Summer Training at
Bharat Serums and Vaccines Ltd,
Mumbai

Study of Mucormycosis and Liposomal Amphotericin B Prescription trend amongst the ENT Physicians

By
Naresh Mali

Under the guidance of
Mr. Abhishek Dadhich

MBA Pharmaceutical Management
2015-2017

The IIHMR University, Jaipur
2016

INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
(WHO Collaborating Centre for District Health System Based on Primary Health Care)

IIHMR UNIVERSITY

TO WHOMSOEVER MAY CONCERN

This is to certify that **Mr. Naresh Mali** student of **MBA Pharmaceutical Management** from The IIHMR University: Jaipur has undergone summer training at **Bharat Serums and Vaccines Ltd, Mumbai** from 1st April to 31st May, 2016.

The Candidate has successfully carried out the study designated to him during summer training and his approach to the study has been sincere, scientific and analytical. This training is in fulfillment of the course requirements.

I wish him all success in all his future endeavors.

Col. (Dr). Ashok Kaushik
Dean, Academics and Student Affairs
The IIHMR University, Jaipur

17/06/2016

Mr. Abhishek Dadhich
Assistant Professor
The IIHMR University, Jaipur

Acknowledgement

The satisfaction and euphoria that accompany the successful completion of the project would be incomplete without the mention of the people who made it possible.

First of all, I express my sage sense of gratitude and indebtedness to our President, Dr. S.D.Gupta, and IIHMR University.

I would like extend my sincere and heartfelt thanks to MR. Rakesh Dave, Vice-President, Bharat Serums and Vaccines Ltd. For providing me an opportunity learn and develop professionally.

I would also like to express my deep sense of gratitude to Mr. Aditya Maheshwari and my faculty mentor Mr. Sandeep Narula and Mr. Abhishek Dadhich. I am greatly indebted to both of them for providing their valuable guidance at all stages of the study, their advice, constructive suggestions, positive and supportive attitude and continuous encouragement, without which it would have not been possible to complete the project.

To place on record, I owe a debt of gratitude to all my teachers for grooming me and my classmates for the inspiration needed to work with dedication and motivation throughout as an Intern at Bharat Serum and Vaccines Ltd.

I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards the industry in coming future.

Executive Summary

The study aimed to understand Mucormycosis and Liposomal Amphotericin B Prescription in treatment among the ENT Physicians.

Semi structured questionnaire was utilized for data collection from respondent i.e. 102 doctors comprising of ENT specialist, from Mumbai. Data was analyzed & the findings provided with doctor's opinion and a comprehensive review of the market situation to be used for framing and suggesting the market strategy

The project was carried out in 3 stages:

First stage was to study about the Mucormycosis and prepare a questionnaire followed by stage two which involves meeting with the ENT specialists in various government and private hospitals and conduct the survey. After the completion of the survey last stage followed which includes analyzing the data and getting conclusion.

Following findings were observed after meeting with ENT specialists:

- From the respondent collected from the survey reported that 59% of doctors examine 0-5 patients on monthly basis. 49% of physicians do not examine the cases of Mucormycosis.

- It was also observed that majority of the patients suffering from the Mucormycosis were immunocmpromised which includes underlying causes, like Diabetes, Cancer, AIDS or use of immunosuppressant agents in case of organ transplant.

- This study shows that Liposomal Amphotericin B is most prescribed drug and surgery is also preferable by doctors in severe cases.

Table of Contents

Company Profile

Bharat Serums and Vaccines Limited (BSV) is one of the fastest growing biopharmaceutical companies in India and have been ranked amongst the top 10 Indian biopharmaceutical companies. The Company, founded in 1971 by Dr. Gautam and Bharat Daftary, the company has 2 manufacturing units in Ambernath, Maharashtra, 3 independent R&D facilities and a horse farm in outskirts of Maharashtra and over 900 employees.

BSV researches, develops, manufactures, and markets injectable biological, pharmaceutical, and biotech products. Its product portfolio comprises 25 brands which include plasma derivatives, monoclonal, fertility hormones, antifungals, anesthetics, cardiovascular drugs and equine immunoglobulin's / antitoxins. BSV provides its products to retail outlets and hospitals through distributors primarily in India and also internationally. In addition to its commercial operation, the Company has an extensive research and development platform working on the development of new drug delivery systems, biotechnology / recombinant therapeutics, and biological / equine products.

BSV currently has two private equity investors, Kotak Private Equity and Orbimed.

Bharat Serums And Vaccines Limited is a company with a noble mission to give life to life. BSV is a company that focuses their scientific knowledge to for the research, development, manufacturing and marketing of specialized biological, pharmaceutical and biotechnology products that combat disease and enhance quality of life.

BSV pursue the purpose by bringing to the world a wide range of plasma derivatives, monoclonal, hormones, equine anti toxins and serums, antifungals, anesthetics, cardiovascular and diagnostic products. With range of products and their efficacy has made BSV a market leader in many segments and one of India's fastest growing bio-pharmaceutical companies. BSV is looking forward to sustaining this growth in the future by continually evolving and expanding its product portfolio.

BSV is research oriented organization with state of the art R&D facilities in India, Germany and USA. BSV have company owned and joint venture based manufacturing facilities in Ambernath, Ahmedabad, and Aachen, Germany. The company also has a horse farm for production of equine anti sera and anti-toxins. Our brands are marketed all over India and exported to over 45 countries across the world

BSV's mission is to be an innovative, caring and trustworthy partner in bringing life to life. As a part of its mission, the Company is committed to mitigating the anguish and suffering of millions. BSV achieves this with its scientific processes, manufacturing expertise and ethical pursuits that introduce new biological and biotechnology products, as well as novel drug delivery systems.

Vision & Commitment

To Be an Innovative, Caring and Trustworthy Partner in Bringing Life To Life

- Mitigating the anguish and suffering of millions.
- Underlying fairness and transparency in dealings with all stakeholders including employees and business partners.
- The Group is driven by an informal culture fostering cohesion and innovation

Presence

Domestic

Products are sold through 6 specialized divisions and have over 25 brands.

