Intracameral Pilocarpine in Topical Phacoemulsification†

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Abstract

Purpose : To evaluate the efficacy and corneal toxicity of intracameral pilocarpine.

Method : A randomized, control trial using contralateral eye as control was designed to evaluate the effect of intracameral pilocarpine during phacoemulsification in 30 patients. 0.13 mg/ml pilocarpine in BSS was used as an irrigating solution to remove viscoelastic agents at the end of the operation while BSS was used in the control group. The outcome measurements composed of intraoperative pre and post irrigation pupil diameter, pre and post operative endothelial cell count and corneal thickness.

Setting : Priests Hospital.

Results : The pre-irrigation pupil size in the pilocarpine group and the control group was 7.62 ± 0.75 mm and 7.60 ± 0.77 mm respectively. The post-irrigation pupil size in the pilocarpine group and the control group was 5.40 ± 0.79 mm and 7.18 ± 0.79 mm. There were no statistically differences in pre and post-operative endothelial cell density, central corneal thickness, and the average corneal thickness between the pilocarpine group and the control group during six months follow-up.

Conclusion : Intracameral pilocarpine in a low concentration (0.13 mg/ml) effectively constricts the pupil without significant changes of corneal endothelium compared to the control group.

Key word : Pilocarpine, Phacoemulsification

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Miotic agents are advocated in cataract and glaucoma surgery to produce pupillary constriction to prevent iris incarceration in the operative wound, iris capture by intraocular lenses, dislocation of implanted intraocular lenses and postoperative peripheral anterior synechiae[1]. The commercial preparation of miotic agents such as acetylcholine and carbachol are expensive and unavailable in rural areas. The relative toxicity of these agents have been noted[2,3]. Pilocarpine eye drop is available in any operating room. Although pilocarpine is commonly used by some surgeons to induce pupillary constriction during intraocular surgery, its efficacy and toxicity in humans has not been documented. This study was designed to study the effect of intracameral pilocarpine on the human corneal endothelium.

SUBJECTS AND METHOD

Thirty patients with bilateral cataract were enrolled in the study. Phacoemulsification was done in the right eye first and then in the left eye two days later. One eye of each patient was randomly assigned to the intraocular pilocarpine group and the other eye was assigned to the control group.

Phacoemulsification was performed by one surgeon (SW.) under topical anesthesia using the same technique. One per cent Mydriacyl eye drop was used to dilate the pupil preoperatively. Each patient was anesthetized with 0.5 per cent tetracaine hydrochloride eye drop. A temporal clear corneal incision was used to enter the anterior chamber and viscoelastic (Viscoat) was injected. After a continuous capsulorrhexis and hydrodissection, the nucleus was removed by phacoemulsification using the chopping technique. The residual cortex was removed with irrigation and aspiration. Viscoat was instilled into the chamber, the wound was enlarged to 5 mm, and a one-piece PMMA IOL was inserted. The remaining Viscoat was removed by manual irrigation using a 10 ml syringe connected to a 26 gauge cannula. The irrigation fluid was 10 ml BSS in the control group, and 10 ml BSS plus two drops of 2 per cent pilocarpine eye drop (2% pilocarpine hydrochloride, 0.01% benzalkonium chloride and 0.5% methylcellulose) in the pilocarpine group. Horizontal pupil diameter was measured before and immediately after irrigation using a sterile ruler under the operating microscope. The wound was checked for leakage and no suture was needed. The same pre and post operative medication was used in all patients.

All the patients were asked to report any discomfort within 6 hours postoperatively. The endothelial cell count was performed using a non-contact specular microscope (Konan ROBO-CA) preoperatively, 1 week, 2 weeks, 2 months and 6 months postoperatively. Ultrasonic pachymetry (CompuScan ^{TM}P) to measure central corneal thickness and 8 midperipheral locations were done prior to the operation and 2 weeks, 8 weeks, and 6 months postoperatively. The "average corneal thickness" was calculated from the central and 8 midperipheral corneal thickness value.

Statistical analysis

The descriptive statistics, *t*-test and ANOVA were used to analyse the results. The analysis was performed using the SPSS/PC statistical program.

RESULTS

The patients were between 46 and 83 years of age. The mean age was 70.5 years with a standard deviation of 7.30 years. All operations were uneventful.

