



Comparison of preoperative prophylaxis with povidone–iodine (5%) and moxifloxacin (0.5%) versus povidone–iodine (5%) alone: a prospective study from India

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Abstract

Purpose To compare the effect of povidone-iodine (PI) 5% and moxifloxacin 0.5% solutions versus PI 5% solution alone on the conjunctival bacterial flora.

Methodology This is a comparative study in which the study population comprised adult patients scheduled for elective small incision cataract surgery. The eye to be operated (control eye) received topical moxifloxacin 0.5% drops 4 times, 1 day before surgery and 2 applications on the day of surgery. As placebo, the contralateral eye (study eye) received saline 0.90% drops as per the same schedule. Before surgery, on table, PI 5% was instilled in the conjunctival sac in both eyes. Conjunctival swabs were taken before initiation of therapy and 3 min after instillation of PI.

Results Of the 96 pairs of eyes included in the study, conjunctival cultures before prophylaxis were similar between the two groups ($p=0.31$), with 54 samples (56%) of the study group and 49 (51%) of the control group showing growth. With positive cultures reducing to 7 (14%) in the study group and 8 (16%) in the control group, both the prophylaxis methods appeared equally efficacious ($p=0.79$). Both the groups showed a significant reduction in positive cultures following prophylaxis ($p<0.0001$).

Conclusions PI 5% alone as preoperative prophylaxis was as effective as its combination therapy with moxifloxacin 0.5% in the reduction in conjunctival bacterial colonization.

Keywords Povidone-iodine · Antibiotics · Resistance · Coagulase-negative *Staphylococcus epidermidis* · Cataract surgery

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Introduction

Cataract surgery is one of the most commonly performed ophthalmic surgical procedures worldwide [1]. It is a safe procedure with good surgical and visual outcomes [2]. Every incisional surgery carries the risk of postoperative infection. Acute postoperative endophthalmitis, one of the most dreaded complications following cataract surgery, has a significant toll on visual recovery. Fortunately, the incidence of this complication has declined in recent times following

better understanding of the risk factors, modifications in preoperative, intraoperative and postoperative antimicrobial therapy, surgical techniques and sterilization procedures [3, 4].

With the breach in ocular surface during cataract surgery, the ocular commensals become the main source of infection [5]. Recognition of this has made the use of preoperative antibiotics almost universal [6]. However, the choice of antimicrobial agents, timing and route of administration of antibiotics is not uniform. Further, the increased use and misuse of antibiotics has led to the emergence and dissemination of antimicrobial resistance (AMR), which is a major global health challenge [7].

Povidone–iodine (PI) has been recommended for periocular skin and conjunctival antiseptics just prior to surgery [8]. Low risk for development of resistance and wide spectrum of antimicrobial effects gives PI an advantage over topical antibiotics. While frequently used as an adjunct to topical antibiotic prophylaxis, the role of PI as a replacement to antibiotics has not been unequivocally established [9]. Therefore, this study was done to compare the effectiveness of preoperative PI alone versus its combination with topical moxifloxacin eye drops on the conjunctival bacterial flora.

Subjects and methods

This comparative study was conducted at the Department of Ophthalmology of a tertiary care hospital between January 2021 and June 2022 after approval from the Institutional human ethics committee (IHEC no: Res/01/2020/112/IHEC/326). Patients above 18 years of age and scheduled for elective small incision cataract surgery were enrolled for the study by simple random sampling. Immuno-compromised patients, those on local or systemic antibiotics or steroids within the past 3 months, and those with local infectious diseases were excluded. Informed consent was obtained from all participants, and the study was conducted in accordance to the tenets of the Declaration of Helsinki.

The eye planned for surgery was taken as the control eye and the fellow eye was taken as the study eye. The sample size was calculated with prevalence of coagulase-negative staphylococcus at 30.40% [10], and found to be 82 in each group.