- **DIVA**: prime division of BSV, operating in Gynaecology and Obstetrics segment

  Flagship Brand: Rhoclone and Hucog

- **ASPIRE**: A complete solution in AST (Assisted reproductive Technology)

  Flagship Brand: Foligraf

- **ELITE**: A tender division of BSV, operating in hospital based emergency medicine and Casualty
  Flagship Brand: Tetglob, Equirab and ASVS

- **ALTIUS**: Second largest division of the company and operating in Critical Care segment
  Flagship Brand: Gamma IV and Albumin

- **ANAGEN**: Offering corner stone therapies in Transplantation and Aplastic Anemia
  Flagship Brand: Thymogam and Ampholip

- **UROCARE**: Offering corner stone therapies in Urological problems
  Flagship Brand: Luprodex

International

- With a zest born out of the desire to improve health and quality of life globally, BSV started its international business operations in early 2000. The international business operation got a major boost with the commissioning of the new Ambernath plant in 2003.
- The Company's products are registered in more than 45 countries and its manufacturing facilities are accredited and certified by various regulatory authorities from Asia, Latin America, Middle East, Africa etc.
- The company also has global subsidiaries namely
    - BSV BIOSCIENCES, INC (United States)
    - BSV BIOSCIENCE,GMPH (Germany)

Timeline

1971	Incorporation of Bharat Serums and Vaccines Limited
1972	Establishes Blood Bank
1972	Exports Polyclonal Sera
1978	Commissioning of the Thane Plant
1980	Launch of Indigenously developed Plasma fractions
1982	Import Substitution Awards from the Indian Government for Anti D Blood Grouping Sera Strips for detection of Diabetes
1982	Receives R&D recognition by Department of Scientific and Industrial Research, Government of India
1983	Launch of Pseudoglob- India's first Pseudomonas globulin
1996	Sets up three independent focused R&D divisions
1998	Launch of Rhoclone – World's First monoclonal Anti D
1999	Filing of the first Product Patent Application
2000	Equity Investment from reputed Indian Institutional Investors
2001	Commissioning of the Animal Farm at Khoni, near Mumbai
2003	Commissioning of the injectable Manufacturing Facility at Amberanth, near Mumbai
2003	Incorporation of BSV Bio Inc. USA
2005	Formation of Zydus BSV Pharma, a 50:50 Joint Venture with Zydus Cadila
2007	Incorporation of BSV Bio GMbh, Germany
2007	Equity Investment from reputed Indian Institutional Investors
2008	Equity Investment from reputed Global Institutional Investors
2008	Launch of Foligraf- India's first recombinant FSH Biosimilar Product
2010	EU approval of the German Subsidiary, BSV Bio
2011	Commissioning of the Biotech facility at Ambernath, near Mumbai
2012	Launch of U-Tryp- India's first Ulinastatin formulation for Sepsis
2012	Frost and Sullivan award for the Fastest Growing Biotech Company

Introduction

The Zygomycoses (Mucormycosis) are infections caused by fungi of the class Zygomycetes, comprised of the orders Mucorales and Entomophthorales. The Entomophthorales are rare causes of subcutaneous and mucocutaneous infections known as entomophthoromycosis, which largely afflict immunocompetent hosts in developing countries. In contrast, fungi of the order Mucorales are causes of Mucormycosis, a life-threatening fungal infection almost uniformly affecting immunocompromised hosts in either developing or industrialized countries.

Fungi belonging to the order Mucorales are distributed into six families, all of which can cause cutaneous and deep infections. Species belonging to the family Mucoraceae are isolated more frequently from patients with Mucormycosis than any other family. Among the Mucoraceae, Rhizopus oryzae (Rhizopus arrhizus) is by far the most common cause of infection. Other less frequently isolated species of the Mucoraceaefamily that cause a similar spectrum of infections include Rhizopus microsporus var. rhizopodiformis, Absidia corymbifera, Apophysomyces elegans, Mucor species, and Rhizomucor pusillus Increasing cases of Mucormycosis have been also reported due to infection with Cunninghamella spp. (in the Cunninghamellaceae family) . To date, rare case reports have demonstrated the ability of species belonging to the remaining four families to cause Mucormycosis.

Both mononuclear and polymorph nuclear phagocytes of normal hosts kill Mucorales by the generation of oxidative metabolites and the cationic peptides defensins. Clinical evidence demonstrates that these phagocytes are the major host defense mechanism against Mucormycosis. For example, neutropenic patients are at increased risk of developing Mucormycosis. Furthermore, patients with dysfunctional phagocytes are also at higher risk for developing Mucormycosis. Hyperglycemia and acidosis are known to impair the ability of phagocytes to move toward and kill the organisms by both oxidative and nonoxidative mechanisms. Additionally, corticosteroid treatment affects the ability of mouse bronchoalveolar macrophages to prevent germination of the spores in vitro or after in vivo infection induced by intranasal inoculation. The exact mechanisms by which ketoacidosis, diabetes, or steroids impair the function of these phagocytes remain unknown.

Mucormuycosis is less common than other opportunistic fungal infections, such as those caused by Candidaand Aspergillus spp. One population-based study estimated the incidence of Mucormycosis to be 1.7 cases per million people per year, which translates to approximately 500 cases per year in the United States. In autopsy series, the prevalence of Mucormycosis has ranged from 1 to 5 cases per 10,000 autopsies, making the infection 10- to 50-fold less common than invasive Candida or Aspergillus infections. Finally, in patients at higher risk, such as that undergoing allogeneic bone marrow transplantation, the prevalence of Mucormycosis has been described to be as high as 2 to 3%.

Based on clinical presentation and the involvement of a particular anatomic site, Mucormycosis can be divided into at least six clinical categories: (i) Rhinocerebral, (ii) Pulmonary, (iii) Cutaneous, (iv) Gastrointestinal (v) Disseminated, and (vi) miscellaneous.