The mean pre and post irrigation pupil sizes of both the pilocarpine and the control group are shown in Table 1. There was no statistically significant difference of the pre-irrigation between the two groups. The post irrigation pupil size in the pilocarpine group decreased significantly compared to the control group. The preoperative and postoperative endothelial cell density of the two groups is shown in Table 2. Both groups had statistically significant endothelial cell loss after phacoemulsification, but there was no demonstrable statistically significant difference

Table 1. Pre and post-irrigation pupil size in pilocarpine and control group.*

	Pilocarpine group	Control group	p value
Pre-irrigation	7.62 ± 0.75	7.60 ± 0.77	0.895
Post-irrigation	5.40 ± 0.79	7.18 ± 0.79	0.000

* The pre and post-irrigation pupil size is presented as mean ± standard deviation.

between the two groups during the same pre and postoperative period. Eight weeks after surgery, the cell loss was 7.45 per cent in the pilocarpine group and 7.26 per cent in the control group. The differences in postoperative cell loss between two groups were not statistically significant.

The preoperative and postoperative central corneal thickness and average corneal thickness are shown in Table 3 and 4. There was no statistical significance between the two groups in pre and postoperative central corneal thickness and average corneal thickness.

The patients reported postoperative discomfort in 7 of 30 eyes in the pilocarpine group and 8 of 30 eyes of the control group, which was not statistically significant. No endophthalmitis occurred in this study.

DISCUSSION

Pilocarpine is a direct-acting parasympathomimetic agent. The ocular effects of pilocarpine are contraction of the iris sphincter, producing miosis and contraction of the ciliary muscle, increasing the outflow of aqueous humor. Pilocarpine toxicity to the corneal endothelium can be demonstrated both functionally and by electron microscopy. Pilocarpine causes steady increase in corneal thickness. The severity and onset are dose related. Based on an *in vitro* perfusion model of the rabbit corneal endothelium, Coles[4] has shown that the concentration of pilocarpine above 2.5 mg/ml is toxic to the corneal endothelium. The highest pilocarpine concentration in the aqueous is 0.15 mg/ml with topically applied 0.1 ml of 8 per cent pilocarpine[5]. In this study, the concentration of pilocarpine used to irrigate the anterior chamber was 0.13 mg/ml, which is about 20 times lower than the concentration found toxic to the corneal endothelium.

The proliferative capacity of corneal endothelium is limited. After surgical trauma, the undamaged endothelial cells undergo morphologic changes to cover the defect, resulting in a decrease in cell density (cell count). The corneal endo-

Table 2. Pre- and post-operative mean endothelial cell density (cells/mm^2).*

	Preoperative (n=30)	1 week (n=29)	2 weeks (n=29)	8 weeks (n=21)	6 months (n=4)
Pilocarpine group	2336 ± 244	2196 ± 276 (-5.98%)	2196 ± 289 (-7.58%)	2162 ± 295 (-7.45%)	2282 ± 100 (-2.29%)
Control group	2351 ± 219	2232 ± 255 (-5.06%)	2219 ± 298 (-5.61%)	2182 ± 252 (-7.26%)	2263 ± 115 (-3.79%)
p-value	0.498	0.197	0.066	0.433	0.330

* The endothelial cell density is presented in mean ± standard deviation. The numbers in parentheses are the percentage of cell reduction compared to the preoperative cell density.

Table 3. Preoperative and postoperative central corneal thickness.*

	Pre-operative (n=30)	2 weeks (n=28)	8 weeks (n=23)	6 months (n=3)
Pilocarpine group	524 ± 37	530 ± 37 (+1.15%)	515 ± 36 (-1.74%)	509 ± 35 (-2.99%)
Control group	525 ± 38	535 ± 41 (+1.89%)	516 ± 33 (-1.67%)	507 ± 35 (-3.50%)
p-value	0.875	0.417	0.885	0.667

* The central corneal thickness in micron is presented in mean ± standard deviation. The numbers in parentheses are the percentage of thickness change compared to the preoperative value.

Table 4. Pre-operative and post-operative average central corneal thickness.*

	Pre-operative (n=30)	2 weeks (n=27)	8 weeks (n=23)	6 months (n=3)
Pilocarpine group	584 ± 47	596 ± 52 (+2.05%)	575 ± 36 (-1.54%)	561 ± 35 (-3.94%)
Control group	584 ± 43	593 ± 44 (+1.61%)	570 ± 36 (-2.38%)	579 ± 32 (-0.91%)
p-value	1.000	0.704	0.503	0.100

* The average corneal thickness derived from one central corneal measurement and eight midperipheral corneal thickness measurement. The average corneal thickness in micron is presented in mean ± standard deviation. The numbers in parentheses are the percentage of thickness change compared to the preoperative value.

thelium maintains the cornea in a deturgescent state. If the endothelial cell destruction exceeds the ability of the remaining endothelial cells to recover, corneal edema occurs. An increase in stromal thickness indicates a deterioration of endothelial cell ability to deturgesce the cornea. Cell count is used to detect morphologic alterations in the endothelium. Stromal thickness is an index of endothelial cell function[6].