The first conjunctival swab was obtained from the inferior cul-de-sac of both the eyes before application of any ocular drops, using sterile dacron swabs, without touching the eyelid margin or eye lashes. The control eye received topical moxifloxacin 0.5% drops (Mosi eye drops, FDC private limited) 1 drop each at an interval of 6 h, into the conjunctival sac, the day prior to surgery and 2 applications on the day of surgery, with the last drop being instilled at least 2 h before surgery. As a placebo, the study eye received normal saline 0.9% drops as per the same schedule. Povidone-iodine 5% solution (Apidine 5% eye drops, Appasamy ocular devices private limited) was instilled in the conjunctival sac in both groups before surgery. After a contact time of 3 min, the second conjunctival swab was taken from the inferior cul-de-sac of both eyes. All the swabs were sent for microbiological examination which included gram staining and culture (with Blood agar and MacConkey agar). The cultures were incubated for 24–48 h under aerobic conditions at 37 °C.

From positive cultures, colony count was obtained as per the Canadian Microbiology Proficiency Testing (CMPT) program's recommended gram stain reporting criteria-based on reading of more than 10 fields [11]. All patients were postoperatively followed up as per the standard guidelines for evidence of endophthalmitis. Data were entered in Microsoft Excel 2019, and statistical analysis was done using Statistical Package for Social Sciences (SPSS) software version 16.0 (SPSS Inc., Chicago, Ill., USA).

Results

Of the 100 patients enrolled for the study, samples of 4 patients developed cross-contamination in the culture plate and hence excluded. Among the 96 patients, 61 (63.54%) were women and 35 (36.45%) were men. The mean age of the study population was 59.10 ± 8.38 years. There were 12 diabetics, 17 hypertensive and 5 patients with meibomian gland dysfunction.

Pre-treatment culture plates showed growth from the conjunctival sac in 54 (56.25%) eyes of the study group and 49 (51.04%) eyes in the control group. Ninety-seven of the 103 culture plates had only a single bacterial isolate. (Fig. 1) Coagulase-negative *Staphylococcus epidermidis* (S.

epidermidis) was the most commonly observed isolate (69 plates, 67%). (Table 1) Additional growth of yeast was observed in 10 plates—6 belonging to study group and 4 belonging to control group. There was no significant difference observed between the study group and control group with respect to pre-treatment culture results ($p=0.31$). (Table 2).

Post-treatment culture plates showed growth from the conjunctival sac in 7 (7.29%) eyes of the study group and 8 (8.33%) eyes in the control group. Twelve out of the 15 culture plates had only a single bacterial isolate. *S. epidermidis* was again the most commonly observed isolate in 8 plates (4 each in both the study and control group). (Table 1) Additional growth of yeast was observed in 3 plates—1 belonging to study

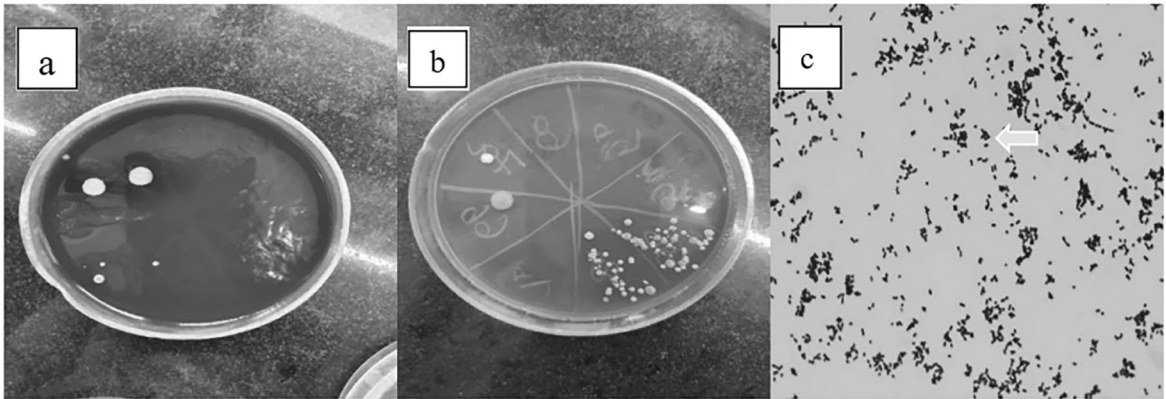


Fig. 1 Culture showing growth in, **a** blood agar, **b** MacConkey agar, **c** Gram staining showing gram-positive cocci in clusters (white arrow)