These categories of invasive Mucormycosis tend to occur in patients with specific defects in host defense. For example, diabetics in ketoacidosis typically develop the rhinocerebral form of the disease, and much more rarely develop pulmonary or disseminated disease.

Rhinocerebral Mucormycosis

Rhinocerebral Mucormycosis continues to be the most common form of the disease, accounting for between one-third and one-half of all cases of Mucormycosis. About 70% of rhinocerebral cases (occasionally referred to as craniofacial) are found in diabetic patients in ketoacidosis. More rarely, rhinocerebral Mucormycosis has also occurred in patients who received a solid organ transplant or those with prolonged neutropenia recently, rhinocerebral disease has been an increasing problem in patients undergoing hematopoietic stem cell transplantation. These cases have largely been associated with steroid use for graft-versus-host disease.

The initial symptoms of rhinocerebral Mucormycosis are consistent with either sinusitis or periorbital cellulitis and include eye or facial pain and facial numbness, followed by the onset of conjunctival suffusion, blurry vision, and soft tissue swelling. Fever is variable and may be absent in up to half of cases white blood cell counts are typically elevated, as long as the patient has functioning bone marrow If untreated, infection usually spreads from the ethmoid sinus to the orbit, resulting in loss of extraocular muscle function and proptosis. Marked chemosis may also be seen. The infection may rapidly extend into the neighboring tissues. Onset of signs and symptoms in the contralateral eye, with resulting bilateral proptosis, chemosis, vision loss, and ophthalmoplegia, is an ominous sign that suggests the development of cavernous sinus thrombosis.

Pulmonary Mucormycosis

Mucormycosis of the lung occurs most commonly in leukemic patients who are receiving chemotherapy or in patients undergoing hematopoietic stem cell transplants. Indeed, the pulmonary form of the disease is the most common form found in neutropenic and stem cell-transplant patients. These patients typically have severe neutropenia and are frequently receiving broad-spectrum antibiotics for unremitting fever, while in patients undergoing allogeneic stem cell transplantation, the disease often occurs postengraftment and is strongly associated with graft-versus-host disease. Patients with diabetic ketoacidosis can also develop pulmonary Mucormycosis, although infections in these patients are less common and less fulminant and follow a more subacute course than is typically seen in patients with neutropenia.

Pulmonary Mucormycosis may develop as a result of inhalation or by hematogenous or lymphatic spread. Symptoms of pulmonary Mucormycosis include dyspnea, cough, and chest pain. In a recent series of 32 cases of pulmonary Mucormycosis, fever was present in the majority of patients. Angioinvasion results in necrosis of tissue parenchyma, which may

ultimately lead to cavitation and/or hemoptysis, which may be fatal if a major blood vessel is involved.

Cutaneous Mucormycosis

Cutaneous Mucormycosis are those with disruption of the normal protective cutaneous barrier. The agents of Mucormycosis are typically incapable of penetrating intact skin. However, burns, traumatic disruption of skin, and persistent maceration of skin enable the organisms to penetrate into deeper tissues. A typical case results from traumatic implantation of soil, for example, as a result of a motor vehicle accident or penetrating injury with plant material (e.g., a thorn). In diabetic and immunocmpromised patients, cutaneous lesions may also arise at insulin injection or catheter insertion sites contaminated surgical dressings have also been implicated as a source of cutaneous Mucormycosis Cutaneous Mucormycosis has also occurred in the context of contaminated tape used to secure an endotracheal tube in a ventilated patient.

Cutaneous disease can be very invasive locally and penetrate from the cutaneous and subcutaneous tissues into the adjacent fat, muscle, fascia, and even bone. Secondary vascular invasion may also lead to hematogenously disseminated infection of the deep organs. Cutaneous and subcutaneous disease may lead to necrotizing fasciitis, which has a mortality approaching 80% However; isolated cutaneous Mucormycosis (i.e., not disseminated disease) has a favorable prognosis and a low mortality if aggressive surgical debridement is done promptly.

Gastrointestinal Mucormycosis

Mucormycosis of the gastrointestinal tract is rare. It mainly occurs in patients who are extremely malnourished (especially infants or children) and is thought to arise from ingestion of the fungi. In particular, gastrointestinal Mucormycosis has been seen in premature neonates, often in association with widespread disseminated disease. Necrotizing enterocolitis has been described largely in premature neonates and more rarely in neutropenic adults. Rare cases of gastrointestinal Mucormycosis have been described in association with other immune-compromising conditions, including AIDS, systemic lupus erythematosus, and organ transplantation.

Disseminated Mucormycosis

Hematogenously disseminated Mucormycosis may originate from any primary site of infection. Pulmonary Mucormycosis in severely neutropenia patients has the highest incidence of dissemination. Less commonly, dissemination can arise from the gastrointestinal tract, the sinuses, or cutaneous lesions, the last occurring particularly in burn patients. The most common site of dissemination is the brain, but metastatic lesions may also be found in the spleen, heart, skin, and other organs. Cerebral infection following dissemination is distinct from rhinocerebral Mucormycosis and results in abscess formation and infarction. Patients present with sudden

onset of focal neurological deficits or coma. The mortality associated with dissemination to the brain approaches 100%. Even without central nervous system involvement, disseminated Mucormycosis has a mortality of >90% in patients undergoing hematopoietic stem cell transplantation, the 1-year mortality is >95% due to a combination of underlying disease, graft-versus-host disease, and the infection.

TREATMENT

Four factors are critical for eradicating Mucormycosis: rapidity of diagnosis, reversal of the underlying predisposing factors (if possible), appropriate surgical debridement of infected tissue, and appropriate antifungal therapy. In general, primary antifungal therapy for Mucormycosis should be based on a polyene, if possible. Although amphotericin B deoxycholate (AmB) was the cornerstone of Mucormycosis therapy for decades, lipid formulations of AmB are significantly less nephrotoxic and can be safely administered at higher doses for a longer period of time than AmB. Furthermore, treatment of Mucormycosis with liposomal amphotericin B (LAmB) was associated with a 67% survival rate, compared to 39% survival when patients were treated with AmB ($p = 0.02$). Multiple other, more recent case series also found initial therapy with LAmB to be substantially more effective than other options. Therefore, most experts now prefer to use lipid polyenes rather than AmB for the treatment of Mucormycosis.

