

Safety and efficacy of intracameral moxifloxacin injection for prophylaxis of endophthalmitis after phacoemulsification

Segurança e eficácia na injeção intracameral de moxifloxacino para profilaxia da endoftalmite após a facoemulsificação

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ABSTRACT

Purpose: To evaluate the safety and efficacy of 0.05 mL intracameral injection of moxifloxacin in patients who underwent phacoemulsification and intraocular lens (IOL) implant.

Methods: Retrospective study comprising patients who underwent phacoemulsification and IOL implant between January 2009 and December 2013. Patients were divided into two groups. Group A followed standard endophthalmitis prevention protocol and group B followed the same protocol plus intracameral injection of 0.05 mL of moxifloxacin hydrochloride at 5.45 mg/mL, immediately after IOL implant.

Results: Medical records from 7,195 eyes of 3,751 patients (median age: 67.8 ± 8.96, range: 48-83 years, 53.8% female) were evaluated. Group A included 3,515 eyes of 1,838 patients and group B included 3,680 eyes of 1,913 patients. The incidence of endophthalmitis in group A was 0.22% (8:3,515 eyes) and in group B was 0.03% (1:3,680 eyes, $p=0.0198$, Fischer's exact test). No toxicity or inflammation related to the use of moxifloxacin was observed.

Conclusions: There was a 7.3-fold lower ratio of endophthalmitis in the group that received moxifloxacin intracameral injection. This study provides further evidence that moxifloxacin is an effective intracameral prophylactic antibiotic.

Keywords: Endophthalmitis; Cataract; Phacoemulsification; Anti-bacterial agents; Injections; Antibiotic prophylaxis

RESUMO

Objetivo: Avaliar a segurança e a eficácia da injeção intracameral de 0,05 mL de moxifloxacina em pacientes que realizaram facoemulsificação e implante de lente intraocular.

Métodos: Estudo retrospectivo envolvendo pacientes submetidos a facoemulsificação e implante de lente intraocular entre janeiro de 2009 a dezembro de 2013. Os pacientes foram divididos em dois grupos. O grupo A seguiu o protocolo padrão de prevenção de endoftalmite e o grupo B seguiu o mesmo protocolo associado à injeção intracameral de 0,05 mL de cloridrato de moxifloxacino a 5,45 mg/mL, imediatamente após o implante de lentes intra-oculares (LIO).

Resultados: Foram avaliados registros clínicos de 7.195 olhos de 3.751 pacientes (mediana de idade de 67,8 ± 8,96, faixa de 48-83 anos, 53,8% de mulheres). O grupo A incluiu 3.515 olhos de 1.838 pacientes e o grupo B incluiu 3.680 olhos de 1.913 pacientes. A incidência de endoftalmite no grupo A foi de 0,22% (8:3.515 olhos) e no grupo B de 0,03% (1:3.680 olhos, $p=0,0198$, teste exato de Fischer). Não foi observada toxicidade ou inflamação relacionada com o uso de moxifloxacino intracameral.

Conclusões: Houve uma proporção 7,3 vezes menor de endoftalmite no grupo que recebeu injeção de moxifloxacino. Este estudo fornece mais evidências que o moxifloxacino intracameral é um antibiótico profilático intracameral eficaz.

Descritores: Endoftalmite; Catarata; Facoemulsificação; Antibacterianos; Injeções; Antibioticoprofilaxia

INTRODUCTION

Although rare, postoperative endophthalmitis is one of the most feared complications of cataract surgery. It may significantly compromise visual function and even the anatomical integrity of the eye. At the beginning of the twentieth century, before the development of antibiotics, the incidence of postoperative ocular infection was approximately 1%-5%⁽¹⁾; nowadays, the percentage of endophthalmitis after intraocular surgery has been lowered to 0.04% to 0.2%⁽²⁻⁴⁾. Despite the significant reduction in recent years, considering the millions of people who undergo cataract surgery each year, postoperative endophthalmitis still poses a significant public health issue, which has been addressed in several studies^(5,6). The preoperative use of povidone-iodine is an effective method to prevent endophthalmitis⁽⁵⁾. However, administration of systemic or periocular injections

of antibiotics is controversial and there is insufficient evidence to support its use⁽⁶⁾.