Table 1 Bacterial growth distribution in the study and control groups before and after prophylaxis

Parameters	Positive cultures before prophylaxis		Positive cultures after prophylaxis	
	Study group (96 eyes) <i>n</i> (%)	Control group (96 eyes) <i>n</i> (%)	Study group (96 eyes) <i>n</i> (%)	Control group (96 eyes) <i>n</i> (%)
Over all	54 (56.25)	49 (51.04)	7 (7.29)	8 (8.33)
<i>S. epidermidis</i> *	35 (36.50)	34 (35.41)	4 (4.16)	4 (4.16)
<i>Staphylococcus aureus</i>	15 (15.60)	13 (13.54)	2 (2.08)	3 (3.12)
Gram-negative bacilli (GNB)	4 (4.16)	2 (2.08)	1 (1.04)	1 (1.04)
Yeast	6 (6.25)	4 (4.16)	1 (1.04)	2 (2.08)

Coagulase-negative *Staphylococcus epidermidis* was the most commonly observed isolate. Gram-negative bacilli (GNB) was the least commonly observed isolate and all were indole positive and oxidase negative suggestive of Enterobacteriaceae

**S.epidermidis*: Coagulase-negative *Staphylococcus epidermidis*

Table 2 Comparison of positive conjunctival cultures before and after treatment

Positive growth	Pre prophylaxis <i>n</i> (%)	Post prophylaxis <i>n</i> (%)	<i>p</i> value
PI <i>n</i> =96	54 (56)	7 (14)	< 0.0001 [#]
PI + Moxifloxacin <i>n</i> =96	49 (51)	8 (16)	< 0.0001 [#]
<i>p</i> value	0.31*	0.79*	

*Chi-square test

[#]McNemar test

group and 2 belonging to control group. The post-treatment culture results in both study and control group were similar ($p=0.79$) (Table 2).

Total number of positive cultures reduced from 103 to 15 following either prophylaxis (Fig. 2). In the study group, 54 eyes, that had shown positive cultures before prophylaxis reduced to 7 following application of PI ($p<0.0001$). In the control group, following application of both PI and moxifloxacin, the 49 eyes that had positive growths reduced to 8 ($p<0.0001$) (Table 2). The reduction in growth, observed after prophylaxis was significant in both the study and control groups (Table 2). No discomfort or irritation was recorded for both PI and moxifloxacin eye drops.

An analysis of pre and post prophylaxis colony count was performed for the 15 culture plates that

continued to remain positive after prophylaxis (Fig. 3). Of the 7 positive culture plates in the study group, it was observed that the colony count reduced from moderate to few in 6 plates and was maintained at few in 1 plate. Of the 8 positive culture plates in the control group, the colony count reduced from moderate to few in 6 plates and remained at moderate colony count, but with reduction in the absolute number of colonies in 2 plates. Reduction in colony count was therefore observed in both the study and control groups even in plates showing positive culture after prophylaxis.

All patients, including those with post prophylaxis positive culture growth, were treated and followed up as per the standard guidelines and none of these patients developed endophthalmitis in the postoperative period.