Available data indicate advantages of LAmB over amphotericin B lipid complex (ABLC) for the treatment of CNS Mucormycosis. For example, LAmB levels achieved in rabbit brain were fivefold above ABLC levels. Furthermore, while similarly effective in neutropenic mice, LAmB was markedly superior to ABLC in diabetic ketoacidotic (DKA) mice infected with Rhizopus oryzae, primarily because of superior clearance of fungus from the brain.

Itraconazole is the only marketed azole drug that has in vitro activity against Mucorales. There are case reports of successful therapy with itraconazole alone. However, as mentioned above, itraconazole prophylaxis has been described as a risk factor for breakthrough Mucormycosis. Voriconazole, Posaconazole and Ravuconazole a recently approved second-generation broad-spectrum triazole, posaconazole is more efficacious than itraconazole but less efficacious than amphotericin B deoxycholate. There are increasing reports of salvage posaconazole therapy for refractory Mucormycosis.

Research Methodology

Objective & Scope of Study

Objective

The main objective to conduct this research is to understand the Mucormycosis and Liposomal amphotericin B market & suggest the Market developing strategies.

Primary Objectives

- To Find the Prescription pattern of liposomal amphotericin B in management of Mucormycosis.
- To understand the incidence, stages, first line therapy and duration of treatment of Mucormycosis.
- To study and understand the concept and process of marketing research.

Scope of the Study

The project scope involves the study of Mucormycosis fungal infection. Understand the liposomal amphotericin B Prescription pattern, their usages duration of treatment. The project scope also involves the finding of doctor's preferences in current antifungal therapy available with the marketing research and developing a marketing strategy for increasing the sales liposomal amphotericin B from the above collected data.

Managerial Usefulness of the Study

This study helps to understand marketing research basic terminologies & different strategies for different market situation.

Methodology

Sample Design:

Descriptive study

Sampling:

Non probability convenience sampling

Sample Size:

Respondents: 102

Sample Frame:

Private Doctors: 89

Government Doctors: 13

Sample population:

ENT Specialists (99)

ICU Consultants (03)

Sample area:

Different areas of Mumbai (zone wise)

Zones	Areas
Western	Churchgate, Mumbai central, Dadar, Bandra, Andheri, Borivali, Bhayander, Vasai,Virar
Central	Thane, Mulund, Byculla, Sion
Harbour	Vashi, Belapur, Nerul

Tools Used For Data Collection: Direct Questionnaire method

Type of Questionnaire: Semi-Structured

Type of Questions: closed and open ended

Tools Used for data analysis: MS-Excel

Data Collection:

Primary- primary data has been collected by the means of questionnaire.

Secondary- The secondary data involved in this project has been gathered from the medical journals, literatures and internet.

Study duration:

Two months

Findings and Interpretation

1) Number Mucormycosis patients Examine per month?

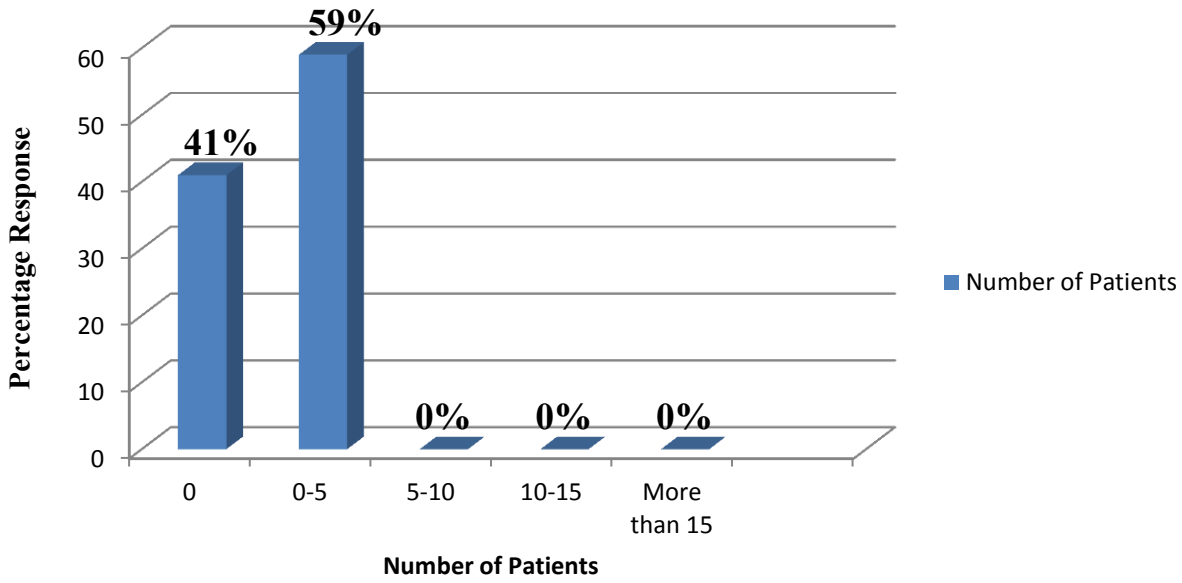

Figure 1: Total No of Patients examine vs. Percentage Response (Per Month)

INTERPRETATION

- 41% of doctors do not examine the Mucormycosis Disease.
- 59% of doctors examine 0-5 patents per months.
- As Mucormycosis is rare disease as described by the doctors, no doctors is found who examine more case of Mucormycosis greater than 5 per months.

2) Stage of Mucormycosis disease Detection.