Several studies have shown that endothelial cell loss following phacoemulsification ranged from 5.9 to 26 per cent[7-9]. In this study, the endothelial cell loss after phacoemulsification of 7.45 per cent in the pilocarpine group and 7.26 per cent in the control group compared favorably with 6.5 to 8.8 per cent reported in other series that used Viscoat as a viscoelastic substance[7-9]. There was no statistical significance between the two groups in endothelial cell density at any postoperative period. This suggests that intracameral pilocarpine does not effect the loss of the endothelial cell. The slightly increase in endothelial cell count at 6 months postoperatively may be due to mitosis and cell division but the number of patients is too few to support this hypothesis[10].

In both the pilocarpine group and the control group, there was no significant difference between pre and post operative corneal thickness. This implies that endothelial cell loss following phacoemulsification does not effect the function of the remaining endothelial cells. There was no significant difference in the corneal thickness between the two groups in this study. This suggests that intracameral pilocarpine does not induce any functional toxicity to the human corneal endothelium. The same result of the analysis is reached when we calculate by central corneal thickness or the average of the central and eight midperipheral corneal thickness.

Benzalkonium chloride in the concentration used in eye drops caused irreversible destruction of rabbit corneal endothelial function. The highest safe concentration of 0.001 per cent for intraocular use has been reported[11]. In this study the concentration of benzalkonium chloride in the irrigating solution used in the pilocarpine group was 0.000066 per cent.

Although there was no endophthalmitis reported in this study, we recommend to use of a new bottle of pilocarpine eye drops in every case. The suitable sterilization for pilocarpine is autoclave.

In our study, intracameral pilocarpine effectively produced miosis and did not cause corneal endothelial cell loss or any functional toxicity. Pilocarpine eye drops should be diluted with BSS to get the proper concentration before intracameral use.

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ผลการใช้พิโลคาร์พีนในช่องด้านหน้าของตาในการผ่าตัดต้อกระจกด้วยเครื่องคลื่นเสียงความถี่สูง

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บทนำ : ศึกษาฤทธิ์ต่อม่านตาและผลกระทบต่อกระจกตาของ pilocarpine eye dropที่ถูกฉีดในช่องด้านหน้าของตาขณะการผ่าตัดต้อกระจกโดยเปรียบเทียบกับตาอีกข้างของผู้ป่วยเองที่ได้รับการผ่าตัดแบบเดียวกัน

วัตถุและวิธีการ : ได้ทำการศึกษาขนาดของรูม่านตา จำนวน endothelium cell และความหนาของกระจกตาก่อนและหลังผ่าตัดของผู้ป่วยจำนวน 30 คนที่ได้รับการผ่าตัดต้อกระจกโดยจักษุแพทย์คนเดียวและใช้วิธีการผ่าตัดแบบเดียวกันโดยตาข้างหนึ่งได้รับ 0.13 mg/ml pilocarpine ใน BSS เป็น irrigating solution ส่วนตาอีกข้างได้รับ BSS อย่างเดียวเป็น control group

ผลการศึกษา : ขนาดของรูม่านตาก่อน irrigation ใน pilocarpine group และ control group เป็น 7.62 ± 0.75 มม. and 7.60 ± 0.77 มม. ตามลำดับ ขนาดของรูม่านตาหลัง irrigation ในกลุ่ม pilocarpine group และ control group เป็น 5.40 ± 0.79 มม. and 7.18 ± 0.79 มม. และพบว่าไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติของจำนวน endothelium cell ความหนาของกระจกตาตรงกลาง และ ความหนาของกระจกตาโดยเฉลี่ยระหว่าง pilocarpine group และ control group ในการติดตาม 6 เดือน

วิจารณ์ : การฉีด pilocarpine eye dropในขนาดความเข้มข้นต่ำ (0.13 mg/ml) ในช่องด้านหน้าของตาสามารถทำให้รูม่านตาหดได้อย่างมีนัยสำคัญทางสถิติโดยไม่มีผลเสียต่อ endothelium cell ของกระจกตา

คำสำคัญ : พิโลคาร์พีน, Phacoemulsification

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