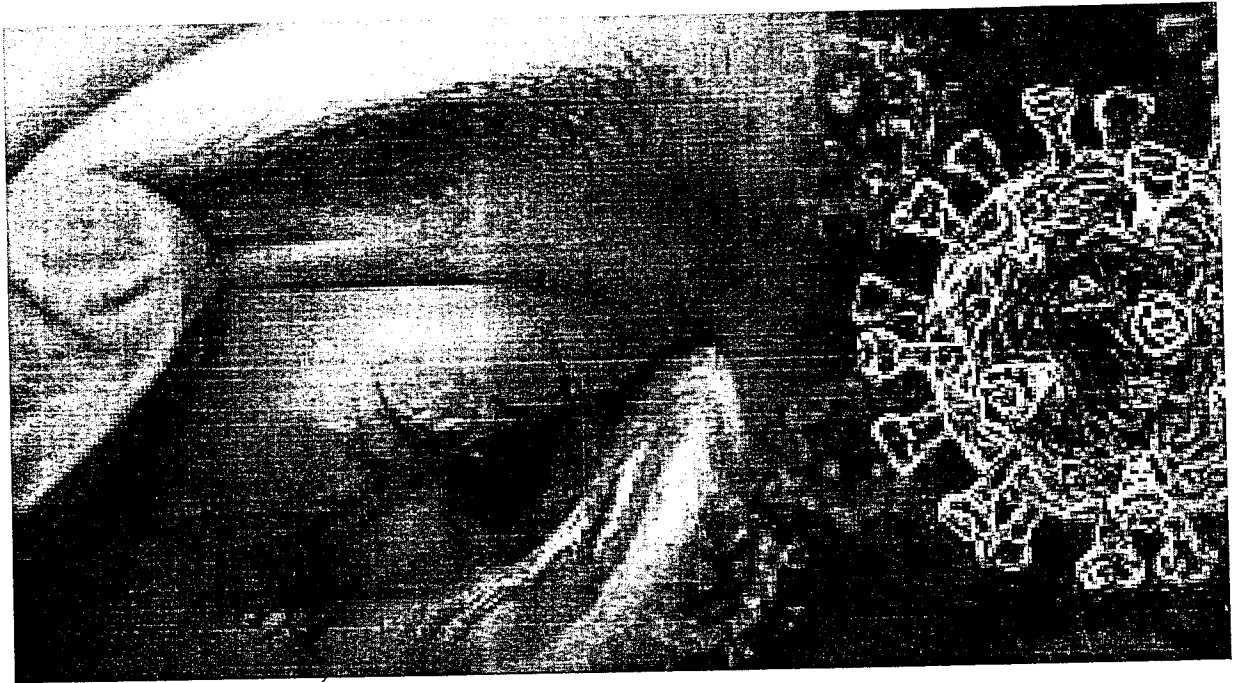
✓ The Health and Family Welfare (Data cell) Department, Chennai - 600 009.
Stock File / Spare Copy.

//FORWARDED BY ORDER//

B. S. Srinivasan
SECTION OFFICER
2/6/21

MUCORMYCOSIS

MANAGEMENT GUIDELINES



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Annexure to G.O.(Ms).No.262, Health and Family Welfare (P1)
Department, dated 02.06.2021

INTRODUCTION

Mucormycosis is an aggressive, opportunistic devastating fungal infection commonly involving Nasal, Orbital and Cerebral regions. It is acquired primarily via inhalation of spores through nasal route. It is a rapidly progressive fungal disorder and any delay in identification & management leads to high morbidity & mortality.

The fungus is angio-invasive causing occlusion of blood vessels, leading to tissue necrosis. Other forms of clinical presentation are Pulmonary, Cutaneous, Gastrointestinal, bone & joint infection and disseminated Mucormycosis.