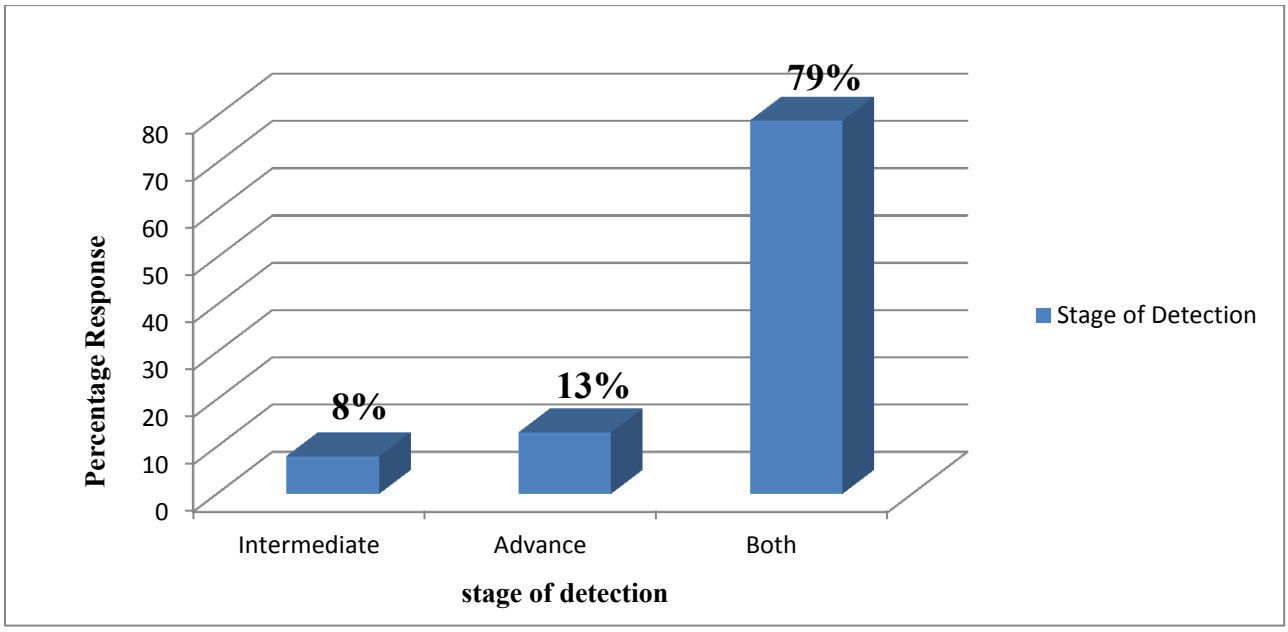

Figure 2: Stage of Detection vs. Percentage Response

INTERPRETATION

- It was found that 8% of doctors detect the Mucormycosis cases at intermediate stage, in initial stage of disease it is difficult to identify between Mucormycosis and other fungal Infection.
- 13% of doctors detect the Mucormycosis cases at Advance stage and later stage of disease.
- 79% doctors detect the major cases at both stage intermediate and advanced stage.

3) Management of Mucormycosis patients by doctors.

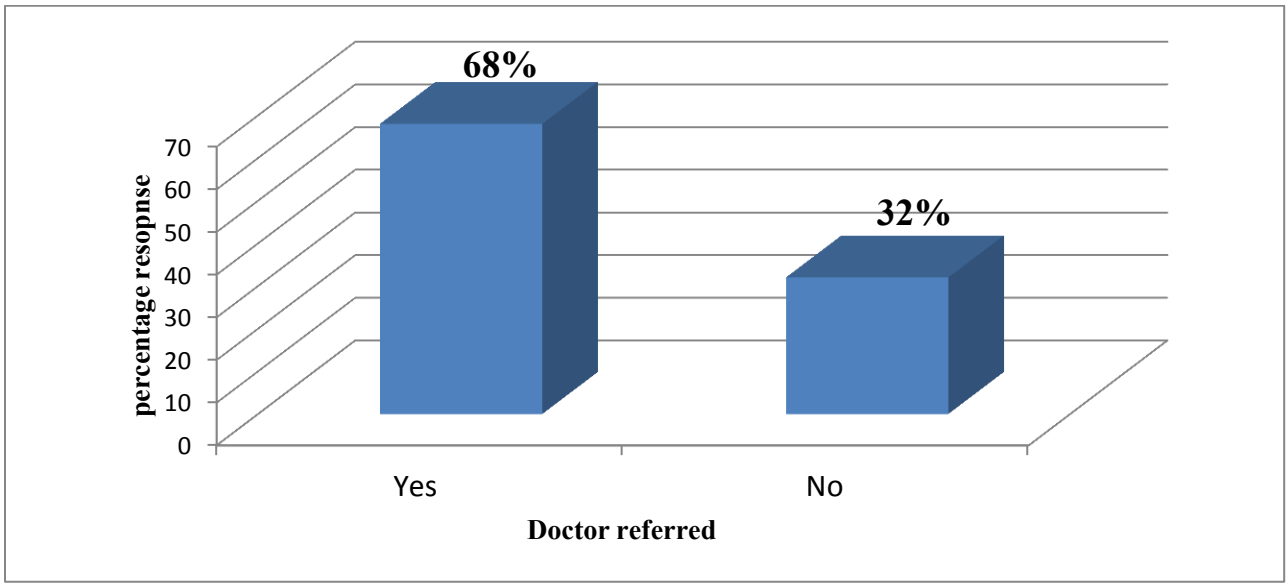

Figure 3: doctor referred vs. Percentage Response

INTERPRETATION

- 68% of doctors referred their Patients to other hospital or senior doctors for further treatment, 41% of doctors who do not examine disease they all referred their patients to other doctors and hospital.
- 32% of doctors who are specialist in Mucormycosis treat patient by self and do not refereed to other doctors.
- It was found that doctors involve the intensive care department and other physician for treating severe cases of Mucormycosis.

4) First line of treatment preferred by doctors.

