Combined Topical and Intracameral Injection of Amphotericin B Versus Topical Amphotericin B in Management of Fungal Keratitis in Mansoura Ophthalmic center, Egypt

Rania A Abdullah[1], Eman A Awad[2], Tarek A Mohsen[2], Tharwat H. Mokbel[2]

1- Ophthalmic hospital, Mansoura, Egypt

2- Ophthalmic Center, Faculty of Medicine, Mansoura University, Mansoura, Egypt.

Corresponding author: Eman A Awad. Ophthalmology Center, Faculty of Medicine, Mansoura University, Mansoura, Egypt. Tel 002-050-2216440 Fax 002-050-2256104 **Email**: dr_emanazmy @hotmail.com

Received: 31/12/2020, Accepted: 3/3/2021, Published online:11/3/2021, EJO(MOC) 2021;1:1-11.

***Running title**:* Intracameral injection in fungal keratitis

Abstract:

Aims: This study aimed to evaluate the efficacy of a combination of topical and intracameral injections of amphotericin B in the treatment of severe fungal keratitis.

Mthods: This prospective, comparative interventional randomized study included 40 patients of fungal keratitis attended outpatient clinic of MOC, faculty of medicine Mansoura University, Egypt, in the period from January 2017 to December 2018.The patients were randomly divided into 2 groups: Group A: underwent only topical amphotericin B. Group B: underwent combined topical & intracameral injection of antimicrobials. Patients were followed up at 1 day, 1 week, 2W, first month, then monthly till the 6th month.

Results: Both groups were sex and age matched. Trauma was the most common risk factor recorded. Asperigulus was the commonest causative agent (85%). In group A, the size of corneal ulcer improved from 32.44±19.37to 29.71±17.16 at 1st week to 18.81±10.04 in the 1st month, in group B the ulcer size decreased from 30.24±16.09 to 21.81 ±11.04 ($p<0.001$) in the 1st week the ulcer achieved complete healing within 3 months. The mean duration for the complete healing in group A, was 48.82 ± 5.31 days while the mean duration in group B, that was 29.59 ± 3.24 days ($p< 0.001$).

Conclusions: Intrcameral Amphotericin B injection is safe and effective technique in treatment of fungal keratitis.

Keyword: Intracameral injection, Amphotericin B, Fungal keratitis, MOC.

Introduction:

Fungal keratitis or keratomycosis refers to an infective process of the cornea caused by any fungal species capable of invading the ocular surface. It is a result of fungal colonization or epithelial infiltration and/or invasion of the corneal stroma. It is most typically a slow, relentless disease that must be differentiated from other types of corneal conditions with similar presentation; especially bacterial conditions[1].

A hot, humid climate and an agriculture-based occupation of a large population make fungal keratitis more frequent in Egypt. Aspergillus species were the most common fungi, involved in 41% of the fungal cases, followed by Fusarium species (26.2%)[2,3].

Amphotericin and natamycin are usually the first drugs of choice for fungal keratitis. It is effective against Candida and Aspergillus species. It has been used by systemic, topical, and intravitreal routes in the treatment of fungal keratitis. Currently, the major route of administration for antifungal agents is topical. However, topical antifungal agents have serious limitations including few commercially available ocular preparations, poor ocular penetration or bioavailability and toxicity[4,5].

However, topical Amphotericin B is not effective in eradicating fungi in the anterior chamber, because it penetrates poorly into the aqueous humor and may not reach adequate therapeutic levels, to try to successfully treat those fungi that had penetrated into the anterior chamber, the intracameral injection of amphotericin B was introduced as a line of therapy [6,7].

This study aimed to compare the efficacy of combined topical antifungal and intracameral injection of amphoteracin B versus topical antifungal in the management of fungal keratitis at Mansoura ophthalmic center (MOC), Egypt.

Patients and methods*:*

This prospective, comparative interventional randomized study included 40 patients of culture proved fungal keratitis recruited from outpatient clinic of Mansoura ophthalmic center, faculty of medicine Mansoura University, Egypt, in the period from January 2017 to December 2018.

Pregnant and lactating women, Children < 12 years of age, One-eyed patients, Patients with concurrent sclera involvement and Patients with impending perforations, elevated intraocular pressure were excluded from the study.

