

# Comparison of 0.3% Gatifloxacin Ophthalmic Solution Against 0.3% Ofloxacin Ophthalmic Solution as Preoperative Ocular Disinfectant in Cataract Surgery: A Prospective Randomized Double-blind Study

Rama Sikka, Ph.D. (Medical Microbiology)\*,  
Chand Singh Dhull, MS, FIAO, DCEH\*\*,  
Ritu Aggarwal, M.D.\*,  
Sanjeev Jindal, M.S.\*\*

## ABSTRACT

Aim of the study was to compare the bactericidal efficacy of 0.3 percent ofloxacin ophthalmic solution with 0.3 percent gatifloxacin solution on conjunctival flora. It was a prospective and randomized double blind study. One hundred patients of senile cataract were admitted to undergo cataract surgery and were divided into two groups of 50 each, with topical ofloxacin solution being instilled in group I patients and topical gatifloxacin solution being instilled in group II patients, thrice a day for one day prior to surgery. Conjunctival swabs were taken from patients of both the groups before and after 24 hours of instillation of first dose of ophthalmic solution. Bacterial isolates were identified and colony forming units (CFU) were calculated. Overall decrease in median CFU count was 33.33 percent and 60 percent after instillation of ofloxacin and gatifloxacin respectively which was statistically significant ( $p=0.019$ ). Preoperative prophylaxis with gatifloxacin was more effective in decreasing the human conjunctival bacterial flora. (*J Infect Dis Antimicrob Agents* 2010;27:85-9.)

## INTRODUCTION

In the early 1900s, the incidence of endophthalmitis following intraocular surgery was 5-10 percent. The incidence of endophthalmitis in mid 1900s

has been reported to vary from 0.5 percent to 0.7 percent, due to better preoperative sterilization. Rate of endophthalmitis in the years 1963 to 1999 was 0.109 percent, while rate from 2000-2003 was 0.265 percent

\*Department of Microbiology, Pt.B.D. Sharma PGIMS, Rohtak (Haryana), India.

\*\*Department of Ophthalmology, Pt.B.D. Sharma PGIMS, Rohtak (Haryana), India.

Received for publication: May 31, 2010.

Reprint request: Dr. Ritu Aggarwal, H no.717, sector-1, Rohtak, (124001), Haryana, India.

E.mail: drritu252@yahoo.com

**Keywords:** cataract, colony forming unit, gatifloxacin, ofloxacin

representing an almost 2.5 fold increase in its incidence. It has been suggested that reported increase in the incidence of endophthalmitis may be due to increased use of self healing clear corneal incisions as compared with previous decades.<sup>1</sup>

Preoperatively, the most important source of potentially infectious organisms is the patient's own natural conjunctival and skin flora and periocular microbes, comprising predominantly of *Staphylococcus epidermidis*, followed by *Staphylococcus aureus*, and rarely, gram-negative rods and *Candida*.<sup>2</sup> It is hypothesized that decreasing the number of bacteria on eye lids and conjunctiva reduces the risk of developing endophthalmitis after surgery. Povidone iodine has been shown to be an effective antiseptic for use as an ophthalmic solution.<sup>3</sup> Some authors have reported, that antibiotic and povidone-iodine solutions when used individually caused a similar decrease in the number of colonies and species of bacteria cultured from the ocular surface, and when both regimens were used together, the decrease was more pronounced, with 83 percent of the conjunctivae being sterile.<sup>4</sup> Hence, the choice of antibiotic used for prophylaxis is important.