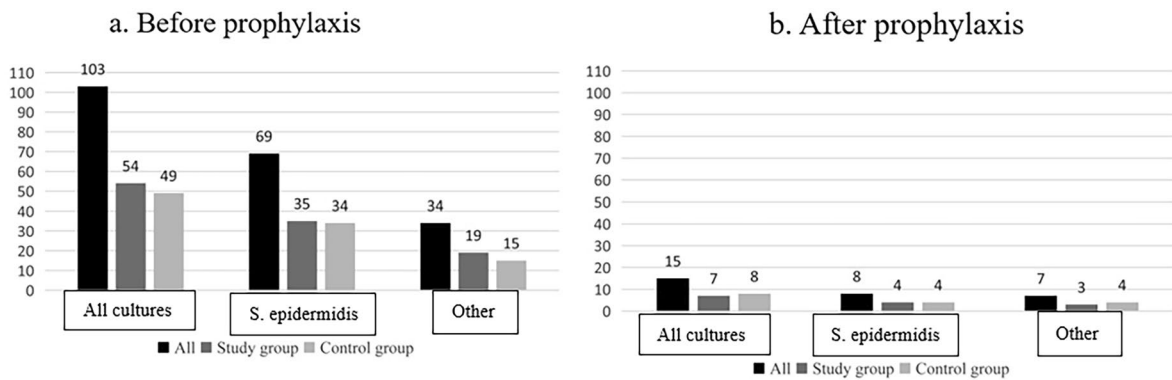


Fig. 2 Graphical representation of number of eyes with positive growth a before prophylaxis, b after prophylaxis

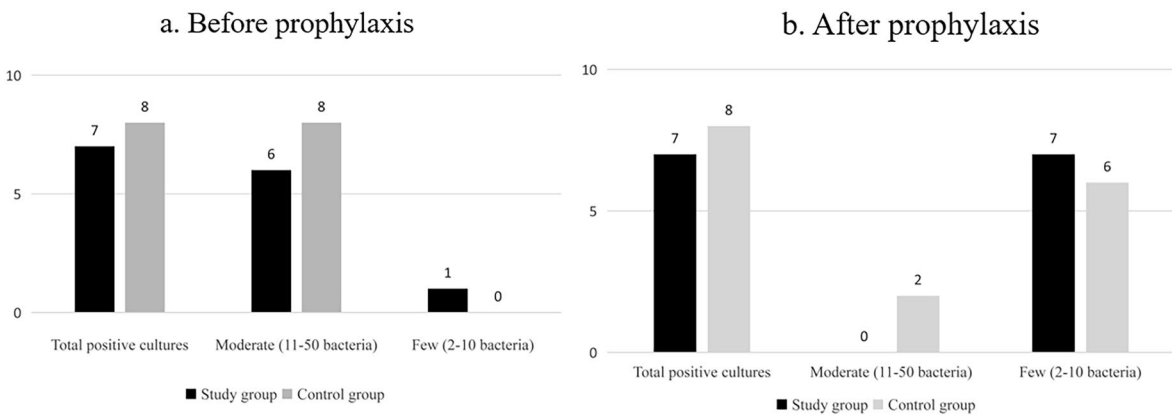


Fig. 3 Graphical representation of colony count as per CMPT criteria, a before prophylaxis, b after prophylaxis

Discussion

Postoperative endophthalmitis, despite an incidence of only 0.04 to 0.44% can be devastating to both the patient and surgeon [12]. Some patients may develop poor visual outcome and sequelae despite extensive medical care and hospitalization [12]. In most cases the causative bacteria for ocular infection originate from the conjunctival sac, making preoperative conjunctival disinfection essential for prevention of endophthalmitis [10].

In the present study, we found that preoperative prophylaxis with 5% PI alone showed similar and significant reduction in positive conjunctival cultures when compared to its combination with 0.5% moxifloxacin eye drops. Both PI alone and PI with moxifloxacin combination also showed similar reduction in bacterial colony count from moderate to few after prophylactic treatment. Coagulase negative *S. epidermidis* was the most commonly observed isolate and Enterobacteriaceae was least commonly observed. None of the patients had any adverse effects such as ocular discomfort or irritation following instillation of PI 5% eye drops for a contact time of 3 min.

Conjunctival flora has been identified as the most important source of infection for postoperative endophthalmitis. Coagulase negative Staph. epidermidis, the most frequently encountered conjunctival commensal, is also the commonest isolate from culture positive endophthalmitis cases. Streptococcus on the other hand, which constitutes <3% of the commensals observed in various studies, is encountered much more frequently in culture positive endophthalmitis, more so in diabetics [13–16].

With conjunctival flora being the most important source of infection for postoperative endophthalmitis, the use of preoperative antibiotics is almost universal. Numerous studies have established the superiority of topical antibiotic regimes over systemic antibiotics [17, 18]. However, there is wide variation in the antibiotic regimen followed in different centres [19, 20]. Chloramphenicol, sulfonamides, polymyxins, bacitracin, aminoglycosides and early-generation fluoroquinolones have been found to be less effective than the advanced-generation fluoroquinolones. This has been attributed to limited spectrum of activity and the development of pathogen resistance [21].