PREDISPOSING FACTORS

- Concurrent /Recently treated COVID -19
- Uncontrolled Diabetes Mellitus
- Inappropriate use of Steroids
 - High doses of steroids
 - Using for prolonged periods
- Immunocompromised individuals
 - Malignancy
 - Transplant recipients
- Prolonged use of broad-spectrum antibiotics
- People under long standing Oxygen therapy
- Prolonged ICU stays
- People under mechanical ventilation
- Nosocomial – Contaminated dirty linen, ICU gadgets –if not properly sterilized.

CLINICAL PRESENTATION

I.Generalized Symptoms:

- i. Headache
- ii. Low Grade Fever
- iii. Malaise & Lethargy

II. Nasal Symptoms:

- i. Nasal Obstruction
- ii. Nasal Discharge often bloody, brownish, or blackish.

III. Ocular Manifestations:

- i. Pain and redness around eyes, watering
- ii. Periorbital Swelling / Discoloration, Proptosis
- iii. Diplopia / Diminution of vision
- iv. Ptosis
- v. Ophthalmoplegia
- vi. Facial Swelling & pain, paresthesia, Numbness in the infra orbital region

IV. Oral Manifestations:

- i. Toothache/Loosening of teeth
- ii. Blackish discoloration of oral mucosa
- iii. Loss of sensation/numbness, ulceration/perforation over palatal region

V. Pulmonary Manifestations:

- i. Refractory fever on broad-spectrum antibiotics,
- ii. Non-productive cough, progressive dyspnea,
- iii. Pleuritic chest pain

VI. Cutaneous and soft tissue mucormycosis

- i. Erythema, induration,
- ii. black eschar at trauma/puncture site,
- iii. muscle pain with deeper involvement

VII. Gastrointestinal mucormycosis:

- i. Fever
- ii. Bleeding per anus
- iii. Mass like lesions
- iv. Perforation of gut

VIII. Mucormycosis of bones and joints: Local pain and tenderness, cellulitis

IX. Cerebral involvement: Altered sensorium

START INJ. AMPHOTERICIN – B IMMEDIATELY WITHOUT WAITING FOR INVESTIGATION REPORTS IN CASE OF VERY HIGH CLINICAL SUSPICION.

IF FACILITIES FOR SURGICAL MANAGEMENT, ADMINISTRATION AND MONITORING OF THE DRUG IS NOT AVAILABLE, TAKE PROMPT DECISION TO REFER THE PATIENT TO DESIGNATED REGIONAL CENTERS.

As per Annexure I

DIAGNOSIS

Nasal endoscopy: Ulceration / Blackish necrotic eschar

Oral Examination: Black eschar on the Palate

Ocular Examination :

- Redness, watering
- Proptosis, Periorbital edema, ecchymosis
- Restricted eye movement, Ophthalmoplegia
- Decreased Corneal Sensation
- Fundus examination: cherry red spot or disc edema or both.

Microbiology:

I. KOH smear

Specimen:

- Nasal mucosal scraping in normal saline
- Tissue biopsy from suspected mucosa in normal saline

II. Fungal culture

Pathology:

Specimen:

- Debrided tissue in 10% Formalin.

Radiology:

- HRCT Scan of Orbit, Paranasal sinuses & Brain, with contrast if renal status permits.
- MRI Paranasal sinuses and orbits (optional)

General Investigations:

- a. CBC
- b. Fasting and Post Prandial Blood Sugar Monitoring
- c. HbA1C
- d. LFT
- e. RFT with electrolytes

TREATMENT ALGORITHM

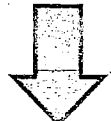
POSSIBLE OR PROVEN ROOM



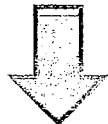
URGENT SURGICAL
DEBRIDEMENT
+
STRICT GLYCEMIC
CONTROL

+

Inj. Amphotericin B Deoxycholate
(0.75-1mg/kg/day)
OR
Inj. Liposomal amphotericin B
(5-10mg/kg/day)
(Central nervous system involvement: 10mg/kg/day)
OR
Inj. Amphotericin B lipid complex 5mg/kg/day
FOR 2-6 WEEKS (depending on severity)