This study was performed in accordance with ethical standards of the Declaration of Helsinki and was approved by the Institutional Research Board (IRB) of Mansoura faculty of medicine. The time of presentation of infection was 8±3.2 days before start of specific treatment. The patients were randomly divided into 2 groups**:** Group A: underwent only topical antimicrobials. Group B: underwent combined topical & intracameral injection of antimicrobials. Each patient in both groups underwent full history taking from each patient this included: occupation, history of systemic diseases such as diabetes mellitus & immunocompromised conditions, corticosteroid use either systemic or topical, history of resistant corneal ulcer and drugs, previous corneal scars, trauma by organic matter, history of corneal surgery as keratoplasty and Lasik, history of topical treatment prior to presentation and contact lens wearing. Full ophthalmic examination: included record of visual acuity using Landolt's broken rings chart and converted to Log MAR chart values, intraocular pressure assessed digitally, B scan ultrasound to assess posterior segment, photo-slit photography. Slit-lamp biomicroscope with assessment of corneal ulcer size (the longest vertical and horizontal diameters of the ulcer were measured), the product of both axes was used for statistical purpose, size of infiltrates using beam of slit lamb light. Level of hypopyon using the slit lamp grading, fixed or mobile nature of hypopyon. The indications of hospitalizations were Presence of thinning, descematocele or perforation. Patients with > 1.5 mm infiltrate, with Hypopyon, intra stromal Purulent exudate (abscess), Severe corneal thinning& Impending perforation, and Poor compliance.

The samples were collected from corneal scrape which obtained from the base and the edges of the ulcer using a disposable surgical blade No 15 after instillation of local anesthetic eye drops (benoxinate Hcl 0.4%) to decrease ocular discomfort on slitlamp

in outpatient clinic , and investigated and the data were recorded by 2 methods: Staining by Potassium hydroxide 10% (KOH) preparation with direct microscopic evaluation to detect hyphae and Culture on Sabaraud dextrose agar, blood agar & enrichment media.

Processing of the samples was done in Microbiological Diagnostic & Infection Control Unit (MDICU) of faculty of medicine at Mansoura University. Patients were randomly classified using closed envelop technique to be included in either groups.

Group A: included 20 patients**,** treated by topical amphotericin B eye drops only in a concentration of1.5 mg/ml amphotrecin B, prepared from the commercially available Fungizone 50mg,(Bristol Myers Squibb). The vial is diluted in 10 ml saline, 3ml was taken and 7ml distilled water was added to obtain the target concentration (1.5 mg/ml).

The product was labeled, dating and refrigerated, as it is available for one week. Using a sterile 10-ml syringe, 5 ml was transferred into a brown sterile eye dropper, away from light as far as possible, received topical application once per hour.

Topical cases that started to show deterioration by increasing size of ulcer, infiltration and hypopyon level, superadded intracameral injection was given and the patient was excluded from the study.

Group B: included 20 eyes**,** treated by combined Topical & Intracameral amphotericin B. intracameral injection one dose of 50 µgm/0.1 ml amphotericin B.

The preparation (fungizone 50 mg vial, Bristol_ Myers Squibb, New York, USA) was diluted in 10 cm distilled water, then 0.1 cm was taken and 9.9 cm distilled water was added to obtain the target concentration of 0.005 to 0.01 mg/0.1ml to be used for injection .

Injection was performed under full aseptic conditions, in an operating theatre. Under topical anesthesia with preserved benoxinate Hcl 0.4% the insulin needle inserted in an area of the superior limbus that was free from infiltrate to make gentle pressure on the paracentesis allowed egress of the aqueous. Using a 27 gauge (insulin) needle the preloaded drug was injected under operating microscope introduce in to the anterior chamber. Following the injection all patient resumed their preoperative topical and systemic antimicrobial therapy with frequent corneal debridement (Itrapex 100 mg, Itranox 100 mg, tab commercial available 2 tab twice daily for 21 day). All patients underwent liver function test before and during the course of systemic antifungal.

The patients also continued their topical natamycin, fluconazole, and atropine after treatment. Patients were followed up at 1 day, 1 week, continued weekly for the first month after injection then every 2 weeks for another month after then monthly till the 6th month.

Patients were evaluated on day 1 to exclude complications of the injection , then starting at day 3 evaluation of the following parameters were done: Pain severity, visual acuity, size of epithelial defect, infiltration size, hypopyon height, Intraocular pressure and development of complications.

Fungal keratitis was considered resolved and complete healing was achieved when there was epithelial defect healing with resolution of stromal infiltrate and scar formation.

The study was performed at 95% level of significance and power of 80%. The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (SPSS Inc, Chicago, IL, USA). Qualitative data was presented as number

(frequency) and Percent. Quantitative data was tested for normality by Kolmogorov-Smirnov test. Data was presented as mean ± SD.