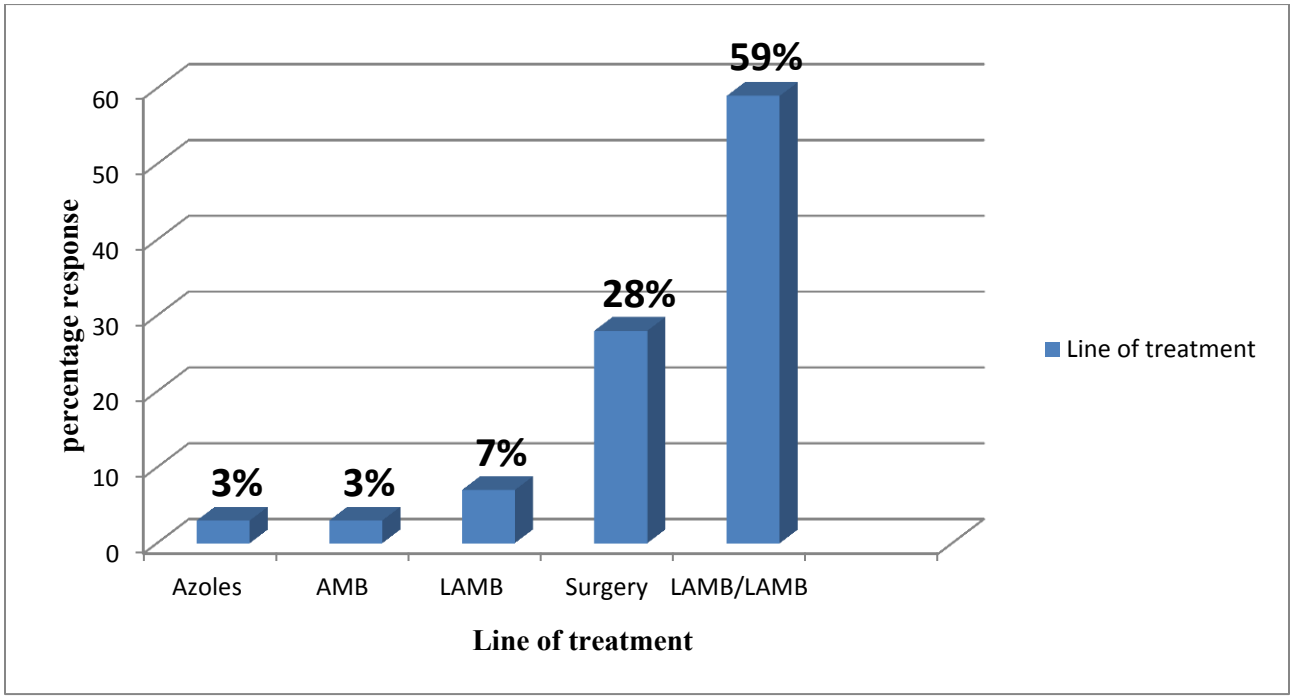

Figure 4: Preferred Line of Treatment vs. Percentage Response

INTERPRETATION

- 59% of doctors preferred amphotericin and liposomal amphotericin B as their first line therapy of treating Mucormycosis disease.
- 28% doctors who are specialized in surgery preferred the surgery as first line therapy and these doctors detect the major cases at advance stage.
- 7% of doctors use liposomal amphotericin B as preferred line of treatment, 3% of doctors preferred azoles and 3% of doctors preferred amphotericin as first line therapy.

5) Brand preference by doctors.

- Majority of doctors not disclose the brand preference for treatment.
- 10% of doctors are selective about the brands, depending upon the cost and patient compliance and clinical data.
- Some doctors are not particular about the brand, as they change their preferences according to new product and invention comes in market.
- Some brands like AMPFONEX, AMFOCAN, PHOSOME and AMPHOTRAET is commonly preferred by the doctors.

6) Number of patients treated with Amphotericin B.

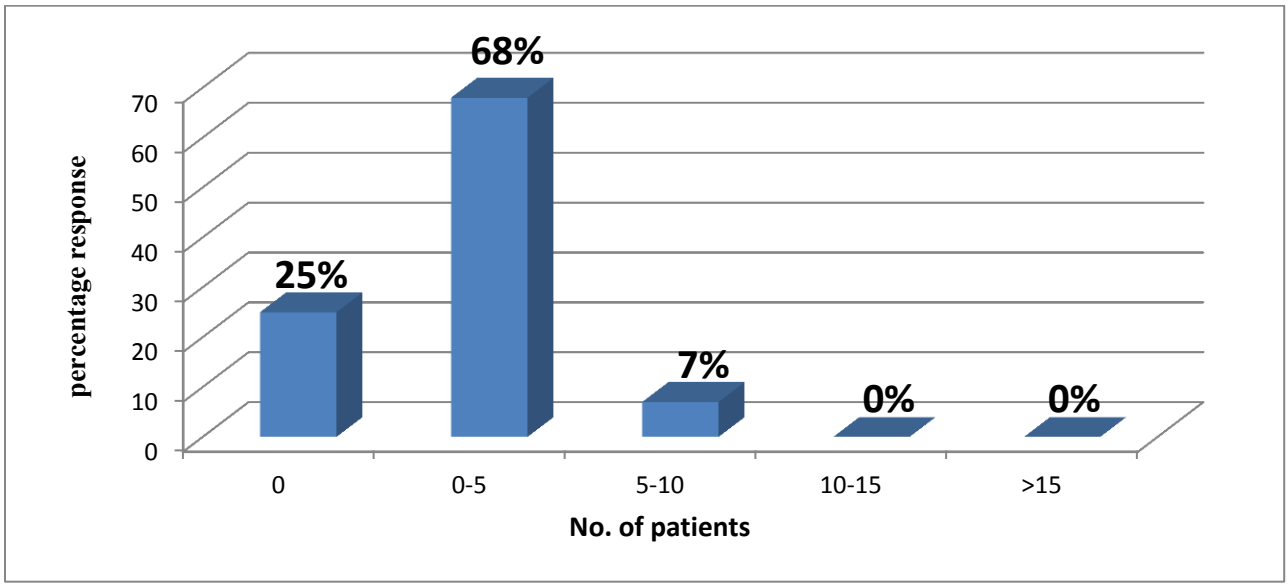

Figure 5: Total Number of Patients Treated with Amphotericin B vs Percentage Response (Per Month)

INTERPRETATION

- It was found that 25% of doctors do not prescribe amphotericin B for treatment.
- 68% of doctors prescribed amphotericin B to 0-5 patients per months.
- 7% of doctors prescribed amphotericin B to 0-5 patients per months.

