IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 11 Ver. II (Nov. 2017), PP 15-19
www.iosrjournals.org

Evaluation of Moxifloxacin 0.5% Eye Drops in Treatment of Bacterial Corneal Ulcers

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Abstract
Purpose: *To compare the equivalence of moxifloxacin 0.5% with a combination of fortifiedcefazolin sodium 5% and tobramycin sulfate 1.3% eye drops in the treatment of moderate bacterial corneal ulcers.*
Design:*Randomized, controlled, equivalence clinical trial.*
Participants and Controls: *Microbiologically proven cases of bacterial corneal ulcers wereenrolled in the study and were allocated randomly to 1 of the 2 treatment groups.*
Intervention: *Group A was given combination therapy (fortified cefazolin sodium 5% andtobramycin sulfate) and group B was given monotherapy (moxifloxacin 0.5%).*
Main Outcome Measures: *The primary outcome variable for the study was percentage ofthe ulcers healed at 3 months. The secondary outcome variables were best-corrected visual acuity and resolution of infiltrates.*
Results: *Of a total of 30 patients with bacterial keratitis, 15 patients each wererandomized to group A, and group B. The mean ulcer size in groups A and B were 4.2±2 and 4.41±1.5 mm, respectively.. A complete resolution of keratitis and healing of ulcers occurred in 12 patients (80%) in group A and 13 patients (86.6%) in group B at 3 months. . Worsening of ulcer was seen in 20% cases in group A and in 13.3% cases in group B. Mean time to epithelialization was similar, and there was no significant difference in the 2 groups . No serious events attributable to therapy were reported.*
Conclusions: *Corneal healingusing0.5% moxifloxacin monotherapy is equivalentto that of combination therapy using fortified cefazolin and tobramycin in the treatment of moderate bacterial corneal ulcers*
Keywords:*moderate corneal ulcer,moxifloxicilin,fortifieddrops,ulcer healing*

Date of Submission: 26 -10-2017 Date of acceptance: 04-11-2017

I. Introduction

Microbial keratitis is an ophthalmic emergency and requires meticulous management to prevent sight-threatening com- plications.(1) Bacterial keratitis accounts for a significant proportion of infectious keratitis worldwide and may have diverse clinical presentation depending on the geo- graphical location and climatic conditions. Gram-positive bacteriasuch as coagulase-negative Staphylococcus, Staphylococcus aureus, and Streptococcus species account for most the organisms isolated.(2) The protocol for the management of bacterial keratitis ideally involves collection of corneal scraping material for smear and culture and starting empirical intensive antimicrobial therapy until culture and antibiotic sensitivity re- ports are available. The regimens of empirical therapy practiced across the world are either monotherapy with a broad-spectrum antibiotic or a combination of 2 antibacterial drugs to cover both gram- negative and gram-positive organisms(.3)

This prospective, randomized study was conducted to evaluate and compare the efficacy and safety of combination therapy of fortified 5% cefazolin sodium and 1.3% tobramycin sulphate eye drops versus monotherapy with 0.5% moxifloxacin hydrochloride eye drops in patients with bacterial corneal ulcers.

II. Patients And Methods

Study Design

A randomized, prospective study was conducted in which 30 patients with proven bacterial corneal ulcers were enrolled from our center. They were assigned randomly into 1 of the 2 groups . One eye of each patient was enrolled.). Bacterial corneal ulcers measuring 2 to 8 mm were identified as well as the presence of

infiltrate, for which a diagnostic scraping had been performed and that showed a significant presence of bacteria on corneal scraping or culture. Group A received topical fortified cefazolin sodium (50 mg/ml) and fortified tobramycin sulphate (14 mg/ml) eye drops, whereas group B received topical moxifloxacin hydrochloride (0.5%). The study was approved by the ethics committee of the hospital written informed consent was obtained from all the patients included in the study.Patients with suspected fungal, viral, or acanthamoeba ulcers and patients with known allergy to fluoroquinolones, aminoglycosides, penicillins, or cephalosporins were excluded from the study. Pregnant and lactating women and patients younger than 12 years also were excluded from the study.