Alarming, studies have reported bacterial isolates from the conjunctival sac exhibiting resistance

to newer generation fluoroquinolones. Bertino et al. observed that above 65% of *S. epidermidis* isolates that were resistant to ciprofloxacin also demonstrated in vitro cross-resistance to gatifloxacin and moxifloxacin. In 2009, a study of endophthalmitis in Mexico showed that more than 20% of them were resistant to gatifloxacin, moxifloxacin and balofloxacin [22]. Multidrug resistant strains are being increasingly observed among staphylococcus aureus and *S. epidermidis* that have traditionally been considered ocular commensals. [7, 23] Therefore, there is a need to search for a newer agent with a broad spectrum of antimicrobial action and low risk of antibiotic resistance.

When compared to antibiotics, PI has a broad antimicrobial spectrum with activity against gram-positive organisms like *Staphylococcus* spp, *Streptococcus* spp and gram-negative bacteria, including antibiotic sensitive and resistant strains, fungi, and protozoa [24]. Moreover, bacterial resistance has not been observed so far with it [23]. In addition, minimal toxicity and low cost make PI an ideal antiseptic agent to reduce the bacterial load of the conjunctival sac and periocular adnexa [25]. Depending on the type of application and ophthalmic use, the concentration of PI and contact time varies [9]. PI 5% with a bactericidal rate of 96.7% and significant reduction in bacterial colonies, is most widely accepted for ocular use [9]. Lower concentrations of 0.02%, 0.2% and 1% of PI have been successfully used as ocular surface irrigating solutions. 10% PI while found to be marginally more bactericidal than 5% PI, is not widely used due to increased complaints of ocular irritation [26]. A contact time of 3 min has been found to be adequately bactericidal without significant increase in ocular surface toxicity [10].

Apt L et al. compared 5% PI with a combination antibiotics (neomycin, polymyxin B, and gramicidin). After 24 h of surgery, it was observed that PI significantly reduced the colony forming units, when compared to the antibiotic combination [27]. Moss et al. compared topical application of 10% PI alone and 10% PI with topical gatifloxacin among patients undergoing intravitreal injections. They observed similar reduction in conjunctival flora in both the groups with 30 s contact time [28]. PI, in different studies, has been found to have bactericidal effect similar to topical antibiotics [9]. A retrospective chart review done to correlate the incidence of postoperative endophthalmitis over a 20-year

period showed reduction in rate of postoperative endophthalmitis from 0.29 to 0.06% with the increase in the copious use of PI preoperatively [29].

Approximately 92.50% cataract surgeries performed in India each year are through centrally sponsored outreach camps [30]. Large volume surgeries in resource scarce nations require endophthalmitis prophylaxis to be economical with minimal risk of development of resistance. The widespread use of antibiotic agents has led to a notorious increase in the resistance, making it necessary to find newer more effective alternatives. Newer generation antibiotics appear to run the risk of cross-resistance with the added disadvantage of being expensive.

In the present study, the two eyes of a single patient were allocated as the study and control groups. By doing so, we were able to compare the effect of both PI and moxifloxacin on the same type of ocular flora and thereby get a more accurate comparison. In this study, the colony count was assessed for only the post prophylaxis culture positive samples and not for all culture samples. This was a limitation of the study.

We conclude that PI 5% alone in the conjunctival sac with a contact time of 3 min is effective in reducing the conjunctival bacterial load. This has been found to be as effective as a combination of 5% PI and 0.5% moxifloxacin in reducing conjunctival flora. PI 5% alone can therefore be considered for preoperative endophthalmitis prophylaxis.

Author contributions Substantial contributions to conception and design, along with drafting the article or revising it critically for important intellectual content was done by ARR, SN and SSS. Acquisition of data along with analysis and interpretation of data was done by SSS, JME and PR. All authors reviewed the manuscript and gave the final approval of the version to be published.

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Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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