Normally distributed quantitative data within two groups was compared by Student t-test. Abnormally distributed quantitative data within two groups was compared by Mann Whitney U test.

Comparison between quantitative data at different time points in the same group was compared by using paired samples t-test or by Wilixon Signed Rank test. Paired samples t-test was used to compare patients in the same groups at different time points. $P < 0.05$ was considered to be statistically significant. Visual acuity was measured in landolt notation which was converted to LogMAR notation as it is more suitable for statistical analysis.

Results:

The mean age of the patients within group A is 45.35 ± 16.22 years and it was 48.65 ± 10.31 years in-group B with no significant difference between the two groups. There were 9 males and 11 females in group A while there were 14 males and 6 females in group B, both groups were age and sex matched.

There were 18 cases came from rural areas in group A while there were 16 cases in group B with no significant difference between the two groups**.**

Regarding the associated systemic diseases of the patients within the two groups; combined DM and HTN was the most prevalent comorbidity and was found in 6 cases in group A and 4 cases in group B. Trauma was present in 10 cases in group A and 11 cases in group B, absent in 10 cases in group A and 9 cases in group B with no significant difference between the two groups. The use of contact lenses was found in 2 cases in group A, but no cases used them in group B with no statistically significant difference between the two groups.

The analysis of the causative organisms results from culture and sensitivity tests within the two groups as detected from culture and sensitivity tests was illustrated in table (1). Aspergilus was the most common infectious organism and it was detected in 17 cases (85%) in group A and in 18 cases (90%) in group B. Mixed fungal infections were present in two cases in each group while fungal infection was mixed with staph aureus and pseudomonas in one case in group B.

The base line visual acuity (before treatment) in group A, was 2.42 ± 0.28 which was fixed at the same value at 2 days and 1st week after treatment. Significant improvement of the visual acuity started after that where the mean visual acuity at 1 month after treatment was 2.40 ± 0.25.Values changed from 2.21 ± 0.31 to 2.15 ± 0.33 at 3 months and 6 months after treatment. In group B, the base line visual acuity (before treatment) was 2.43 ± 0.23 which started to show significant improvement at the first week after treatment 2.37 ± 0.25.

Table 1: Analysis of causative organisms in the two studied groups

Items	Group A (Topical treatment) n=20	Group B (treatment with injection) n=20	Test of significance
Fungal			
Aspergilus	17 (85%)	18 (90%)	P= 0.678
Candida	1 (5%)	1 (5%)	
Stemphylium walroth	1 (5%)	0 (0%)	
Mucor	0 (0%)	1 (5%)	
Bipolaris	1 (5%)	0 (0%)	
Penicillium	0 (0%)	1 (5%)	
Alternia	0 (0%)	1 (5%)	
Mixed fungal infection	2 (10%)	2 (10%)	
Mixed bacterial & fungal			
Staph aureus	0 (0%)	1 (5%)	P= 0.714
pseudomonas	0 (0%)	1 (5%)	

P: Probability. Categorical data expressed as Number (%)

Regarding the inter groups significance, the effect of treatment began to show significant difference between the two groups at the 1 month after treatment (p= 0.003). The difference increased in the second month (p<0.0001) and the difference decreased at 3 rd (p= 0.007). These data were illustrated in table (2). The base line size of cornel ulcer (before treatment) in group A, was 32.44 ± 19.37mm which decreased at 1st week after treatment to 29.71 ± 17.16 mm so there was no significant difference in size.

Table (2): Analysis of visual acuity along the follow up periods (LogMar score):

Time	Group A (Topical treatment) n=20	Group B (treatment with injection) n=20	Test of significance
Before treatment	2.42 ± 0.28	2.43 ± 0.23	P = 0.926
At 2 day	2.42 ± 0.28	2.43 ± 0.23	P = 0.926
At 1week	2.42 ± 0.28	2.37 ± 0.25	P = 0.529
At 1months	2.40 ± 0.25	2.11 ± 0.28	P = 0.003*
At 3months	2.21 ± 0.31	1.84 ± 0.59	P = 0.007*
At 6months	2.15 ± 0.33	1.84 ± 0.59	P = 0.007*

P: probability. Continuous data expressed as mean±SD

**: significant value < 0.05*

***: highly significant value < 0.001*

Significant improvement of the cornel ulcer size started after 2nd week where the mean size of cornel ulcer at 1 month after treatment were 18.81 ± 10.04 mm. The ulcer size decreased in most of cases at 6th months after treatment.

In group B, the base line size of cornel ulcer (before treatment) was 30.24 ± 16.09 mm which started to show significant improvement at the first week after treatment 21.81 ± 11.04 mm. The size of the ulcer size decreased in most of cases at 3rd months after treatment.