7) Number of patients treated with Liposomal Amphotericin B.

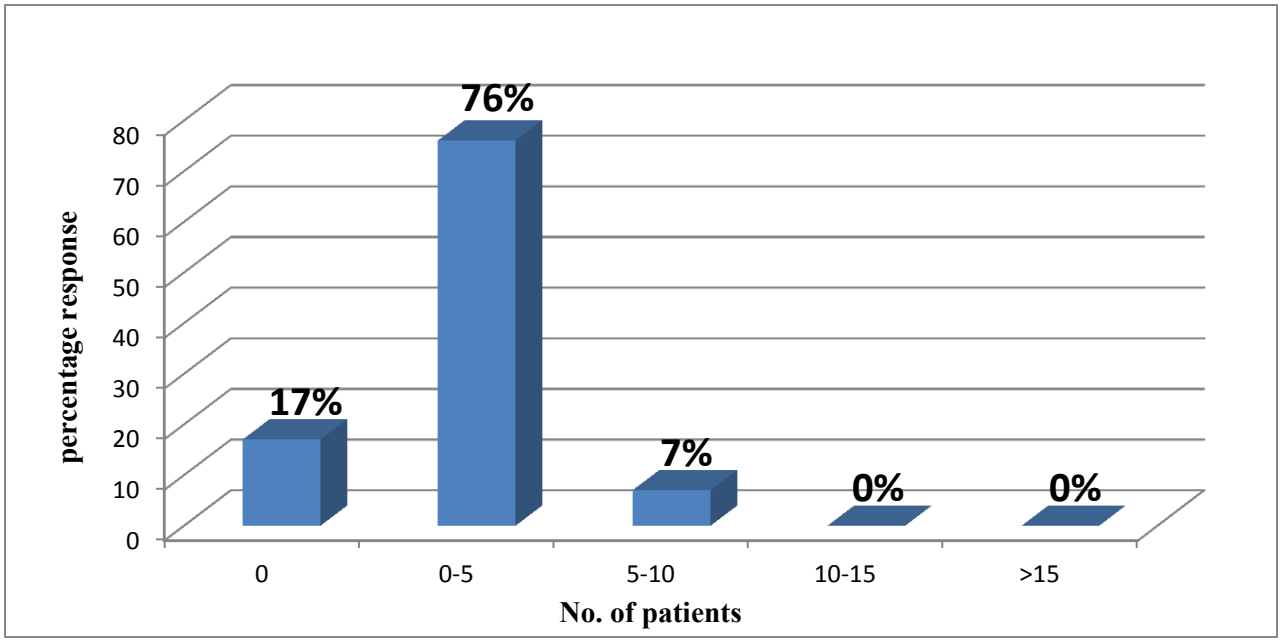

Figure 6: Total Number of Patients Treated with Liposomal Amphotericin B vs. Percentage Response (Per Month)

INTERPRETATION

- 17% of doctors do not prescribe Liposomal amphotericin B to 0-5 patients; they either prefer surgery, amphotericin B or Azoles for treatment.
- 76% of doctors prescribed Liposomal amphotericin B to 0-5 patients per months.
- 7% of doctors prescribed Liposomal amphotericin B to 0-5 patients per months.

8) Duration of Treatment in terms of Dose Rx (No. of Vials?)

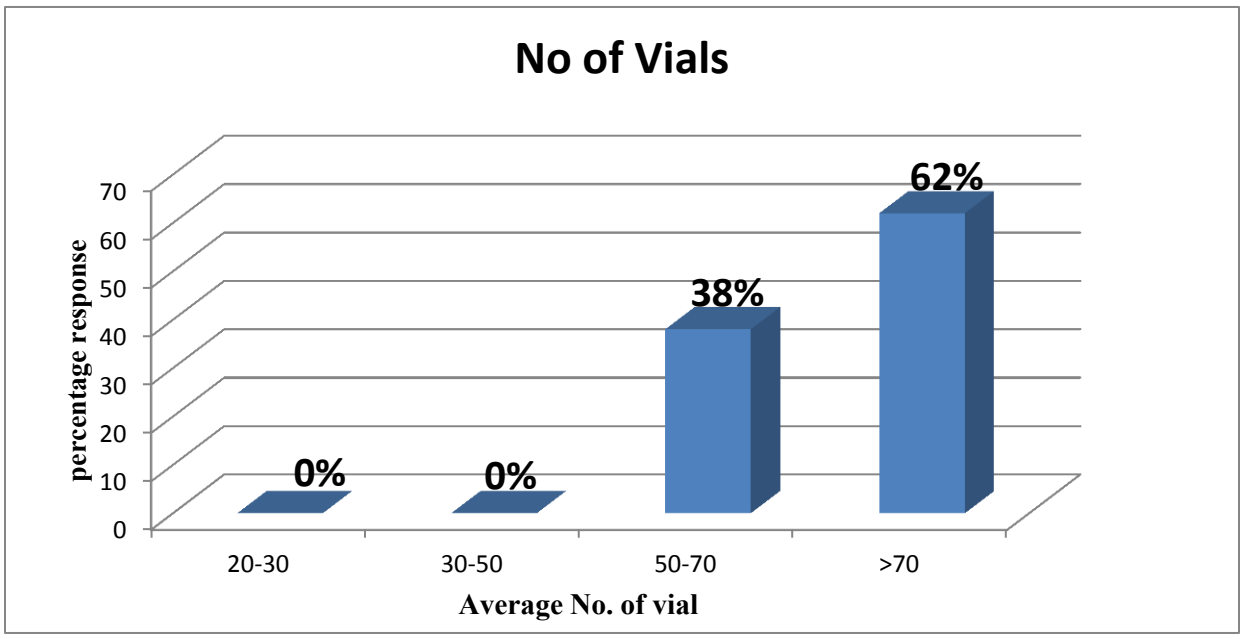

Figure 7: Average Number of Vials vs. Percentage Response

INTERPRETATION

- 38% of doctors use average 50-70 vials for treating Mucormycosis disease.
- 62% of doctors use average 50-70 vials for treating Mucormycosis disease.
- It was also found that dose of amphotericin B is varying with disease severity.