In the last decade, several studies have suggested that the intracameral (IC) use of antibiotics may reduce endophthalmitis risk^(7,8). The administration of antibiotics in the anterior chamber after surgery is theoretically the most direct method for prophylaxis. The dissemination of this practice started after a multicenter, prospective, randomized controlled trial performed by the European Society of Cataract and Refractive Surgeons (ESCRS) showed a 4.92 increase in the risk of total postoperative endophthalmitis in the group that did not receive cefuroxime in the anterior chamber⁽⁷⁾.

Since then, studies have tested the safety and efficacy of IC injection of other antibiotics, such as moxifloxacin⁽⁹⁻¹¹⁾. This antibiotic has been widely used in the anterior segment and, due to the lack

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of preservatives in its commercial eye drop formula, it has been used intracamerally with no reports of ocular toxicity⁽¹²⁾. The choice of moxifloxacin instead of cefuroxime may be based on the rapid medication turnover after surgery, lending favor to moxifloxacin (which is concentration-dependent) over cefuroxime (which is time-dependent)⁽¹³⁾.

Considering the reports of reduction in endophthalmitis with IC antibiotic injection and the absence of evidence or consensus as to which antibiotic is superior in preventing endophthalmitis⁽¹⁴⁾, our service decided to adopt IC injection of commercially-available moxifloxacin at the end of phacoemulsification starting June 06, 2011. In view of the perceivable reduction in endophthalmitis after the adoption of IC antibiotic prophylaxis and the absence of similar studies in Brazil, we decided to retrospectively evaluate our data, which is the focus of the current study.

METHODS

This is a retrospective clinical registry-based study. Its protocol was conducted according to the principles described in the declaration of Helsinki. All data were collected, manipulated, and analyzed without personal identification of patients.

The study population comprised all patients ≥ 18 years old who underwent phacoemulsification with intraocular implant between January 2009 and December 2013 at a private ophthalmologic hospital in Brasilia, Brazil. Patients were divided into two groups: group A received one drop of 5% povidone-iodine (Ophthalmos, São Paulo, Brazil) 15 minutes before surgery and postoperative antibiotics eye drops 4 times per day for 10 days; group B received the same prophylaxis for endophthalmitis as group A, plus an IC injection of 0.05 mL of commercially available moxifloxacin hydrochloride at 5.45 mg/mL (Vigamox®, Alcon Laboratories, Inc., Fort Worth, TX) immediately after IOL implant.

All patients had scheduled consultations at one, seven, and thirty days after surgery, and were instructed to return to the clinic in case of alarming signals between follow-up evaluations.

Postoperative endophthalmitis was defined as inflammation in the anterior chamber or vitreous cavity occurring within 6 weeks after surgery that responded to intravitreal antibiotics or presented positive cultures. The data was analyzed by descriptive statistics and Fisher's exact test to compare groups, statistical significance level ($p < 0.05$).

RESULTS

A total of 7,195 eyes of 3,751 patients were retrospectively evaluated (median age: 67.8 ± 8.96 years, range: 48-83 years, 53.8% female). Group A included 3,515 eyes of 1,838 patients (median age: 68.1 ± 8.92 years, range: 52-83 years, 54.4% female), and group B included 3,680 eyes of 1,913 patients (median age: 67.7 ± 9.03 years, range: 48-82 years, 53.5% female), as shown in table 1.

The incidence of endophthalmitis in group A was 0.22% (8:3,515 eyes) and in group B was 0.03% (1:3,680 eyes, $p = 0.0198$, Fisher's exact test).

Table 1. Patient sex and age profile (n=3,751)

Parameter	Group A	Group B	Total
Age (years)	68.1 ± 8.92	67.7 ± 9.03	67.8 ± 8.96
Female (%)	54.4	53.5	53.8
Male (%)	45.6	46.6	46.2

DISCUSSION

Gram-positive bacteria are the most common cause of postoperative endophthalmitis in the West⁽³⁾. However, the prevalence of certain causative agents may vary according to geographic region. A study conducted in Brazil pointed to coagulase negative agents such as *Staphylococci* and *Streptococcus viridans* as the primary pathogens in a university-based hospital; however, the wide spectrum of detected microorganisms also includes gram-negative bacteria such as *Pseudomonas aeruginosa* and *Haemophilus sp.* As such, prophylactic antibiotics are usually chosen based on their low toxicity and large spectrum.

Despite many studies pointing to a reduction in endophthalmitis cases after IC administration following cataract surgery, many surgeons justify not introducing this practice into their routine due to risks associated with the procedure, such as dilution errors, contamination, and drug toxicity⁽¹¹⁾. Their concerns are justifiable; due to the absence of a commercial formula, IC antibiotics must be prepared in a sterile environment and diluted by the surgeon. Dilution errors with cefuroxime have been documented as a possible cause for postoperative toxic anterior segment syndrome and even more severe adverse effects such as macular infarction⁽¹⁵⁾. Toxicity may result not only from the drug itself but also from preservatives or abnormal osmolality or pH⁽³⁾.