FOLLOWED BY



FOR 2 TO 4 WEEKS (depending on severity)

ADMINISTRATION OF DRUG:

Inj. Amphotericin B Deoxycholate (C-AmB)

Test dose	<ul style="list-style-type: none">• 1 mg in 100 mL D5 over 20 minutes
Pre-hydration	<ul style="list-style-type: none">• 500 mL NS over 30 minutes
DAY 1	<ul style="list-style-type: none">• 0.5mg/kg in 100ml D5 over 1 HOUR
DAY 2	<ul style="list-style-type: none">• 0.75mg/kg in 100ml D5 over 2-3 hours
Post-hydration	<ul style="list-style-type: none">• 500 mL NS over 30 minutes
Watch for	<ul style="list-style-type: none">• Urine output , Renal function Test• Fill Amphotericin monitoring chart

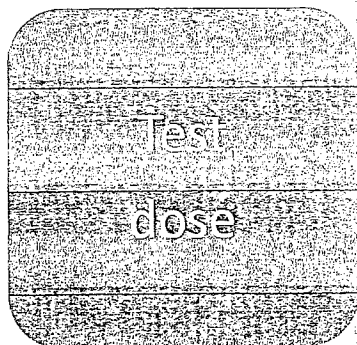
45 mg/day is given daily until a cumulative dose of 2 g is reached.

If the patient becomes normal before the stipulated dose of 2g the treatment schedule can be tailored as per tissue response.

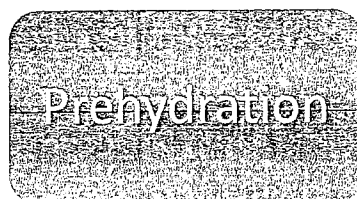
CREATININE MONITORING TO ASSESS RENAL FUNCTION

SERUM CREATININE (mg/dl)	DOSE OF DRUG
<1.1	0.75mg/kg/body weight/day (full dose)
<i>Mild renal failure</i> - 1.2-2.5	0.35mg/kg/body weight/day (half dose)
<i>Moderate renal failure</i> -2.5-3.5	0.25mg/kg/body weight/day on alternate days
>5	0.25mg/kg/body/weight/day (Once in 3 days)

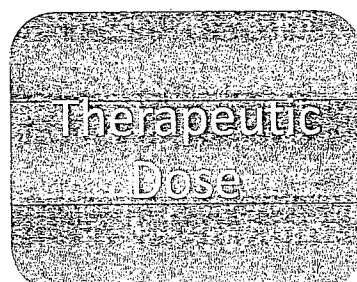
Inj. Liposomal amphotericin B (LAmB):



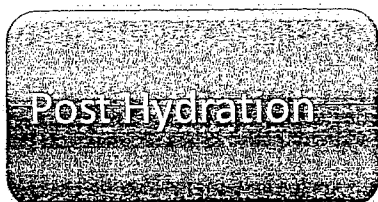
- Inj. Liposomal Amphotericin- B 1 vial (50 mg) to be diluted in 12 ml of the diluent and 0.25ml (1 mg) of solution made, to be mixed in 100ml Dextrose and to be infused in 30 minutes.
- Observe for fever and reactions



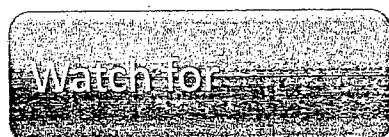
- 500 mL NS over 30 minutes
- To reduce the risk of renal toxicity and hypokalaemia :- 500ml Normal Saline + 1 Amp (20mmol) KCL



- 5-10 mg /kg/day Amphotericin B in 500 mL D5 with 10 Units HIR (Human Insulin Regular) over 3 hrs
- To be covered in black sheet



- 500 mL NS over 30 minutes






- Urine output , Renal function Test after every dose
- Fill Amphotericin monitoring chart

Inj Amphotericin B lipid complex (ABLC)