FINDINGS FROM THE RESEARCH

There are much critical information were found out from the study:

- It was found that the disease conditions is rare, less cases were found in Mumbai, doctors which is practicing from last 10-15 years have seen vary less cases of Mucormycosis.
- Some doctors are not aware about the disease conditions and their treatment.
- Rhinocerebral Mucormycosis is found to be the most common form of the disease, About 50-60% of Rhinocerebral cases are found in diabetic patients and 20% cases is found in immunocmpromised patient.
- In Rhinocerebral Mucormycosis cases initial symptoms was found that eye or facial pain and facial numbness and edema in some cases as well as fluid discharge from cerebral region.
- It was also found that doctors are using combination therapy for treating the disease with liposomal amphotericin B and itraconazole, posaconazole or both.
- Some doctors are preferred surgery over medications due to Dose required for the treatment is very high.

Conclusion

Mucormycosis is frequently rapidly progressive, and antifungal therapy (liposomal amphotericin B) alone is often inadequate to control the infection. The rapidly progressive nature of Rhinocerebral Mucormycosis and the mortality rate associated with disease is 40-50% after treating with antifungal therapy. Early diagnosis is important because small, focal lesions can often be surgically excised before they progress to involve critical structures or disseminate. Unfortunately, there are no serologic or PCR-based tests to allow rapid diagnosis. It was found that up to half the cases of Mucormycosis are diagnosed postmortem and tissue necrosis in disease result in poor penetration of anti-infective (azoles and amphotericin B) agents to the site of infection. Finally, surgery is necessary due to the massive amount of tissue necrosis occurring during Mucormycosis, which may not be prevented by killing the organism. Surgical debridement of infected and necrotic tissue should be performed in severe cases.

- The overall finding of the study helped us to understand the prescription behavior of the ENT specialist and surgeon, the reason that influence them to prescribe the various brands of liposomal amphotericin B.
- The cost and dose are the two main factors that influence the prescription of liposomal amphotericin B.

Suggestions (Marketing Strategy)

- Introduce the Competitive Pricing Policy, as there is significance difference in the price of competitive Brands. This will lead to more prescription generation by doctors.
- Attractive Discounting Policy that will attract more customers, as cost of therapy is high.
- Institutional supply source to be maintained well with including the separate field professional for institution.
- Identify the Key Opinion Leader and served with more frequently with excellent customer service.
- Introduce the Cross Promotional strategy (either with own Product or competitors Product)
- Segment the Market based on Number of prescription Generation by Physicians.
- Mucormycosis Market is diffused market, so Increased Area of coverage amongst the ENT physician and other Physician.
- Introduce the Subjective Positioning Strategy for liposomal Amphotericin B.
- Awareness about the Mucormycosis disease to the doctors who do not examine the Mucormycosis cases.
- Providing favorable studies and data on Liposomal amphotericin B therapeutic efficacy in Mucormycosis to doctors as the prescription trend may shift towards combination therapy and new generation of azole derivative (e.g. posaconazole).

- Focus should be shifted from only ENT doctors to other Physicians, because it was found that ENT doctors involve other Physician also.
- Medical Representative should update doctors about Mucormycosis through online journals and research studies.

Limitation of the Study

- The sample area and sample size has been limited due to time constraint.
- Doctors (respondents) are reluctant for their feedbacks & opinions, and authenticity of their statements can't be verified too.
- All the observation and recommendation will be made on the feedback obtained from survey.

Annexure

Questionnaire

Name of Doctor: _____

Date of Visit: _____

Specialty: _____

Hospital Attached: _____

Contact No: _____

Name of student: _____

Q-1 – How many of Number Mucormycosis patients detected in your practice / month?

☐ 0-5 ☐ 5-10 ☐ 10-15 ☐ > 15

Q-2 – At what Stage Mucormycosis disease is detected?

A:-_____

_____

Q-3 - How do you manage these patients?

☐ Refer to other Drs /Hospital ☐ treat in your hospital

Q-4 – If you refer – can you please share name of Dr/Hospital?

A: _____

Q-5- What is your line of treatment?

☐ Azoles ☐ Amphotericin ☐ Liposomal Amphotericin B

Q-6 – What is your preference?

1) Azole - Preferred Drugs a)_____ b)_____c)_____
2) Liposomal Amphotericin B brands – a) _____
   b) _____
   c) _____

Q-7- How many patients are treated with Amphotericin B?

☐ 0-5 ☐ 5-10 ☐ 10-15 ☐ > 15

Q-8 - How many patients are treated with Liposomal Amphotericin B?

☐ 0-5 ☐ 5-10 ☐ 10-15 ☐ > 15

Q-9: What is the Duration of Treatment in terms of Dose Rx (No. of Vials?)

☐ 20-30 ☐ 30-50 ☐ 50-70 ☐ >70

Q-10 would like to share any other critical Information Related to Mucormycosis?

A: _____

_____

Reference

- Brad Spellberg, John Edwards, Jr. Ashraf Ibrahim. Novel Perspectives on Mucormycosis: Pathophysiology, Presentation, and Management, Clinical Microbiology Review. 2005 Jul; 18(3): 556–569.
- Atahan A Çagatay, Serkan S Oncu, Semra S Çalangu, Rhinocerebral Mucormycosis treated with 32 gram liposomal amphotericin B and incomplete surgery: a case report. BMC Infectious Disease. 2001; 1: 22.1471-2334-1-22.
- George Petrikkos, Anna Skiada, Olivier Lortholary, Emmanuel Roilides, Epidemiology and Clinical Manifestations of Mucormycosis.2012 Volume 54, page no S23-S34.
- https://www.bharatserums.com.