Study Protocol

All patients underwent a meticulous history taking, which included the demographic profile, duration and type of symptoms, and risk factors. A complete initial ocular examination including record of best-corrected visual acuity; slit- lamp biomicroscopy to assess the size, depth, and location of theulcer; anterior chamber reaction; and presence and height of hy- popyon was undertaken.. A standard protocol was used for the initial microbiologic investigation of all patients with keratitis. At presentation, corneal scrapings were collected from the base and edges of the ulcer and examined with gram's stain and potassium hydroxide wet mount. Any patients who demonstrated hyphae or acanthamoeba cyst on potassium hydrox- ide mount were excluded from the study. Corneal scrapings were plated directly on culture plates of blood agar, chocolate agar, Sabouraud's dextrose agar, and thioglycolate broth. Growth in culture media was considered significant if the same organism was isolated on more than 1 culture medium with direct microscopy of corneal scrapes revealing bacterial morphologic features consistent with those of bacteria isolated on culture. Susceptibility of the isolates to antimicrobials was assessed by the Kirby-Bauer disk diffusion method.

Dosage Schedule.

The dosage schedule was as follows. For the first 72 hours, antibiotics were given every hour, day and night. After 72 hours, the same medications were administered every 2 hours for next 7 days, then tapered according to the clinical response. The additional supportive treatment included cycloplegic and antiglaucoma therapy if required.The examination findings were recorded on days 1, 4, 7, 14, and 21 and at 3 months. Slit-lamp biomicroscopy with fluorescein staining was carried out at each visit to assess the size, depth, and location of the ulcer; anterior chamber reaction; and presence and height of hypopyon. To distinguish between stromal infiltrates and corneal scarring, fluorescein staining was performed at each follow-up visit. Stromal infiltrate is yellowish and shows evidence of staining, whereas a scar is whitish and does not stain with fluorescein.. The above-mentioned parameters were evaluated at each visit. Healing was defined as closure of the epithelial defect with disappearance of the stromal infiltrates at or before 3months. Clinical response to medication was poor if the ulcer size remained the same or increased for 72 hours. If the keratitis worsened, the treatment code was broken, and the patient was administered alternate treatment regimen.

III. Result

Of a total of 30 patients with bacterial keratitis enrolled in the study, 15 patients were randomized to the fortified tobramycin and cefazolin group (group A) and 15 patients were randomized to the moxifloxacin group (group B). Microbiologic AnalysisAmong 30 gram-stain specimens analyzed, 27.5% were gram-positive cocci and 5.9% were gram-negative bacilli. Positive bacterial culture results were obtained in patients 80.7%, and no growth was seen in 19.4% Among the bacterial isolates, coagulase-negative Staphylococcus 40.9% in group A and 48.2% in group B was seen most com- monly in both groups, followed by Staphylococcus aureus 19.1% in group A and 21.3% in group B. Pseudomonas aeruginosa was isolated in 5.4% in group A and in 4.6% in group B. There was no significant difference in the organisms isolated in either groupThe antibiotic sensitivity of the isolated organisms was analyzed by the Kirby-Bauer disk diffusion method. The isolates were considered resistant, intermediate, or susceptible to an antibiotic based on the zone of inhibition It showed that 100% samples of Staphylococcus, Streptococcus, and Pseudomonas species were sensitive to moxifloxacin. All the isolates of Pseudomonas species, Proteus and Klebsiella species were sensitive to tobramycin. In

comparison, sensitivity to cefazolin was seen in 90.6% isolates of coagulase-negative Staphylococcus, 76.6% isolates of S aureus, and 45.5% isolates of Psuedomonasaeruginosa .

