LETTER TO THE EDITOR

Pharmacokinetics of subconjunctival injection of moxifloxacin in humans

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Dear Editor,

Postoperative endophthalmitis remains one of the most devastating complications of cataract surgery. Eye drops are currently the standard means of preventing infection. However, as the elderly comprise a large number of patients undergoing cataract surgery, administration of eye drops and compliance with postoperative instructions is difficult. Furthermore, patients unaccustomed to eye drops are exposed to risks that exceed possible side-effects from drugs.

Since the release of the European Society of Cataract and Refractive Surgeons multicenter study report on intracameral cefuroxime, a number of reports about the efficacy and safety of intracameral moxifloxacin have been published. However, many practitioners have reservations about the safety of these drugs, and hence, they are not widely used in practice [1].

In contrast, subconjunctival injection of antibiotics has a long history of widespread international use and is performed by 16 % of American [1] and 77 % of British [2] practitioners. However, there are no reports available on the effects and pharmacokinetics of subconjunctival injection of moxifloxacin.

After obtaining written informed consent, we administered subconjunctival injections of moxifloxacin (0.2 cc, 5,000 μg/ml) to patient groups varying according to the time of injection with at 1, 3, 5, and 6 h prior to cataract surgeries (n=5–6 in each group). Upon commencement of surgery, a 29-gauge needle was used to extract 0.1 ml of the anterior chamber fluid, and densitometry was performed using high-performance liquid chromatography.

The following average concentrations were obtained according to the time of subconjunctival injection: 1 h, 3.03 μg/ml; 3 h, 1.91 μg/ml; 5 h, 0.53 μg/ml; and 6 h, 0.30 μg/ml. Therefore, we hypothesize that minimum inhibitory concentration to inhibit the growth of 90 % organisms of moxifloxacin for Enterococcus faecalis (0.5 μg/ml) can be maintained for approximately 5 h after subconjunctival injection (Fig. 1).

While moxifloxacin has a high maximum aqueous concentration (AQCmax), it cannot be ensured that one drop of ophthalmic solution is sufficient to be retained in the conjunctival sac and maintain effective intracameral concentrations under postoperative conditions in which edema, inflammation, hemorrhage, and lacrimation predominate. For frequent eye drop usage, the solution concentration is set to an amount of 1.8–2.3 μg/ml [3]. Subconjunctival injection of moxifloxacin resulted in slightly higher concentrations than those obtained from frequent usage of eye drops.

Despite multiple peer-reviewed reports regarding the safety and efficacy of intracameral injections, many practitioners have reservations about its use [1] because of risk of tissue injury, contamination, and incorrect administration [4].

In contrast, because subconjunctival injection involves administration of undiluted solutions, risk of incorrect administration or contamination during dilution is low.

Reports on the reduced risk of infection by subconjunctival injection of gentamicin and cefuroxime [5, 6] and those on the pharmacokinetics of these drugs [7, 8] have been available for a long time.

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However, *E. faecalis* shows no sensitivity to cefuroxime and low sensitivity to gentamicin. In addition, there are reports of tissue injury with gentamicin [9] and anaphylaxis with cefuroxime [10].

Considering all these facts, we suggest that moxifloxacin is the most appropriate drug for subconjunctival injection because of its broad antibacterial spectrum, high AQCMAX, and absence of reports regarding serious tissue injury or allergies.

While subconjunctival injection is inferior to intracameral administration from the perspective of drug concentration or antimicrobial activity, it meets with little psychological resistance from practitioners because of its simple technique and preparation. On the other hand, the surgeon should consider that there is a growing evidence about the efficacy and safety of using intracameral injections of antibiotics for preventing postoperative endophthalmitis.

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References


Fig. 1 Minimum inhibitory concentration to inhibit the growth of 90 % organisms of moxifloxacin for *Enterococcus faecalis* (0.5 μg/ml) can be maintained for approximately 5 h after subconjunctival injection of moxifloxacin (average + standard deviation)