Effects of Intracameral Triamcinolone and Gentamicin Injections Following Cataract Surgery

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Objective: *Evaluate the anti-inflammatory efficacy of intracameral triamcinolone acetonide and gentamicin injections compared with topical dexamethasone and tobramycin combination eye drops in cataract surgery patients.*
Material and Method: *The present prospective study enrolled 60 patients scheduled to receive phacoemulsification surgery. After surgery, patients were randomized to receive either single intracameral injections of triamcinolone acetonide and gentamicin followed by topical tobramycin eye drops four times daily for one week (IC TA group, n = 30), or topical dexamethasone-tobramycin combination eyedrops four times daily until no inflammation was seen (Topical group, n = 30). Postoperative evaluations included grading of anterior chamber cells, log MAR best-corrected visual acuity (BCVA), intraocular pressure (IOP) and adverse effects.*
Results: *There was no significant difference between the treatment groups in anterior chamber cells at one day and one week after surgery (p = 0.50 and 0.328, respectively). However, the anterior chamber cells were significantly less in the IC TA group than in the Topical group, one month postoperatively (p = 0.006). No significant between-group difference in mean BCVA or IOP was noted at any time point (p > 0.05). No adverse effects or endophthalmitis were observed.*
Conclusion: *Intracameral injections of triamcinolone acetonide and gentamicin appear to be a promising treatment option for the control of post-operative inflammation following cataract surgery.*

Keywords: *Anti-inflammatory agents, Cataract extraction, Gentamicins, Injections, Phacoemulsification, Triamcinolone acetonide*

J Med Assoc Thai 2011; 94 (7): 819-25
Full text. e-Journal: *http://www.mat.or.th/journal*

Phacoemusification with intraocular lens (IOL) implantation is currently the most common ophthalmic surgical procedure because of the high incidence of cataract combined with surgical advances that make modern cataract surgery highly successful and easy to perform as an outpatient procedure. Nonetheless, postoperative inflammation is common and can lead to decreased visual outcomes if not properly controlled[1,2].

Corticosteroid therapy is widely used to control post-cataract surgery inflammation[3]. Although topical formulations are routinely effective and well tolerated, there can be patient compliance problems, especially in the elderly. Potential for corneal and ocular surface toxicity increases with frequent and prolonged application. Triamcinolone acetonide (TA) is a potent corticosteroid that has recently been reported to be safe and effective for controlling postsurgical inflammation when administered as a sub-tenon injection after uneventful phacoemulsification surgery[3,4]. Variable doses of TA injected into the anterior chamber have also been reported to adequately control postoperative inflammation after cataract surgery without serious complications[5-8]. In addition, intracameral TA injection has been shown to be effective in preventing postoperative fibrin formation after cataract surgery in patients with juvenile iridocyclitis[9].

Gentamicin is an aminoglycoside antibiotic that has a broad spectrum of activity against common ocular pathogens and a low rate of bacterial resistance (data from the annual report of antimicrobial susceptibility, Ramathibodi Hospital, 2006-2007). Because of its effectiveness, safety and availability, the prophylactic use of topical or subconjunctival gentamicin has become common in cataract surgery[8].

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Intraocular injection of gentamicin has also been shown to be effective in the prevention of posttraumatic and postoperative endophthalmitis[11-13]. Additionally, it appears that low doses of gentamicin (50-200 μg) can be injected into the anterior chamber without any damage to the cornea, lens or retina[13].

The present study evaluated intracameral TA and gentamicin injections compared with topical dexamethasone-tobramycin eye drops for the prophylaxis of postoperative inflammation following uncomplicated phacoemulsification surgery. To the best of the authors' knowledge, this is the first randomized study evaluating the effect of intracameral TA and gentamicin injections on post-cataract surgery inflammation.

Material and Method

This randomized, prospective study was conducted at the Department of Ophthalmology, Ramathibodi Hospital, Bangkok, Thailand. All patients consented to participation in the present study and the protocol was approved by the Research Ethics Committee of Mahidol University, Thailand.

Sixty patients with uncomplicated senile cataract, scheduled to undergo phacoemulsification and foldable intraocular lens implantation, were enrolled into the present study. Exclusion criteria included patients with glaucoma, a family history of glaucoma, a history of elevated intraocular pressure (IOP) in response to topical ophthalmic steroid treatment, a history of uveitis, previous eye trauma, previous intraocular surgery, diabetes mellitus, corneal endothelium disease, other anterior or posterior segment abnormalities, or cognitive impairment. Patients were also excluded if they were monocular, experienced complications during cataract surgery, or were using oral or topical anti-inflammatory agents.

All surgeries were performed by the same surgeon (P. Simaroj) and conducted under topical and peribulbar anesthesia (2% lidocaine with hyarulonidase). All operated eyes were dilated with topical tropicamide 1% and phenylephrine 2.5%. Standard phacoemulsification was performed through a 3-mm clear corneal incision using the stop-and-chop technique. The setting parameters of the Infiniti phacoemulsifier (Alcon, Fort Worth, Texas) were as follows: vacuum level 150-200 mmHg, flow rate 22-25 mL/min, ultrasound power 50-60% and bottle height 70 cm. After cortical removal, the anterior chamber was refilled with viscoelastic agent and a foldable acrylic IOL (SN60WF, Alcon) was implanted into the capsular bag. The viscoelastic agent was aspirated at the end of surgery.