Outcome

A complete resolution of keratitis and healing of ulcer occurred in 81% patients at 3 months. Of these, 81.8% were in group A and 81.4% were in group B. Worsening of ulcer was seen in 20% of cases in group A and in 13.6% of cases in group B. Mean time to epithelialization wassimilar, and there was no significant difference in the 2 groups . No serious events directly attributable to therapy were reported during the study. However, a change in therapy guided by repeat microbiologic examination led to resolution of ulcers in these cases, so that no therapeutic keratoplasty was required in either groups.

IV. Discussion

The standard treatment of microbial keratitis consists of a combination of fortified topical antibiotics or fluoroquinolones. It generally is advocated that for nonsevere ulcers that are not threatening the visual axis, fluoroquinolones are preferred over combination therapy, whereas in cases of severe bacterial ulcers threatening the visual axis, combination therapy with fortified antibiotics is preferred. There are factors favoring monotherapy, such as ease of procurement of medicine, simplicity of application and storage, and less chance of toxicity. With the advent of newer fourth-generation fluoro-quinolones with enhanced gram-positive coverage while retaining efficacy against gram-negative organisms, there has been a renewed interest in newer-generation fluoroquinolone monotherapy for bacterial keratitis. This has been accomplished by substitution of the methoxy group at position 8 of the quinolone ring, which helps in simultaneous inhibition of both DNA gyrase and topoisomerase 4 in gram positive bacteria. This not only increases the efficacy of the action of moxifloxacin and gatifloxacin but also reduces the risk of resistance because concomitant mutations in both genes are less likely to occur than the single mutation required for developing resistance to older fluoroquinolones. This structural modification also decreases the suscep-tibility to efflux the drug from the bacterial cell, thereby reducing risk of resistance development[(4)]

The points supporting combination fortified antibiotic therapy are better coverage of gram-positive and gram- negative organisms and less chance of development of antibiotic resistance. Fortified antibiotics have the disadvan-tage that they need to be prepared under sterile conditions at a pharmacy for use. Concerns have been expressed about their shelf life, appropriate method of storage, and the duration for which they can be used safely before replace-ment. Fortified drops also have the theoretical risk of the first drug being washed away if both the medicines are applied simultaneously. Using 2 drugs as a combination may enhance ocular toxicity and may prevent re-epithelialization.[(5)]

Monotherapy with ciprofloxacin and ofloxacin were studied in the past and were found to be equally effective. In a study by Gangopadhyay et al,[(6)] monotherapy with fluoroquinolone eye drops led to shorter duration of intensive therapy and a shorter hospital stay compared with combined forties therapy (tobramycin and cefazolin). How ever, serious complications were encountered more commonly in the fluoroquinolone group, such as corneal perforation, evisceration, or enucleation of the affected eye. The limitation of this study was that it was retrospective.(6) There are only 2 prospective, randomized, controlled clinical trials comparing the efficacy of moxifloxacin with combination fortified therapy in bacterial keratitis.[(7)(8)] In a pilot prospective study comparing moxifloxacin (0.5%), gatifloxacin (0.3%), and fortified tobramycin(1.33%) plus cefazolin (5%) with 20 patients with corneal ulcers in each group, similar outcomes were seen.31 However, the sample size of this study was small and the power of the study was only 32%. The only other randomized, controlled clinical trial comparing moxifloxacin and com-bination therapy was carried out by Constantinou et al.(8) They compared moxifloxacin (1%), ofloxacin (0.3%), and fortified tobramycin (1.33%) plus cefazolin (5%) and found similar rates of healing of corneal ulcers. There were 3 differences in the study protocol compared with the present study. The present study used commercially available moxifloxacin hydrochloride 0.5% (Vigamox; Alcon), unlike the study by Constatinou et al, in which 1% moxifloxacin that was reconstituted at a pharmacy was used; the availability of this commercial preparation obviates the need for a hospital pharmacy to prepare the drug. In the study by Constatinou et al, the initial therapy was ceased at 1 week and a preservative-free

prophylactic antibiotic such as chloramphenicol ointment was used subsequently, if required. However, in the present study, because preservative-free moxifloxacin was being used, it was continued until complete healing occurred. Furthermore, in this study, no topical corticosteroids were used, which were used in the study by Constatinou et al as the ulcer was resolving. It has been demonstrated amply in the available randomized clinical trials that topical corticosteroids may not help in enhancing the rate of healing in cases of resolving keratitis.[(9)]