Regarding the inter groups significance, the effect of treatment began to show significant difference between the two groups at the first week after treatment (p= 0.019) and the difference decreased after that. All these data were illustrated in table (3).

The base line of cornel infiltration size (before treatment) in group A was 32.44 ± 19.23 mm which decreased at 1st week after treatment to 31.13 ± 17.2 mm. Significant improvement of the size of cornel infiltration started after that where the mean size of cornel infiltration at 1 month after treatment were 22.86 ± 12.04 mm. The infiltration decreased in size in most of cases at 6 months after treatment.

In group B, the base line of corneal infiltration size (before treatment) was 34.17 ± 18.43 mm. The size of the infiltration started to decrease more in most of cases at 3rd month after treatment. that was illustrated in table (3).

Table (3), shows the base line of hypopyon level (before treatment) in group A was 2.46 ± 1.23 mm which was fixed at the same value at 2nd day. Significant decrease of the level of hypopyon started at 1 month after treatment 1.36 ± 0.43 ml. Values decreased to 0.90 ± 0.31 mm and 0.37 ± 0.17 mm at 2nd and 3rd months. Minimal hypopyon at 6 months in few cases.

In group B, the base line of hypopyon level (before treatment) was 3.22 ± 2.09 mm which started to show improvement at the first week after treatment 1.45 ± 0.62 mm. Values decreased from 1.02 ± 0.61 mm at 2nd weeks to 0.33 ± 0.19 mm at 6th weeks and Minimal level at 2nd months after treatment in few cases.

In group A, the reported complications were staphyloma (2 cases), thinning (6 case), hyphema (2 case) and Atrophi Bulbi (1 case). In group B the complications showed mild variations in distribution as follows; staphyloma (1 case), thinning (3 cases), hyphema (3 cases) and Atrophi Bulbi (1 case). There was no statistically significant difference between

the two groups in the occurrence of complications. The mean time for starting healing in group A, was 25.81 ± 3.17 days while the mean time in group B, that was 8.14 ± 2.78 days with high level of significance between the two groups (p<0.001).

The VA at the end of therapeutic regimen was 2.15 ± 0.33 in group A ,and 1.84 ± 0.59 in group B, with high level of significance between the two groups (p= 0.001).

The incidence of overall complications was 55% in group A, while it was 32% in group B, with no statistically significant difference between the two groups. The mean duration for the complete healing in group A, was 48.82 ± 5.31 days while the mean duration in group B, that was 29.59 ± 3.24 days with high level of significance between the two groups (p< 0.001).

The mean duration for follow up in group A, was 8.95 ± 2.15 months while the mean duration in group B, that was 4.74 ± 0.62 months with high level of significance between the two groups (p< 0.001). These data were shown in table (4). Fig1 represent one of the cases of the study.

Table (3): Assessment of corneal ulcer size, infiltration size and hypopyon level:

	Size of ulcer			Infiltration			Hypopyon level		
	A	**B**	**P**	**A**	**B**	**P**	**A**	**B**	**P**
Before treatment	32.44±19.37	30.24±16.09	P=0.552	32.44±19.23	34.17±18.43	P=0.552	2.46±1.23	3.22±2.09	P=0.004*
At 2 days	32.44±19.37	29.69±18.31	P=0.552	32.44±19.23	33.89±18.31	P=0.935	2.46±1.23	1.9±0.76	P=0.017*
At 1We	29.71±17.16	21.81±11.04	P=0.019*	31.13±17.2	30.67±19.28	P=0.855	2.11±1.46	1.45±0.62	P=0.073
At 1Mo	18.81±10.04	6.95±5.12	P=0.005*	22.86±12.04	14.63±6.32	P=0.0001**	1.36±0.43	0.72±0.31	P=0.025*
At 3Mo	4.39±1.45	2.64±1.12	P=0.009*	7.62±2.51	5.39±2.15	P=0.003*	0.90±0.31	0.31±0.09	P=0.001**
At 6Mo	2.11±0.78	0	P=0.032*	3.06±1.22	0	P=0.042*	0.37±0.17	0	
							0		

P: probability.