Moxifloxacin (Vigamox®, Alcon Laboratories, Inc., Fort Worth, TX) is preservative-free and isotonic, with a pH of 6.8 and an osmolality of approximately 290 mOsm/kg⁽¹³⁾ and has been used as an IC prophylaxis^(11,12,14). These values are very similar to those of the aqueous humor (pH=7.4, osmolality=305 mOsm/kg)⁽¹³⁾, and may help to explain why the use of IC Vigamox has not been associated with ocular toxicity at full strength or with a 50:50 dilution in balanced salt solutions.

Moxifloxacin is a fourth-generation quinolone that exerts its antibacterial effect by preventing bacterial DNA from unwinding and duplicating, mainly acting on DNA gyrases and topoisomerases. Moxifloxacin provides an improved activity against gram-positive bacteria and atypical pathogens than did earlier fluoroquinolone agents such as levofloxacin, ofloxacin, and ciprofloxacin, while maintaining good activity against gram-negative bacteria. Furthermore, it presents high potency, better tissue penetration, and delayed antibiotic resistance^(10,16).

Different methods of IC use for commercially available moxifloxacin have been proposed, such as flushing the anterior chamber with 2 to 3 mL of diluted solution⁽¹¹⁾ or the use of a relatively small volume (0.05 to 0.2 mL) of highly concentrated solution (undiluted or diluted up to 10-fold) at the end of surgery⁽¹³⁾. Considering that this antibiotic has not demonstrated toxicity to endothelial cells in concentrations as high as 500 $\mu\text{g/mL}$ ⁽¹⁰⁾, and given that its mechanism of action is concentration-dependent, we preferred to perform a 0.05 mL IC injection of undiluted moxifloxacin.

We found a 7.3-fold lower ratio of endophthalmitis after cataract surgery in the group that received moxifloxacin during surgery. Although this decrease is higher than other comparable studies, it may be explained by a slightly higher rate of endophthalmitis prior to the adoption of IC injection. A previous study demonstrated that the IC use of commercially available moxifloxacin eye drops led to an endophthalmitis rate of 1:6,265, which is a 3-fold decrease compared with the group that did not receive the antibiotic⁽¹¹⁾. In a recently published study from India, a 4-fold reduction in endophthalmitis was observed in patients that underwent small-incision cataract surgery and received IC injection of commercially available moxifloxacin eye drops after IOL implantation⁽¹⁴⁾.

Despite these favorable results, some researchers believe that other factors may explain the decreased rate of endophthalmitis over time, including increased asepsis and antisepsis concerns, improvement in surgical time and techniques, equipment evolution, changes in post-operative routines, or other unknown factors⁽¹⁷⁾. Considering

this, the adoption of IC antibiotics may be only one of many measures that may reduce infection. As such, all possible precautions should be taken to reduce the possibility of endophthalmitis.

Another claim is that the low incidence of endophthalmitis does not justify antibiotic prophylaxis. Studies performed in the last decade have demonstrated rates of endophthalmitis as low as 0.05% without the introduction of intracameral antibiotics^(18,19). With such a low incidence, even if IC antibiotics reduced the risk 5-fold, it would be necessary to treat 2,500 patients to prevent one event of endophthalmitis; this raises concerns about costs.

Our study did not account for the costs involved in the prophylactic procedure or the treatment of endophthalmitis; nevertheless, previous studies have demonstrated prophylaxis with IC injections to be cost effective^(8,14).

Limitations of this study include its retrospective design as well as the lack of microbiological confirmation of endophthalmitis. To our knowledge, this is the first study in Brazil to evaluate infection rates and the incidence of complications after IC injection of commercially available moxifloxacin eye drop administration.

Although these results align with previous literature and may therefore be considered a clear argument for the routine use of moxifloxacin in cataract surgery, it is important to emphasize the fact that in Brazil, as in many other countries, there are no commercially available IC antibiotic solutions. The decision regarding use of self-prepared or commercially available eye drops for IC injection is left to the surgeon's discretion and is considered off-label.

We believe that approved antibiotic preparations for IC injection should increase the safety of cataract surgery by reducing the risk of endophthalmitis and dilution toxicity.

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