The argument against fluoroquinolone monotherapy is that although these agents are considered very effective and safe, resistance is bound to occur if they are used indiscriminately, and a few cases of moxifloxacin and gatifloxac in resistance already are emerging, especially in cases of infectious keratitis occurring after refractive surgery.[(10)] however, their judicious use in an appropriate setting may be justified. Furthermore, poor patients from rural areas often are uneducated and have poor access to tertiary care hospitals or pharmacy. They may not be able to store the fortified medication at a cool temperature to maintain its shelf life. The combination therapy may enhance the cost of treatment as well. It may be difficult to explain the method of sequential application of fortified topical medication to uneducated patients, and inappropriate application may nullify the advantage of combination therapy. Compliance also is difficult to maintain with more medications and confusing regimens.

To conclude, this study demonstrated that monotherapy with commercially available 0.5% moxifloxacin hydrochloride may be as effective as a combination therapy of fortified cefazolin and tobramycin in cases of nonperforated bacterial keratitis. Moxifloxacin 0.5% may be continued during the entire treatment course because, being preservative free, it is not significantly epitheliotoxic. Further studies are required to evaluate the role of moxifloxacin 0.5% in perforated corneal ulcers.

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Financial support and sponsorship- nil
Conflicts of interest – there are no conflicts of interest.

References-

[1]. Whitcher JP, Srinivasan M, Upadhyay MP. Corneal blindness: a global perspective. Bull World Health Organ 2001;79:214 –21.
[2]. Schaefer F, Bruttin O, Zografos L, Guex-Crosier Y. Bacterial keratitis: a prospective clinical and microbiological study. Br J Ophthalmol 2001;85:842–7.
[3]. Bennett HG, Hay J, Kirkness CM, et al. Antimicrobial man- agement of presumed microbial keratitis: guidelines for treat- ment of central and peripheral ulcers. Br J Ophthalmol 1998; 82:137– 45.
[4]. Blondeau JM. Fluoroquinolones: mechanism of action, clas- sification, and development of resistance. SurvOphthalmol 2004;49(suppl):S73– 8.
[5]. Arici MK, Sümer Z, Güler C, et al. In vitro potency and stability of fortified ophthalmic antibiotics. Aust N Z J Oph- thalmol 1999;27:426 –30.
[6]. Gangopadhyay N, Daniell M, Weih L, Taylor HR. Fluoro- quinolone and fortified antibiotics for treating bacterial cor- neal ulcers. Br J Ophthalmol 2000;84:378 – 84.
[7]. Shah VM, Tandon R, Satpathy G, et al. Randomized clinical study for comparative evaluation of fourth-generation fluoro- quinolones with the combination of fortified antibiotics in the treatment of bacterial corneal ulcers. Cornea 2010;29:751–7.
[8]. Constantinou M, Daniell M, Snibson GR, et al. Clinical efficacy of moxifloxacin in the treatment of bacterial keratitis: a randomized clinical trial. Ophthalmology 2007; 114:1622–9.

[9]. Srinivasan M, Mascarenhas J, Rajaraman R, et al, Steroids for Corneal Ulcers Trial Group. Corticosteroids for bacterial keratitis: the Steroids for Corneal Ulcers Trial (SCUT). Arch Ophthalmol 2012;130:143–50.

[10]. Jhanji V, Sharma N, Satpathy G, Titiyal J. Fourth-generation fluoroquinolone-resistant bacterial keratitis. J Cataract Refract Surg 2007;33:1488-9

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