Fluoroquinolones were chosen after extensive study of the literature as they are unique class of antibacterial agents with a broad spectrum of antimicrobial activity against most aerobic gram-negative and gram-positive bacteria. They have low toxicity, safety, good ocular surface penetration, prolonged tear film concentration, stability at room temperature, and easy availability.<sup>5</sup> Some authors have found their *in vitro* efficacy better than aminoglycosides and erythromycin.<sup>6</sup> Both ofloxacin and gatifloxacin are active against gram-positive bacteria. Ofloxacin belongs to second generation fluoroquinolones and it is more active against gram-negative bacteria but has limited gram-positive coverage. Gatifloxacin belongs to fourth generation fluoquinolones with improved gram-positive

coverage and retained gram-negative activity. Amongst the newer generation quinolones, gatifloxacin in addition has greater affinity for topoisomerase IV and has more activity against gram-positive bacteria.<sup>5</sup>

Gatifloxacin has been compared with ofloxacin as there are increasing reports of resistance among bacteria against second and third generation fluoroquinolones.<sup>5</sup> Hence, the aim of the study was to compare topical gatifloxacin and topical ofloxacin as a preoperative ocular disinfectant in cataract surgery.

## MATERIAL AND METHODS

One hundred patients of senile cataract admitted to undergo cataract surgery, from January 2005 to December 2005 were included in this prospective, randomized and double blind study.

Informed consent was taken from the patients. Following exclusion criteria were: 1) patients with clinical evidence of any type of local (eye) or systemic infection, 2) history of recent use of topical or systemic antimicrobial agents, 3) history of allergy to iodine and topical antibiotics, 4) history of previous intraocular surgery or penetrating injury to the eye, 5) history of intake of steroids and other immunosuppressive agents, 6) history of any malignancy, and 7) pregnant patients.

The patients were divided into two groups of 50 each by systematic random sampling method. Topical ofloxacin ophthalmic solution (0.3%) was instilled in group I (50 patients) and topical gatifloxacin ophthalmic solution (0.3%) was instilled in group II (50 patients). Eyes of both the groups were instilled with respective topical ophthalmic solution thrice a day, one day prior to surgery.

A swab from the inferior conjunctival fornix of the eye to be operated on was taken with sterile cotton tipped applicator before and after 24 hours of instillation of first dose of topical antibiotic solution. These swabs

were then inoculated on chocolate agar, blood agar and Mac Conkey's agar and incubated for 24-48 hours at 37°C aerobically. For isolation of anaerobic bacteria, brain heart infusion agar enriched with blood, vitamin K and haemin were inoculated and incubation was done at 37°C for 48 hours in an anaerobic jar. After incubation, the plates were examined and identification of the growth was carried out on the basis of gram staining, culture characteristics and biochemical tests. In addition, the numbers of colonies in plates were counted, thus giving Colony forming Units (CFU) per eye.<sup>7,8</sup>

Routine preoperative preparation of the patients in both the groups was done. Dilatation of the pupil was done. Eye lashes were trimmed. Brow, both upper and lower eye lids, forehead, nose, cheeks and temporal orbital area were scrubbed with 5 percent povidone iodine for 1 minute. This was followed by cataract surgery.

As the study was double blind, all the patients in both the groups were blinded to the ophthalmic solution they were instilled with. Name of the antibiotic on the ophthalmic solution vial was masked. Vials were marked as I for ofloxacin and II for gatifloxacin. Surgeons who took preantibiotic and postantibiotic swabs were also masked about the grouping of the patients. Microbiologists who processed the samples and isolated and identified the bacteria were also unaware about the grouping of the patients. The results of efficacy were then compiled and compared by using Chi square test, paired T test and Mann-Whitney U test.

## RESULTS

There was no statistically significant difference in number of culture positive cases in group-I and group-II patients before and after instillation with antibiotic (p=0.22). Composition of conjunctival microbial flora

(amongst pre and post antibiotic groups) in those instilled with 0.3 percent ofloxacin or 0.3 percent gatifloxacin ophthalmic solution is shown in Table 1.