Test dose	<ul style="list-style-type: none">• 1 mg in 100 mL D5 over 20 minutes
Pre-hydration	<ul style="list-style-type: none">• 500 mL NS over 30 minutes
Therapeutic dose	<ul style="list-style-type: none">• 5mg /kg/day Amphotericin B in 500 mL D5 with 10 Units HIR (Human Insulin Regular) over 3 hrs• To be covered in black sheet
Post-Hydration	<ul style="list-style-type: none">• 500 mL NS over 30 minutes
Watch for	<ul style="list-style-type: none">• RFT with Serum electrolytes after Every dose of Amphotericin B• Fill Amphotericin monitoring chart

STEP DOWN OR SALVAGE THERAPY:

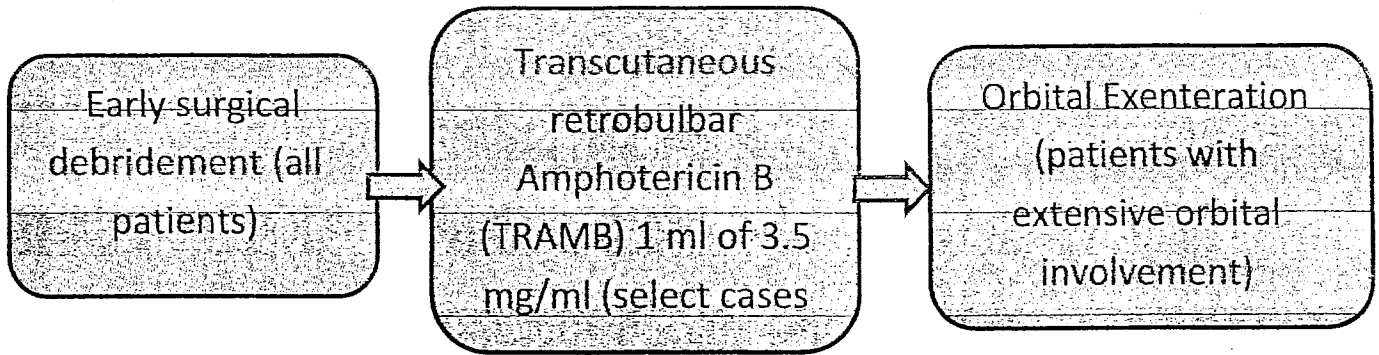
In patients who cannot tolerate Amphotericin B due to severe renal impairment / allergy / selected cases for cerebral mucormycosis,

	300mg IV BD / oral / Day 1 - followed by 300mg OD for 4 - 6 weeks
	
	• 200mg IV TID / oral X 2 days - followed by • 200mg IV OD / oral X 4 - 6 weeks

AMPHOTERICIN B DRUG CHART

Starting Time	Ending Time	Dose	Cumulative Dose	Urea	Creatinine	Na	K	SGOT /SGPT	Any Complications

SURGICAL MANAGEMENT



Nasal and sinus involvement
 Erosion of maxilla/zygoma
 and orbital floor

- Endoscopic sinus surgery debridement

Maxilla involvement

- Maxillectomy (partial/ total)

Maxilla + Maxilla + Zygoma involvement

Maxillectomy (partial/ total) with zygoma debridement

Maxilla + Zygoma + Orbital

- Maxillectomy (partial/total), Zygoma debridement
- Debridement of Orbital floor/walls, Localised debridement of necrosed tissue in early localised orbital disease

Protrusion of eye + Loss of vision

- 1) Vision loss 2) Total ophthalmoplegia 3) Chemosis 4) Necrosis of orbital tissues
- NOTE: Loss of vision in not always the indication of exenteration

Protrusion of eye + Involvement of the skull base

- Anterior table: Debridement
- Posterior table: Cranialization
- Debridement of Osteomyelitic Skull bone and involvement of the cerebral parenchyma (Safe maximum resection)

FOLLOW UP AFTER SURGERY:

Relook nasal endoscopy of weekly intervals for 6 weeks to assess epithelization of nasal cavity and to remove any residual necrotic bone

Daily nasal douching with diluted Amphotericin B solution (50mg vial in 500ml of normal saline)

PREVENTIVE MEASURES:

1. Personal Hygiene

Good Oral Hygiene

2. Medical Management

Judicious use of steroids.
Strict diabetes control

3. Hospital / Institutional level

- A. Use clean, sterile water for humidifiers during oxygen therapy
- B. Disinfecting all gadgets in ICU regularly.
- C. Not to Reuse disposable oxygen delivery devices like Nasal prongs, Face masks etc.

