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"A PROSPECTIVE STUDY ON ANAESTHETIC MANAGEMENT OF RHINOCEREBRAL MUCORMYCOSIS"

Anaesthesiology

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ABSTRACT

Mucormycosis is a progressive, opportunistic fungal infection with a high risk of mortality. Also mucormycosis may attack any organ system and may be accompanied by hemodynamic instability and difficult airway management.

OBJECTIVE: This study aimed to evaluate the anaesthetic management of patients undergoing surgical resection for rhinorcerebral mucormycosis.

METHODOLOGY: The study evaluated 24 patients that underwent surgical resection for rhinocerebral mucormycosis under general anaesthesia. Demographic factors, hemodynamics, monitoring methods, surgical procedures, medical records, and mortality rates were reviewed for each patient.

OBSERVATIONS: The patients had a median age of 58 (range, 25-80) years. Four patients had an American Society of Anaesthesiologists (ASA) score of II while the remaining 20 patients had a score of III. Most common comorbidity was DM (n=15), followed by hematological malignancy (n=3), solid organ malignancy (n=3), and kidney transplantation (n=1). Invasive arterial monitoring was performed in 15 and central venous cannulation was performed in 9 patients. Fifteen patients were transferred to the intensive care unit (ICU) and the mortality rate was 37.5% with an average mortality time was 10 days in 9 cases.

DISCUSSION: In cases of rhinocerebral mucormycosis, necessary precautions should be taken for the difficult airway caused by fungal debris in the oropharyngeal region and supraglottic edema. Postoperative ICU is important due to comorbidities and fungal infection with high mortality.

KEYWORDS

Rhinocerebral mucormycosis, immunocompromised, anaesthetic management, difficult airway, mortality

INTRODUCTION:

Mucormycosis or black fungus is a rare fungal infection caused by a group of molds called mucormycetes. Mucormycosis is a rapidly progressive, rare, opportunistic fungal infection[1]. Patients with a low-immunity level or have compromising health conditions like diabetes, cancer, HIV, hematopoietic stem cell transplant recipients[2]. Use of certain combinations of steroids for treating COVID patients has also emerged to be one prominent reason as to why COVID survivors are complaining of black fungus. Successful treatment of mucormycosis is dependent on four key principles: early diagnosis, treatment of underlying factors, surgical debridement of necrotic tissue and administration of antifungal therapy[3]. Surgical resection for mucormycosis is often indicated in the presence of predisposing factors such as immunodeficiency, DM, and multiple organ failure and in the presence of conditions that require emergency intervention such as sepsis[4]. In particular, airway management of the patients is of paramount importance since the fungal debris in the oropharyngeal region and supra-glottic edema lead to difficult ventilation and endotracheal intubation. Literature reviews indicate that the medical and surgical treatment of mucormycosis has been extensively studied. In this study, we aimed to evaluate the anaesthetic management of patients undergoing surgical resection for rhinocerebral mucormycosis.

AIMS AND OBJECTIVES:

This study aimed to evaluate the anaesthetic management of patients undergoing surgical resection for rhinocerebral mucormycosis in terms of airway management.

MATERIALS AND METHODS:

The present study is a prospective study carried out with 24 patients who underwent surgical resection for rhinocerebral mucormycosis at Civil Hospital, Ahmedabad between March 2021 to June 2021.

Inclusion Criteria:

1. Patients suffering from rhinocerebral mucormycosis who underwent surgery under general anaesthesia.
2. Patient between the age group of 25 to 80 years.

Exclusion Criteria:

1. Breast feeding and pregnant women.
2. Medically unfit patients.
3. Patients not giving consent for participation in the study.

Detailed history were recorded from patients and clinical examination were performed. The findings were recorded in the pro forma.

- **Pre- Operative Preparation:**

All patients underwent the routine blood investigations like complete blood count, random blood sugar, liver function test, renal function test to exclude any major medical disorders. Heart rate and non-invasive blood pressure monitoring were done. Chest x-ray, Electrocardiogram and peripheral oxygen saturation(spO2) were done for anaesthetic fitness.