Continuous data expressed as mean±SD

**: significant value < 0.05*

***: highly significant value < 0.001*

Table 4: The final outcome between the two groups:

Items	**Group A (Topical treatment) n=20**	**Group B treatment with injection) n=20**	**Test of significance**
Mean time for starting healing (days)	25.81 ± 3.17	8.14 ± 2.78	P < 0.001**
VA at the end of treatment	2.15 ± 0.33	1.84 ± 0.59	P = 0.001*
Overall complications	11 (55%)	8 (32%)	P = 0.167
Mean time for complete healing (days)	48.82 ± 5.31	29.59 ± 3.24	P < 0.001**
Mean duration of follow up (months)	8.95 ± 2.15	4.74 ± 0.62	P < 0.001**

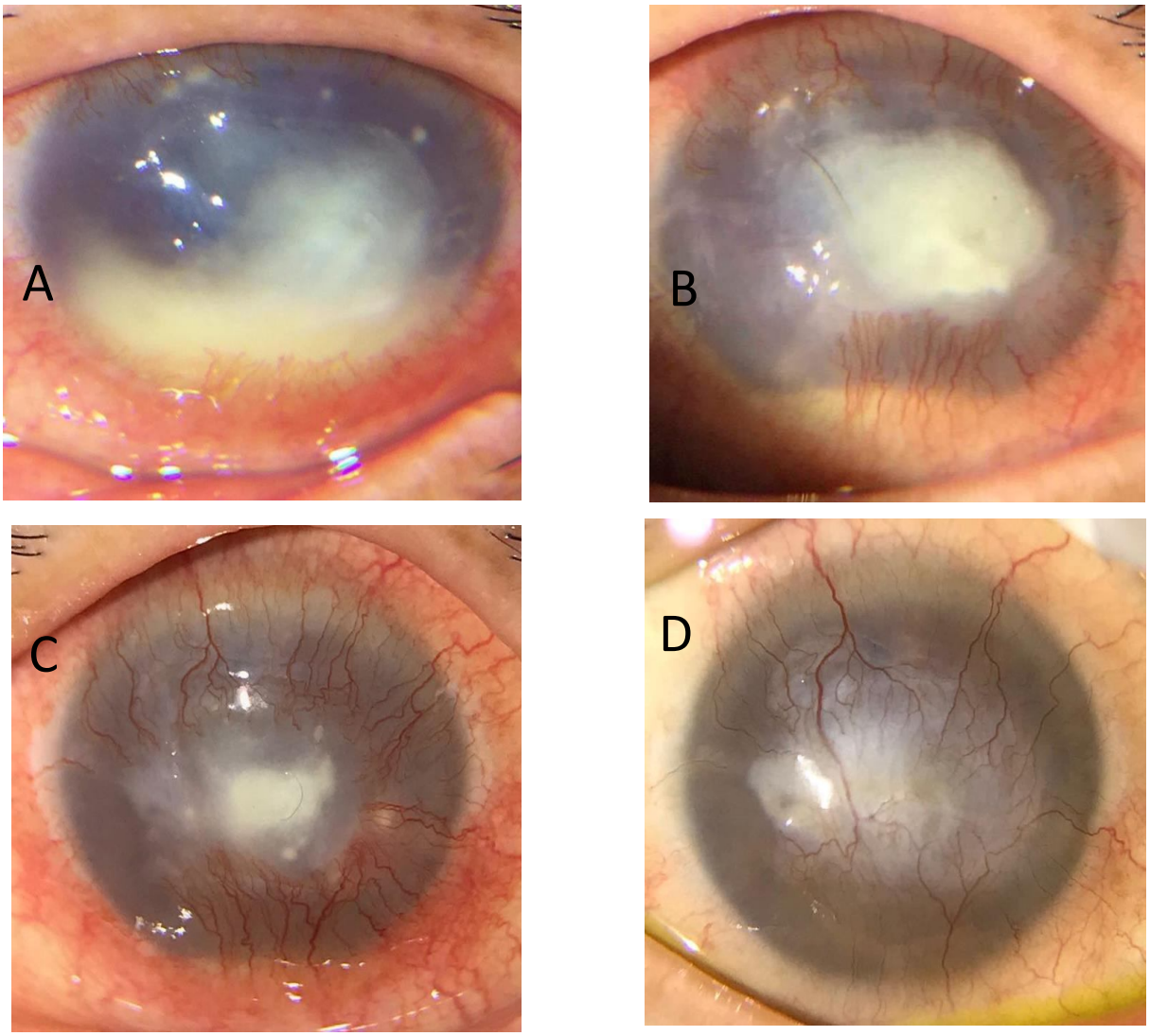

Fig 1: A) female patient aged 55 years old complained painful diminution of vision**,** for 1 month culture showed Pencillium infection. **B)** 1 week after injection (increased corneal vascularization & decreased size of both ulcer & infiltration & level of hypopyon). **C)** 1 month after injection (minimal hypopyon, marked corneal vascularization, small infiltration). **D)** 3 months after injection healing (opacity& vascularization) with visual Acuity 4\60.

