Original Article

Role of Moxifloxacin in Bacterial Keratitis

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Pak J Ophthalmol 2009, Vol. 25 No. 2

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Received for publication
August' 2008

Purpose: To study the safety and efficacy of Moxifloxacin in bacterial keratitis.

Material and Methods: The study was conducted in the department of Ophthalmology, Lahore General Hospital and Civil Hospital, Karachi from February 2007 to June 2007. The study consisted of two arms. The first arm had 13 diagnosed cases of bacterial keratitis were enrolled in this quasi-experimental study. They were diagnosed by microscopy, culture and sensitivity of corneal scrapings. The second arm consisted of 10 cases of keratitis that were culture and microscopy negative and had been resistant to all treatment.

Results: Out of the 13 diagnosed cases of bacterial keratitis, 7 cases had treatment success while 6 cases had treatment failure. The second arm of the study consisted of 10 cases of bacterial keratitis, which were culture and sensitivity negative. All these 10 cases showed treatment success.

Collectively, 17 out of 23 patients of keratitis had treatment success. They showed improvement in signs and symptoms with corneal re-epithelization within 1 to 4 weeks of initiation of the treatment.

6 out of 23 patients showed treatment failure. Out of these 6, 2 had corneal perforation and 1 had endophthalmitis within 3 to 7 days of initiation of therapy.

Conclusion: 74% of the patients had treatment success with monotherapy with Moxifloxacin eye drops. Moxifloxacin has been shown to be safe and effective in treatment of bacterial keratitis.

Bacterial keratitis is a serious ocular disease that can lead to severe visual disability and even loss of the globe. The severity of the corneal infection usually depends on the underlying condition of the cornea and the pathogenecity of the infecting bacteria and presence or absence of the external eye disease. Many patients have a poor clinical outcome if

aggressive and appropriate therapy is not promptly initiated[1].

In the past the mainstay of treatment of microbial keratitis had been combination therapy with two antibiotics (first generation Cephalosporin and an Aminoglycoside)[2], one each with potent gram positive and gram negative coverage. To achieve this broad cover both antibiotics had to be used initially at half hourly intervals. In addition the suprathreshold concentrations caused osmotic damage to the corneal epithelial cells. The pH was always indifferent and the method of preparation meant that the sterility could not be ensured.

Fourth generation fluroquinolone (Moxifloxacin and Gatifloxacin) with their wide spectrum covering both gram positive and gram negative bacteria have opened new possibilities in treatment of microbial keratitis[3]. They have broad spectrum, are bactericidal, have a rapid rate of bacterial kill, achieve therapeutic levels in target tissues and have minimal toxicity.[4] Moxifloxacin is a self preserved antibiotic, therefore in theory should be less toxic to the corneal epithelium. Moxifloxacin is formulated at a physiological pH of 6.8, has acceptable osmolality, and does not precipitate. We conducted this study to ascertain the role of Moxifloxacin in treatment of bacterial keratitis.

MATERIAL AND METHODS

A Quasi-experimental study was conducted at two centers, namely Department of Ophthalmology, Lahore General Hospital affiliated with Post Graduate Medical Institute, Lahore and Department of Ophthalmology, Civil Hospital, Karachi. A total of 23 patients were enrolled in this study from February 2007 to June 2007.

Patients were diagnosed as suffering from bacterial keratitis either by microscopy and gram staining or by culture and sensitivity of corneal scrape. There were 13 diagnosed cases of bacterial keratitis, which showed the causative organism either on gram staining or on culture and sensitivity. Apart from these 13 cases, there were 10 cases which were culture and sensitivity negative and did not show any causative organism.

Informed consent was taken from all patients. Personal profile of the patients, duration of disease and the eye involved were recorded. A detailed examination of the eye was carried out. The condition of the eye before administering Moxifloxacin and after its administration was recorded.