Amongst patients of group I, the median colony forming unit counts before instillation of antibiotic was  $9 \times 10^2$  CFU, which after instillation of antibiotic decreased to  $6 \times 10^2$  CFU, thus causing a decrease of  $3 \times 10^2$  (33.33%) CFU. This reduction in CFU was not significant (Mann-Whitney U; p=0.257). In group-II, the median CFU count decreased from  $1 \times 10^3$  CFU to  $4 \times 10^2$  CFU after instillation of antibiotic, thus causing a decrease of  $6 \times 10^2$  (60%) CFU. This reduction in CFU was significant (Mann-Whitney U; p=0.002). Overall, in this study, decrease in median CFU count after instillation of 0.3 percent gatifloxacin ophthalmic solution was statistically significant (Mann-Whitney U; p=0.019). None of the patients developed postoperative endophthalmitis and no other major side effect or allergic reaction to topical antibiotic ophthalmic solution was observed.

## DISCUSSION

In the present study, 79 percent culture positivity was observed in the eyes of the patients undergoing cataract surgery prior to instillation of antibiotic solution. This is comparable to the study by Kasper et al.<sup>9</sup> However, it differs from the study by Dereklis et al.<sup>10</sup> This difference may be because of the difference in methodology of the two studies.

In this study, coagulase negative staphylococci were the predominant organisms in both the groups, before and after instillation of antibiotic. Other common bacterial isolates were *Corynebacterium* spp. and *Staphylococcus aureus*, followed by gram-negative bacilli. This finding is also in concordance with the findings of Kasper et al and Ferguson et al.<sup>9,11</sup>

A significant fall in median CFU was found in group II after instillation of 0.3 percent gatifloxacin

**Table 1. Types of bacteria found in the two groups.**

| Bacteria                                | Group I, number (%) |                  | Group II, number (%) |                  |
|---|---------------------|------------------|----------------------|------------------|
|   | Pre- antibiotic     | Post- antibiotic | Pre- antibiotic      | Post- antibiotic |
| Coagulase negative staphylococci (CONS) | 30 (57)             | 26(59)           | 28 (55)              | 21 (56)          |
| <i>Corynebacterium</i> spp.             | 12 (23)             | 9 (20)           | 9 (18)               | 7 (18)           |
| <i>Staphylococcus aureus</i>            | 3 (6)               | 3 (6)            | 5 (10)               | 2 (5)            |
| <i>Peptococcus</i> spp.                 | 3 (6)               | 2 (5)            | 2 (4)                | 2 (5)            |
| Alpha-hemolytic streptococci            | 2 (4)               | 2 (5)            | 2 (4)                | 1 (3)            |
| <i>Escherichia coli</i>                 | 2 (4)               | 2 (5)            | 2 (4)                | 2 (5)            |
| <i>Proteus</i> spp.                     | 0                   | 0                | 3 (5)                | 3 (8)            |
| Total                                   | 52                  | 44               | 51                   | 38               |

In both the groups, 12 eyes yielded multiple isolates. In group I, combinations of CONS + *Corynebacterium* spp. (7), *S. aureus* + *Corynebacterium* spp. (2), CONS +  $\infty$  hemolytic streptococci (1), CONS + *Peptococcus* spp. (1) and *S. aureus* + CONS (1) were observed. In group II, combinations of CONS + *Corynebacterium* spp. (4), *S. aureus* + CONS (4), CONS + *Proteus* spp. (3), CONS +  $\infty$  hemolytic streptococci (1), were isolated.

whereas, the fall in the median colony counts was not significant among group I patients instilled with 0.3 percent ofloxacin. This may be due to broader spectrum of activity of gatifloxacin as compared to ofloxacin. But, no definite conclusion can be drawn from this finding as this is a small sample size study.

A statistically significant difference in bactericidal activity of 0.3 percent gatifloxacin and 0.3 percent ofloxacin *in vivo* was observed in the present study, with 0.3 percent gatifloxacin exhibiting more bactericidal activity. However, the number of patients with positive cultures did not differ statistically among the two groups ( $p=0.02$ ). In addition no endophthalmitis case developed in this study. This might be due to small sample size.

Hence, it is suggested that 0.3 percent gatifloxacin ophthalmic solution can be used as preoperative prophylactic regimen for cataract surgery. Considering the small sample size, a study

involving larger sample size may be planned to authenticate or generalize the findings of this study.

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