- **Anaesthetic Management:**

All the surgical procedures were performed under general anaesthesia. Following the 3-5 min pre-oxygenation with 100% O2 (8-10 L/min), anaesthesia was induced with intravenous propofol (2-3 mg/kg) or thiopental (5 mg/kg), succinylcholine (1-2mg/kg) and fentanyl (1-2 mcg/kg). Administration of anaesthetic drugs was based on ideal body weight. Each patient was intubated using orotracheal intubation and was mechanically ventilated using a Dra¨ger Primus ventilator at a frequency of 8-12 breaths per min with a tidal volume of 8-10 ml/kg. Following intubation, the EtCO2 value was monitored continuously. The tidal volume and the ventilation rate were adjusted to maintain the EtCO2 value within a range of 35- 45 mmHg. Anaesthesia was maintained with desflurane in a mixture of 50%-50% oxygen and N2O. Loading dose of atracurium (0.5mg/kg) and incremental dose of atracurium(0.1mg/kg) given. In patients that had no intraoperative complications, intravenous glycopyrrolate(0.008 mg/kg) and neostigmine (0.05 mg/kg) were administered to reverse residual neuromuscular blockade at the end of the surgery. Suitable patients who achieved spontaneous respiration (respiratory rate >12/min, tidal volume >5mL/kg), had a SpO2 levels of >95% and showed good response to verbal commands were extubated. However, hemodynamically unstable patients and those who showed no respiratory effort were transferred to the ICU intubated.

Postoperative analgesia was provided with appropriate doses of tramadol (0.5–1mg/kg, IV) or paracetamol (1 gm, IV) at the beginning of the skin sutures.

OBSERVATIONS AND RESULTS:

Demographic characteristics of patients are presented in table 1.

Table 1: Demographic Data

FACTORS	FREQUENCY
SEX, MALE/FEMALE	18/6

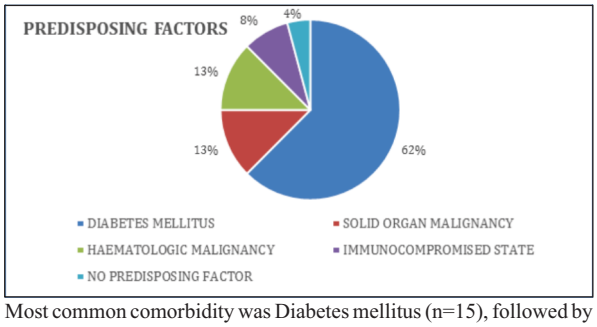
AGE (in years)	58 (25-80)
ASA GRADE II/III/IV	4/20/0
MALLAMPATTI SCORE I/II/III	4/18/2
DIFFICULT INTUBATION	5/24
SMOKING	15/24

The data is summarized as median value. The numbers in brackets indicates range (min-max).

In this study, there were 18 males (75%) and 6 females (25%). The mean age of patients in were 58 years (Range from 25-80 years). Four patients had an American Society of Anaesthesiologists(ASA) score of II while the remaining 20 patients had a score of III. Twenty two (91.75%) patients had a diagnosis of rhino-mucormycosis and 2 (8.25%) patient was diagnosed with Rhinocerebral mucormycosis.

Table 2: Predisposing Factors

FACTORS	PATIENTS
DIABETES MELLITUS	15
SOLID ORGAN MALIGNANCY	3
HAEMATOLOGIC MALIGNANCY	3
IMMUNOCOMPROMISED STATE	2
NO PREDISPOSING FACTOR	1



Most common comorbidity was Diabetes mellitus (n=15), followed by hematological malignancy (n=3), solid organ malignancy (n=3), and kidney transplantation (n=1). Here, immunocompromised state includes HIV and organ transplant patients.

Table 3: Intra Operative

VARIABLE	PATIENTS
INTRA ARTERIAL MONITORING, number	15
CENTRAL VENOUS CATHETER, number	9
TOTAL CRYSTALLOID, ml	1700(200-3000)
TOTAL COLLOID, ml	1000(0-1000)
DURATION ON ANAESTHESIA, in minutes	138.5(92-325)
DURATION OF PROCEDURE, in minutes	120(80-295)

All patients received crystalloids while 3 patients additionally received colloids. Median duration of anaesthesia was 138.5 (range, 92–325) min and the median duration of surgery was 120 (range, 80–295) min. The median time to hospital discharge was 15.5 (range, 9–28) days. Fifteen patients were transferred to the ICU postoperatively. Invasive arterial monitoring was performed in 15 and central venous cannulation was performed in 9 patients. In these 9 patients, central venous cannulation was achieved via femoral vein in 6 and via internal jugular vein in 3 patient. Table 3 presents the procedural data for 24 patients. Liposomal amphotericin B was used as antifungal therapy in all the patients.