At this point, all patients were randomized, using a block randomization, to receive either single intracameral injections of TA (2 mg in 0.1 ml) and gentamicin (0.2 mg in 0.1 ml) (IC TA group, n = 30) or postoperative topical 0.1% dexamethasone-0.3% tobramycin combination eye drops four times daily until the inflammation subsided (Topical group, n = 30). In the IC TA group, the solution was injected through a 27-gauge cannula pointed posteriorly to reduce the amount of medication contacting the corneal endothelium[5]. Patients in the IC TA group were also treated with topical tobramycin for one week.

Outcome measurement

All patients were scheduled for evaluation at one day, one week and one month postoperatively. A complete ophthalmic examination using slit-lamp biomicroscopy was performed at all follow-up visits. The primary outcome was the degree of intraocular inflammatory response at each visit as measured by anterior chamber cell grading using a slit-lamp biomicroscope. Intraocular pressure was also monitored at each visit using Goldmann applanation tonometry. Log MAR best-corrected visual acuity (BCVA) was measured at one month by a masked technician. Adverse events were recorded to assess the safety of the injection.

Anterior chamber cell measurements

At each follow-up visit, the investigator (P. Sinsawad) graded anterior chamber cells through an undilated pupil using a slit-lamp biomicroscope with a 1 mm beam-width and 3 mm beam-height. The following grading scale was used: grade 0 = no cells; grade trace = 1-5 cells; grade 1+ = 6-10 cells; grade 2+ = 11-20 cells; grade 3+ = 21-50 cells; and grade 4+ $\geq$ 50 cells.

Statistical analysis

The unpaired t-test was used when the distribution of the data was continuous and normal and the chi-square test or Fishers' exact test was used for the data that were nominal. A p-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 10.0 (SPSS, Chicago).

Results

Sixty patients were recruited into the trial between February and July 2007. All patients completed

the 4-week follow-up period and there were no intraoperative complications in any patients. Patient baseline characteristics are summarized in Table 1. There was no significant difference between the study groups in age, sex, preoperative visual acuity, level of cataract, baseline IOP and phacoemulsification time.

Fig. 1 shows the typical appearance of an eye on slit-lamp examination following intracameral injection of TA. The "snow-globe effect" due to the presence of TA crystals was noted[5]. The TA crystals disappeared from the anterior chamber within one week in seven eyes (23.33%) and within one month in the remaining cases. The presence of crystals did not interfere with the assessment of cells and flare.

The present study outcomes are summarized in Table 2. There was no statistically significant between-group difference in anterior chamber cells at one day and one week postoperatively (p = 0.5 and 0.328, respectively). However, anterior chamber cells were significantly less in the IC TA group compared to the Topical group at the one month visit (p = 0.006). Moreover, on the first postoperative day almost half of the patients (13/30) in the IC TA group had anterior chamber cells of grade 1+ compared with nine patients with grade 1+ and 14 with grade 2+ in the Topical group. At one week postoperatively, most of the patients in both groups had trace anterior chamber cells (19 cases in IC TA group and 16 cases in Topical group). At one month, 29 of 30 eyes (96.7%) in the IC TA group had no cells in the anterior chamber (grade 0) whereas nine of 30 eyes (30%) in the Topical group still had cells present in trace amounts (p = 0.006).

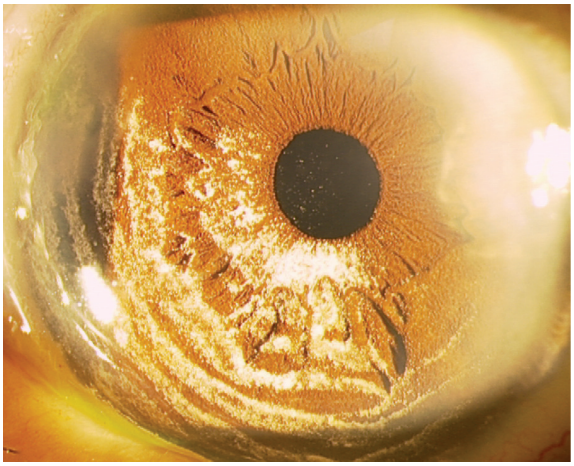

Fig. 1 Example of an eye 1 day after intracameral triamcinolone injection. The presence of crystals in the anterior chamber and iris is noted

There was no significant between-group difference in mean BCVA at either baseline (p = 0.950) or one month postoperatively (p = 0.213) (Table 2). Between baseline and one month postoperatively, mean logMAR BCVA improved from 0.88 to 0.28 in the IC TA group and from 0.88 to 0.23 in the Topical group. There was no statistically significant between-group difference in mean IOP throughout the study period (Table 2). IOP ranged from 8 to 18 mmHg in the IC TA group and from 8 to 20 mmHg in the Topical group. No patients in either group had an IOP greater than 20 mmHg at any time during the present study. Most of