Discussion:

Fungal keratitis accounts for 5 %–20% of all corneal infections[8]. Management of fungal keratitis is challenging in view of fungistatic effect of most of the topical antifungal agents and their poor penetration to the deeper layers of the cornea leading to suboptimal therapeutic levels at the site of infection. Topical antifungal alone or combined with oral antifungal medications seems to be effective in the early stages of the keratitis[9,10].

Targeted drug delivery has the potential to achieve sufficient drug concentrations at the site of infection and serve as an alternative modality of treatment in eyes with resistant fungal keratitis [11]. Among the targeted drug delivery modalities, intracameral injection of antifungal agents has shown promising results[12].

This study aimed to compare the effect of intracameral amphotericin B injection against topical antifungal drugs in treatment of fungal keratitis. Our study, included 40 cases of culture proved fungal

keratitis. The cases were subdivided into two groups according to the treatment regimen. Group A (topical antifungal treatment) and group B (ICAMB and topical antifungal).

In this study, the mean age of the cases within group A is 45.35 ± 16.22 years and it was 48.65 ± 10.31 years in group B with no significant difference between the two groups. There were 9 males and 11 females in group A while there were 14 males and 6 females in group B with no significant difference between the two groups.

Trials included people with a wide range of ages, from seven to 84 years of age, although in general the patient populations were younger rather than older, with average ages between 33 and 47 years. The majority of the participants were male; the percentage male ranged from 57% to 77% in the included trials (median 69%) [13].

There are many factors that increase the risk of fungal keratitis. In our study, combined DM and HTN was the most prevalent comorbidity and was found in 10% of the cases included in the study (6 cases in group A and 4 cases in group B). Trauma was present in 54% of the cases (10 cases in group A and 11 cases in group B).

Mahdy et al ,conducted their study on 48 eyes and they found that 38% were diabetic, and 21% received organic trauma[14] . This was in agreement with that reported by El Gohary *et al.,* who postulated that diabetes, ocular trauma, and presence of preexisting corneal ulcer were considered risk factors for keratomycosis[15]. The risk factors for fungal keratitis were diabetes and plant ocular trauma, 48% of cases were diabetic and 76% of cases had plant ocular trauma[16].

Corneal trauma (primarily with vegetative matter) that has been considered as the predominant predisposing factor in different studies accounts for 40%-60% of patients with fungal keratitis[17,18,19].

The results of culture and sensitivity tests in our study showed that Aspergilus was the most common infectious organism and it was detected in 17 cases (85%) in group A and in 18 cases (90%) in group B. Mixed fungal infections were present in two cases in each group while fungal infection was mixed with staph aureus and pseudomonas in one case for each type. The culture results in another study were reported that 75% of cases presented positive culture results[16].

This was also in accordance with Nayak, who reported 77.8%, and Al Hussaini et al., who reported 75% positive fungal infection by culture and sensitivity tests respectively [20,21] .In our study, the mean duration for the complete healing in group A was 48.82 ± 5.31 days while the mean duration in group B that was 29.59 ± 3.24 days with high level of significance between the two groups ($p<0.001$).

Similar duration was reported by Sharma et al, and found that the mean-time to healing was 51.4 ± 33.5 days (range, 23–131 days) after treatment with topical antifungal agents, 29.1 ± 15.7 days (range, 10–58 days) in the patients treated with intracameral amphotericin B injection, and 43.8 ± 21.3 days (range, 15–89 days) in the patients treated with drainage of hypopyon and intracameral amphotericin B injection [22].

Arora 2011, reported that the average time of complete resolution of corneal infiltrate in 15 patients allocated to natamycin was 24.3 days and in 14 patients (with healed ulcer) allocated to voriconazole was 27.4 days24. In our study, The VA at the end of therapeutic regimen was 2.15 ± 0.33 in group A and 1.84 ± 0.59 in group B with high level of significance between the two groups ($p=0.001$)[23].

Similar study as Yoon et al,[24] concluded that intracameral amphotericin B (ICAMB) seems to be effective in reducing time to disappearance of hypopyon and final improvement in the treatment of fungal keratitis. In this report, the mean time of disappearance of hypopyon was 9.6 ± 9.2 days (range, 1- 26 days) in the ICAMB group as compared with 26.8 ± 20.8 days (range, 14- 62 days) in the conventional treatment group A, greater number of patients showed complete re epithelialization in the ICAMB group (n = 27) than in the other group (n = 14; P < 0.05). In this study, none of the patients reported any adverse effects or discomfort with treatment[24].