Table 4: Vitals Monitoring

TIME	HR (per min)	MAP(mmHg)	ETCO2	SPO2
T0	98(58-133)	58.5(41-82)	-	94(87-98)
T1	115.5(62-140)	66.5(52-89)	40.5(35-48)	96.5(94-99)
T2	84(50-122)	52(40-78)	37(35-41)	96.5(92-99)
T3	85.5(53-125)	58(40-82)	-	94.5(94-99)

T0: before Intubation, T1: After intubation (10 min), T2: Perioperative (30 min), T3: After Surgery; the data are summarized as median (min-max).

Table 4 presents the Heart rate, MAP, SpO2, EtCO2 median values for patients. Mortality occurred in 9 patients during ICU stay. Accordingly, the mortality rate of our patients was 37.5% and the average mortality time was 10 days.

DISCUSSION:

Patients with mucormycosis may experience difficult mask ventilation and endotracheal intubation as a result of epiglottitis and supraglottic edema associated with fungal debris. Eckmann et al., evaluated a 14 year old girl with mucormycosis and reported that they inserted a tracheotomy tube since they could not perform intubation due to supraglottic edema, although the patient had been intubated with no difficulty two months earlier for intraabdominal surgery[5]. In our study, diffuse fungal debris in the oropharyngeal region was detected in 8 patients and in 3 of these patients, endotracheal intubation could not be performed with direct laryngoscopy due to supraglottic edema and thus was performed with video laryngoscopy. Moreover, additional equipment and drugs were used to avoid difficult airway management. Accordingly, anaesthesiologists should verify that operating theatre has adequate facemasks, intubating stylets, tube-changer or gum elastic bougies, laryngeal mask airways, video laryngoscopes, rigid laryngoscope blades of varying designs or sizes, fiberoptic-guided intubation, aspirators and emergency tracheotomy for unexpectedly difficult airway management[6].

Literature indicates that coexistence of diffuse sepsis, multiple organ failure, immunosuppression, and absolute neutropenia leads to increased morbidity and mortality in patients with mucormycosis[7]. Moreover, blood and blood products transfusion, fluid replacement, and intraoperative support may be required in some patients, which may necessitate central venous cannulation.

Celebi et al. reported that a hematoma occurred following internal jugular vein cannulation in a patient who had acute lymphoblastic leukemia (ALL) with pancytopenia and underwent surgery due to mucormycosis[8]. In our study, central venous cannulation was achieved via femoral vein in 6 and via internal jugular vein in 3 patient. We suggest that in such patient groups, interventional procedures such as central venous cannulation should not be performed at a location close to the infected site since these patients are at increased risk of rapid development of immunosuppression, neutropenia, and thrombocytopenia.

A number of volatile anaesthetic drugs have been reported to show antibacterial and antifungal activity in in-vitro studies. However, there is little or no documentation on ideal intravenous and inhaled anaesthetic agents in progressive active fungal infections such as mucormycosis. In a previous in-vitro study, Barodka et al. reported that isoflurane inhibited the growth of Albicans[9]. In our study, desflurane was used as the volatile anaesthetic agent. We consider that although volatile anaesthetic agents have been shown to inhibit the growth of fungal cells in in-vitro studies, the effects of these agents need to be investigated in in-vivo studies as well.

The use of systemic amphotericin B in the treatment of mucormycosis leads to nephrotoxicity and some other side effects including hypokalemia, hypomagnesemia, fever, shivering, dyspnea, and hypotension. Moreover, kidney functions may be affected in more than 80% of the patients and hemodialysis may be required in 15% of them during the treatment. However, to avoid the side effects of amphotericin B, liposomal amphotericin B has emerged as an alternative drug due to its lower nephrotoxicity over the last several years. On the other hand, avoiding hypotensive attacks and achieving hemodynamic stability in the perioperative period is highly critical for securing adequate renal perfusion and preventing the progression of renal damage. Moreover, continuous measurement of arterial blood gas values and intermittent biochemical analyses are essential for anaesthetic management of the patients in terms of metabolic condition, fluid-electrolyte balance, and coagulopathy[10].

In our study, 11 patients developed severe hypotension and thus received positive inotropic support. It should be noted that since patients with mucormycosis are at increased risk of hemodynamic instability and fluid-electrolyte imbalance, continuous monitoring of arterial pressure and arterial blood gas should be performed with invasive arterial blood pressure monitoring.

Our study was limited in several ways. All the patients were from a single center and the sample size was relatively small. Delays in the diagnosis and treatment of Rhinocerebral mucormycosis are associated with high morbidity and mortality. Due to fungal debris and supraglottic edema in the oropharyngeal region, precautions should be taken against the possibility of difficult intubation. Postoperative ICU

management is highly important due to the risk of comorbidities and rapid progressive infection after surgery.

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