All patients were treated with Moxifloxacin eye drops at 1 to 2 hourly intervals along with a cycloplegic agent. All patients above 2 years of age with clinical diagnosis of bacterial keratitis were included in the study. Patients with known history of hypersensitivity to flouroquinolones and patients with history of ocular allergy or ocular surgery within the last 6 months were excluded from the study.

Any improvement or worsening in the verbal pain response, redness, photophobia, size of ulcer, size of abscess, density of abscess, size of infiltrate and size of hypopyon was monitored during the course of treatment. Complications like corneal perforations and endophthalmitis were also taken into account.

Statistical software "SPSS-13.0" was used for statistical analysis. Age was presented by Mean ± SD. The qualitative response variables like sign and symptoms, clinical outcome, patients' overall response and side effects were presented by frequencies and percentages. Non-parametric sign test (chi-square statistic) was applied to compare significance of outcome. For comparison of outcome and response of patients' feeling to well being was compared between genders and age groups by using chi-square test.

Statistical significance was taken at $p \leq 0.05$.

RESULTS

Total 23 patients were recruited in this prospective open ended quasi-experimental study through non-probability purposive sampling, 16 (69.6%) males and 7 (30.4%) females (M: F = 2.3: 1). Fifteen patients were treated in Lahore and 8 patients in Karachi. Mean age of the patients was 45.3±19.1 (Range=5-80) years. Majority of the patients (88.2%) were older than 30 years of age as detailed in (Table-1).

Out of the 13 diagnosed cases of bacterial keratitis, 7 patients had treatment success with Moxifloxacin eye drops while 6 had treatment failure. All of the 10 cases of bacterial keratitis which were culture and sensitivity negative showed treatment success with Moxifloxacin eyedrops.

Collectively, complete resolution of sign and symptoms was observed in 12 (52.2%) patients and 5 (21.7%) showed improvement while deterioration was found in 3 (13%) patients and three (13%) patients showed no change; similar figures were recorded in response of overall feeling of patients well being.

Therefore, 17 patients had treatment success and 6 had treatment failure. Data (74% vs. 26%, p=0.001, Sign test) reveals that Moxifloxacin (Megamox) had dramatic effect for relief in symptoms and patients response (Fig.1 & 2).

There was no difference in outcome gender-wise and age-wise (Table-3).

Transient ocular burning and ocular pain was observed in 2 (13.3%) patients while one patient had fever (Fig. 3).

Pattern of sign and symptoms from baseline to follow up visits is presented in (Table-3).

DISCUSSION

We enrolled 23 patients in our Quasi-experimental study through non probability purposive sampling. Sixteen patients (69.6%) were males and 7 patients (30.4%) were females. Fifteen patients were treated in Lahore and 8 patients in Karachi.

Mean age of the patients was 45.3 ±19.1 (Range=5-80) years. No Gender wise or age wise difference of clinical outcome was observed.

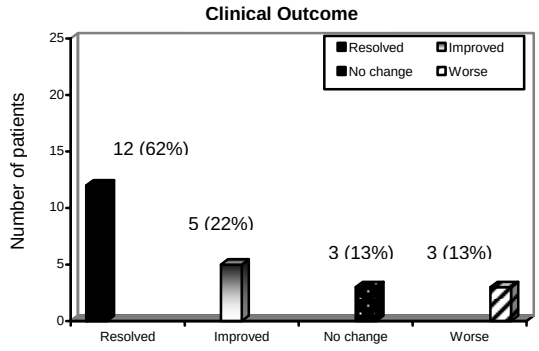
Eight cases out of the 23 patients showed growth of staphylococcus coagulase positive. Four of them responded well to Moxifloxacin, 3 of them worsened while 1 showed no change. This is in accordance with the study, which compared in vitro susceptibility patterns and MIC values of both Gatifloxacin and Moxifloxacin with older generation flouroquinolones against bacterial keratitis isolates. Staphylococcus aureus isolates that were resistant to ciprofloxacin, levofloxacin and ofloxacin showed susceptibility to fourth generation flouroquinolones[7].