In our study, the base line size of hypopyon (before treatment) in group A was 2.46 ± 1.23 mm which was fixed at the same value at 2nd day. Significant decrease of the volume of hypopyon started at 1 month after treatment 1.36 ± 0.43 mm. Values decreased to 0.90 ± 0.31 mm and 0.37 ± 0.17 mm at 2nd and 3rd months. Minimal hypopyon at 6 months in few cases.

In group B, the base line size of hypopyon (before treatment) was 3.22 ± 2.09 mm which started to show improvement at the first week after. Treatment 1.45 ± 0.62 mm. Values decreased from 1.02 ± 0.61 mm at 2nd weeks to 0.33 ± 0.19 mm at 6th weeks and disappeared at 2nd months after treatment in most of cases.

In agreement with Shao et al, compared the improvement in visual acuity, in addition to ulcer healing and disappearance of hypopyon. The mean final visual acuity (log MAR) was 1.6 ± 1.1 in the ICAMB group and 1.3 ± 1.4 in the conventional treatment group (P = 0.24). Treatment success was achieved in 92.9% of the ICAMB group as compared with 82.4% of the conventional treatment group (P=0.38)[12].

In another study, in group A, 87.7% of patients showed ulcer healing in 1 to 3 weeks' time with conventional treatment. The mean time for healing was 13.08 ± 4.33 days. The time for disappearance of hypopyon was 2 to 3 weeks in 50% of patients, with the mean time being 17.12 ± 8.7 days. The final visual outcome in 40.8% of patients was less than 1 logMAR unit. The mean visual outcome was 1.25 ± 0.73 logMAR units[8].

In the same study, in group B, it was observed that in 52.7% of patients the ulcer achieved complete epithelialization and healing in 1 to 2 weeks. The mean time for ulcer healing was 12.37 ± 5.50 days. In 46.6% of patients, hypopyon resolved in 1 to 2 weeks. The mean time for disappearance of hypopyon was 13.4 ± 8.0 days. Eighty percent of patients had final visual acuity between 1 and 2 logMAR units, whereas 20% of patients had visual acuity of less than 1 logMAR unit. The mean final visual acuity was 1.22 ± 0.31 logMAR units.

Regarding the associated complications in our study, in group A the reported complications were staphyloma (2 cases), thinning (6 cases), hyphema (2 cases) and Atrophia Bulbi (1 case). In group B the complications showed mild variations in distribution as follows; staphyloma (1 case), thinning (3 cases), hyphema (3 cases) and Atrophia Bulbi (1 case). This agreed with other studies[23,25,26] who reported corneal perforations or failure of treatment with different anti-fungal drugs.

This study was limited by little number of cases and the use of single agent antifungal therapy further studies with larger number of patients and comparison of different antifungal agents is recommended.

Acknowledgements

Mansoura Ophthalmic Center Staff.

Conflicts of Interest: Non

References:

1.Mravičić I, Dekaris I, Gabrić N, Romac I, Glavota V, Mlinarić-Missoni E. An overview of fungal keratitis and case report on trichophyton keratitis. Keratitis. Intech Open 2012;ch1:1-14.

2. Al-Hussaini AK, Moharram AM , Ismail MA, Gharama AA. Human microbial keratitis in Upper Egypt. Journal of Basic & Applied Mycology 2010;1:1-10.

3. Al-Hussaini A, Moharram A, Ismail M, Gharama A. Human microbial keratitis in upper Egypt. J of Basic and Applied Mycology, 2010;1:1-10.

4. Johns KJ, O'Day DM. Pharmacologic management of keratomycoses. Survey of ophthalmology, 1988;33(3):178-188.

5. Pleyer U, Grammer J, Pleyer J, Kosmidis P, Friess D, Schmidt K, Thiel H. Amphotericin B--bioavailability in the cornea. Studies with local administration of liposome incorporated amphotericin B. Der Ophthalmologe: Zeitschrift der Deutschen Ophthalmologischen Gesellschaft, 1995;92(4):469-475.

6. Green M, Apel A, Stapleton F. A longitudinal study of trends in keratitis in Australia. Cornea, 2008;27(1):33-39.

7. Seo JH, Wee WR, Lee JH, Kim MK. Risk factors affecting efficacy of intracameral amphotericin injection in deep keratomycosis. J of the Korean Ophthalmological Society, 2007;48(9): 1202-1211.