4. Advice to the Patient and care-giver at the time of discharge:

- a. Monitor blood glucose level in diabetics
- b. Inform the patients about early symptoms & signs of Mucormycosis.
 - Nasal blockage/Blood-tinged nasal discharge
 - Pain in the eye/swelling of the eye /double vision.
 - Headache / numbness over the face
 - Tooth ache/loosening of teeth/discomfort duringchewing
 - Follow up on Day-7 and 3 weeks after discharge.

REFERENCE

- Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases - 9th Edition. 2020. E-Book
- Management Protocol for Mucormycosis- AIIMS, Rishikesh
- Honavar SG. Code Mucor: Guidelines for the Diagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis in the Setting of COVID-19. Indian J Ophthalmol 2021;69:1361-5.

ACKNOWLEDGEMENT

All the respected members of State Mucormycosis Task Force Committee, who shared their valuable input in formulating this guideline.

ANNEXURE I

LIST OF REGIONAL CENTERS WHERE MULTIDISCIPLINARY TREATMENT IS AVAILABLE

1. RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL, CHENNAI
2. COIMBATORE MEDICAL COLLEGE HOSPITAL, COIMBATORE
3. GOVERNMENT RAJAJI HOSPITAL, MADURAI
4. THANJAVUR MEDICAL COLLEGE HOSPITAL, THANJAVUR
5. TIRUNELVELI MEDICAL COLLEGE HOSPITAL, TIRUNELVELI
6. GOVERNMENT MOHAN KUMARA MANGALAM MEDICAL COLLEGE HOSPITAL,
SALEM

ANNEXURE-II

COVID-19 DIABETES MANAGEMENT GUIDELINES FOR PREVENTION AND TREATMENT OF MUCORMYCOSIS

1. Regular blood sugar monitoring should be done for all diabetic patient sunder Home Quarantine, COVID Care Centre, COVID Health Centre, Primary Health Centre and COVID Hospitals.
2. Even Non-Diabetic patients may show increase in blood sugar after 3rd day of steroids. Hence blood sugar should be monitored for them too, including pre dinner blood sugar levels.
3. OHA's can be continued for patients who do not have hypoxia or organ dysfunction. Insulin should be added if adequate control is not achieved with OHA's.
4. Insulin should be initiated in all patients on steroids with oxygen support.
5. The regimen should include 3 doses of short acting insulin before break fast, lunch and dinner & morning and night basal insulin.
6. Patients on steroids may require higher dose of Insulin at 1 to 2 units/ kg body weight per day.
7. As and when steroid therapy is modified, insulin dose should be modified accordingly.
8. Patient with poor oral intake require RT feeding/ IV dextrose containing fluids if they are on subcutaneous insulin.
9. If fasting blood sugar is >400 mgs/dl (or) RBS > 500 mgs/dl, insulin infusion should be started at a rate of 5 units/hr. [Kindly add 25 units of regular insulin in 500ml of NS and flow at 100 ml/hr. Hourly CBG monitoring should be done till blood sugar drops to 200mgs/dl]. There after subcutaneous insulin should be given depending on patient's oral intake. All patients started on insulin infusion should be monitored for serum potassium levels.
10. Patients should be monitored for both hypoglycemia and hypokalemia.

J.RADHAKRISHNAN,
PRINCIPAL SECRETARY TO GOVERNMENT

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24/6/24
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2/2024