Table 1: Demographic Features (N=23):

Demographic variables	**Frequency n (%)**
Gender (M/ F)	16/ 7 (69.6/ 30.4)
Age (years)	
≤ 15	2 (8.7)
16 – 30	3 (13.1)
31 – 45	7 (30.4)
> 45	11 (47.8)
Occupation	
Laborer	5 (21.7)
Guard	1 (4.35)
Sweeper	1 (4.35)
Non-working	16 (69.6)

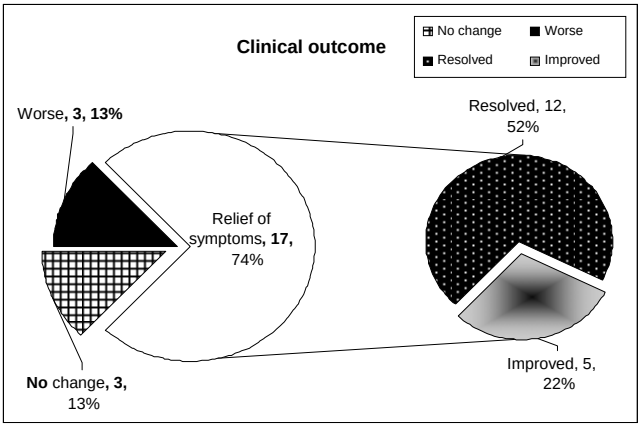
Table 2: Clinical outcome according to demographic variables (n=23)

Demographic variables	**Relief of symptoms**		
	Yes	**No**	**p-value**
Gender			
Male	12 (75)	4 (25)	
Female	5 (71.4)	2 (28.6)	0.845
Age (years)			
≤ 15	2 (100)	0 (0)	
16 – 30	2 (66.7)	1 (33.3)	
31 – 45	5 (71.4)	2(28.6)	
> 45	8 (72.7)	3 (27.3)	0.845



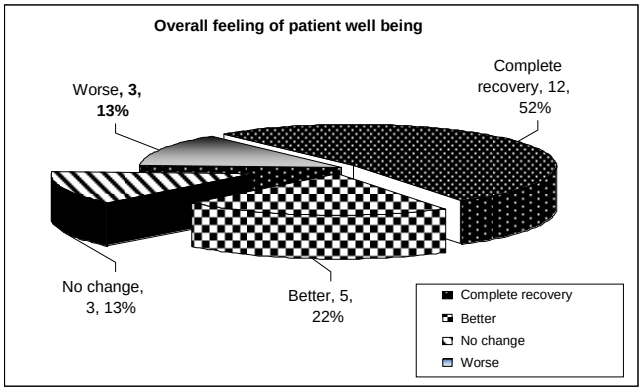
*Significantly high proportion of improvement (p<0.001).

Fig. 1 (a): Clinical outcome and ocular sign and symptoms



*Significantly high proportion of improvement (74% vs. 26%, p<0.001).

Fig.-1 (b): Clinical outcome and ocular sign and symptoms



*Significantly high proportion of improvement (74% vs 26%), (p<0.001).

Fig. 2: Overall feeling of patient well being:

Table 3: Pattern of sign and symptoms from baseline to follow up visits

Signs/ symptoms	Base n (%)	Day 2 n (%)	Day 3 n (%)	Day 4 n (%)	Day 5 n (%)	Day 6 n (%)	Day 7 n (%)
Verbal pain							
0%	1 (4)	3 (13)	6 (26)	7 (30)	7 (30)	9 (39)	11 (47)
25%	4 (17)	2 (9)	1 (4)	1 (4)	6 (26)	5 (22)	4 (17)
50%	4 (17)	5 (22)	4 (17)	9 (39)	3 (13)	5 (22)	6 (26)
75%	0 (0)	2 (9)	8 (35)	4 (17)	6 (26)	2 (9)	0 (0)
100%	14 (61)	11 (47)	4 (17)	2 (9)	1 (4)	2 (9)	2 (9)
Redness							
None	0 (0)	4 (17)	3 (13)	8 (35)	8 (35)	9 (39)	9 (39)
Mild	2 (9)	2 (9)	2 (9)	6 (26)	1 (4)	1 (4)	4 (17)
Moderate	6 (26)	2 (9)	7 (30)	3 (13)	9 (39)	10 (43)	8 (35)
Severe	15 (65)	15 (65)	11 (48)	6 (26)	5 (22)	3 (13)	2 (9)
Photophobia							
None	1 (4)	2 (9)	11 (48)	5 (22)	8 (35)	9 (39)	10 (43)
Mild	3 (13)	4 (17)	2 (9)	6 (26)	2 (9)	5 (22)	8 (35)
Moderate	6 (26)	3 (13)	6 (26)	4 (17)	10 (43)	7 (30)	3 (13)
Severe	13 (57)	14 (61)	4 (17)	8 (35)	3 (13)	2 (9)	2 (9)
Edema of eyelids							
Present	13 (57)	12 (52)	10 (43)	10 (43)	8 (35)	4 (17)	4 (17)

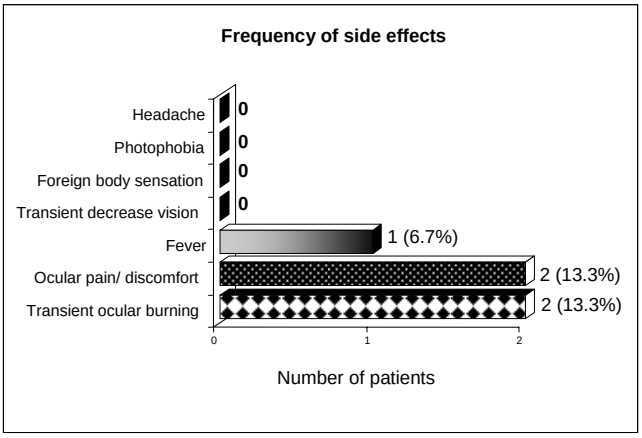
Absent	10 (43)	11 (48)	13 (57)	13 (57)	15 (65)	19 (83)	19 (83)
Discharge							
Present	17 (74)	14 (61)	15 (65)	10 (43)	8 (35)	7 (30)	6 (26)
Absent	6 (26)	9 (39)	8 (35)	13 (57)	15 (65)	16 (70)	17 (74)

Four patients showed gram positive rods on corneal scrapings, 3 of these patients improved while 1 patient showed no change. One patient showed gram negative rods on corneal scrapings. This patient had treatment failure and progressed to corneal perforation and was therefore subjected to surgical application of conjuctival flap[8].

Complete resolution of sign and symptoms was observed in 12 (52.2%) patients and 5 (21.7%) showed improvement while deterioration was found in 3 (13%) patients and three (13%) patients showed no change. Similar figures were recorded in the response of overall feeling of patients well being.

Many prospective randomized controlled trials have examined the efficacy of 2nd generation flouroquinolones such as ofloxacin and ciprofloxacin compared with the traditional combined fortified antibiotics in the treatment of bacterial keratitis[9].

Ofloxacin, fortified tobramycin and Moxifloxacin have shown to be equally effective against a wide range of ocular isolates in the treatment of severe bacterial keratitis. All are safe and well tolerated, no serious events directly attributable to therapy was observed during the study. There was no difference of healing rate or incidence of serious complications such as perforations or enucleation[10].



*Significantly high proportion of patients satisfaction response ($p<0.001$).

Fig. 3: Frequency of side effects of megamox:

CONCLUSION

Seventy four percent of the patients had treatment success with monotherapy with Moxifloxacin eye drops. Moxifloxacin has shown to be safe and effective in treating bacterial keratitis. Large scale and multicenter trials are required to achieve precise results in order to establish recommendations and guidelines for its routine practices.

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