8. Sharma B, Kataria P, Anand R, Gupta R, Kumar K, Kumar S, Gupta R. Efficacy profile of intracameral amphotericin B. the often forgotten step. The Asia-Pacific J of Ophthalmology, 2015;4(6):360-366.

9. Yilmaz S, Ture M, Maden A. Efficacy of intracameral amphotericin B injection in the management of refractory keratomycosis and endophthalmitis. Cornea, 2007;26(4):398-402.

10. Kalaiselvi G, Narayana S, Krishnan T, Sengupta S. Intrastromal voriconazole for deep recalcitrant fungal keratitis: a case series. British J of Ophthalmology, 2015;99(2):195-198.

11. Cruz JP, Sahgal A, Whyne C, Fehlings MG, Smith R. Tumor extravasation following a cement augmentation procedure for vertebral compression fracture in metastatic spinal disease: Report of 2 cases. J of Neurosurgery: Spine, 2014;21(3):372-377.

12. Shao Y, Yu Y, Pei CG, Tan YH, Zhou Q, Yi J, Gao GP. Therapeutic efficacy of intracameral amphotericin B injection for 60 patients with keratomycosis. International J of ophthalmology, 2010;3(3):257.

13. FlorCruz NV, Evans JR. Medical interventions for fungal keratitis. Cochrane Database Syst Rev. 2015;9(4):CD004241.

14.Mahdy RA, Nada WM, Wageh, MM. Topical amphotericin B and subconjunctival injection of fluconazole (combination therapy) versus topical amphotericin B (monotherapy) in treatment of keratomycosis. J of ocular pharmacology and therapeutics, 2010a;26(3):281-285.

15. El-Gohary M, El-Desoky E, El-Shorbagy M. Clinical versus laboratory diagnosis of mycotic keratitis. Bull. Ophthalmol. Soc. Egypt, 1999;92(6):1121-1123.

16. El-Sayed SH, Wagdy FM, El-Hagaa AA, Mottawea EF. Topical amphotericin B versus subconjunctival fluconazole injection in the management of fungal keratitis. Menoufia Medical J, 2016;29(3):601.

17. Gopinathan U, Sharma S, Garg P, Rao GN. Review of epidemiological features, microbiological diagnosis and treatment outcome

of microbial keratitis: experience of over a decade. Indian J of Ophthalmol, 2009;57(4):273.

18. Thomas P, Kaliamurthy J. Mycotic keratitis: epidemiology, diagnosis and management. Clinical Microbiology and Infection, 2013a;19(3):210-220.
19. Punia RS, Kundu R, Chander J, Arya SK, Handa U, Mohan H. Spectrum of fungal keratitis: clinicopathologic study of 44 cases. International J of ophthalmol, 2014;7(1):114.
20. Al-Hussaini M, Abdel-Kader M, Abu-Ghadeer A, AL-Hussaini A. Keratomycosis diagnosis and therapy with ketoconazole. Bull Ophthalmol Soc Egypt, 1988;81:113-7.
21. Nayak N. Fungal infections of the eye: laboratory diagnosis and treatment. Nepal Med Coll J, 2008;10(1):48-63.
22. Sharma N, Sankaran P, Agarwal T, Arora T, Chawla B, Titiyal JS, Tandon R, Satapathy G, Vajpayee RB. Evaluation of intracameral amphotericin B in the management of fungal keratitis: randomized controlled trial. Ocular immunology and inflammation, 2016;24(5):493-497.
23. Arora R, Gupta D, Goyal J, Kaur R. Voriconazole versus natamycin as primary treatment in fungal corneal ulcers. Clinical & experimental ophthalmology, 2011;39(5):434-440.
24. Yoon KC, Jeong IY, Im SK, Chae HJ, Yang SY. Therapeutic effect of intracameral amphotericin B injection in the treatment of fungal keratitis. Cornea, 2007;26(7):814-818
25. Lalitha P, Sun CQ, Prajna NV, Karpagam R, Geetha M, O'Brien KS, Cevallos V, McLeod SD, Acharya NR, Lietman TM. In vitro susceptibility of filamentous fungal isolates from a corneal ulcer clinical trial. Ame J of ophthalmol, 2014;157(2): 318-326.
26. Prajna NV, Krishnan T, Mascarenhas J, Rajaraman R, Prajna L, Srinivasan M, Raghavan A, Oldenburg CE, Ray KJ, Zegans ME, McLeod SD, Porco TC, Acharya NR, Lietman TM; Mycotic Ulcer Treatment Trial Group. The mycotic ulcer treatment trial: a randomized trial comparing natamycin vs voriconazole. JAMA Ophthalmol. 2013;131(4):422-9.