Table 1. Baseline characteristics

Characteristic	IC TA group (n = 30)	Topical group (n = 30)	p-value
Sex			
Female: n (%)	18 (60%)	18 (60%)	
Age (years)			
Mean ± SD	66.77 ± 8.29	65.37 ± 7.97	0.41
Level of cataract			
NS2+	18 (60.0%)	19 (63.33%)	0.79
NS3+	12 (40.0%)	11 (39.67%)	
Ultrasound time (minutes)			
Mean ± SD	0.77 ± 0.78	0.83 ± 0.82	0.36
BCVA (LogMar)			
Mean ± SD	0.88 ± 0.22	0.88 ± 0.19	0.95
IOP (mm Hg)			
Mean ± SD	13.92 ± 2.25	13.81 ± 2.23	0.79

BCVA = best-corrected visual acuity; IOP = intraocular pressure

Table 2. Study outcomes

Characteristic	IC TA group (n = 30)	Topical group (n = 30)	p-value (t-test)
Anterior chamber cell grade: n			
1 day			
Trace	3	2	
1+	13	9	
2+	12	14	
3+	2	5	0.50
1 week			
No cell	5	3	
Trace	19	16	
1+	6	11	0.33
1 month			
No cell	29	21	
Trace	1	9	0.006*
IOP (mm Hg): mean ± SD			
Baseline	13.92 ± 2.25	13.81 ± 2.23	0.79
1 day	13.20 ± 1.88	12.90 ± 2.81	0.63
1 week	12.33 ± 1.81	12.90 ± 2.16	0.27
1 month	12.43 ± 1.87	12.77 ± 2.05	0.51
BCVA (LogMar): mean ± SD			
Baseline	0.88 ± 0.22	0.88 ± 0.19	0.95
1 month	0.28 ± 0.20	0.23 ± 0.16	0.21

* Statistically significant at $p < 0.05$
IOP = intraocular pressure; BCVA = best-corrected visual acuity

the patients in the Topical group had to continue topical combined dexamethasone and tobramycin eye drops for at least two weeks. Nine patients (30%) in the Topical group required eye drops for one month postoperatively.

Discussion

Corticosteroids have long been the mainstay of treatment for postoperative intraocular inflammation associated with cataract surgery. Traditional methods of administration of these agents include topical eye drops and subconjunctival injection. These techniques have certain disadvantages, however, including an unpredictable duration of therapeutic drug levels as well as inconvenience and the risk of poor compliance, which can be a particular problem for elderly patients prescribed frequent dosing with topical eye drops. Poor compliance may result from impaired physical ability, simple forgetfulness, regimen complexity, doctor-patient miscommunication, or socio-economic factors. Frequent topical dosing can also create a hardship for relatives if they need to take time off from work to assist the patient with drug administration. Topical medications may be costly and can have adverse effects on the cornea, causing disruption of the tear film and subsequent irritation[5]. Consequently, sub-Tenon[3,4] and intracameral injection[5] have recently been proposed as alternative routes of corticosteroid delivery to help prevent inflammation following cataract surgery.

High-dose sub-Tenon injections of TA can cause increases in IOP, subconjunctival hemorrhages, and orbital fat prolapse at the site of injection[3]. When TA is injected into the anterior chamber, however, the incidence of elevated IOP seems to be lower than that seen with topical administration of corticosteroids[5,14]. Intracameral TA has also been shown to decrease the rate of clinical cystoid macular edema (CME) in a dose-dependent manner with no occurrences of CME noted at doses of 1.8 mg or higher during three months of follow-up[5]. Based on these results, a 2 mg dose of TA was chosen for the present study.

The most important finding of the present study was that intracameral TA and gentamicin appeared to control postoperative ocular inflammation at least as effectively as topical dexamethasone-tobramycin eye drops without any detectable adverse effects. There was no significant difference between

the IC TA group and the Topical group in anterior chamber cells one day and one week after surgery. However, the anterior chamber cells were significantly lower in the IC TA group than the Topical Group one month after surgery. There was no significant between-group difference in mean IOP at any time during the present study or in BCVA one month after surgery. There were no cases of postoperative endophthalmitis and no serious adverse effects in either treatment group.

At this time, there is insufficient evidence to support any particular method for preventing postoperative endophthalmitis associated with cataract surgery. Only preoperative povidone-iodine applied to the conjunctival fornix has been reliably shown to decrease the rate of endophthalmitis[15], but the use of postoperative topical antibiotic prophylaxis is very common[16]. Some recent prospective studies have suggested the use of intracameral antibiotics for endophthalmitis prophylaxis[17-21]. Gentamicin, a broad-spectrum antibiotic, is associated with a low degree of bacterial resistance, is inexpensive and widely available, and has been shown to be safe and effective when administered intracamerally for the prevention of posttraumatic and postoperative endophthalmitis[11-13]. Because postoperative endophthalmitis is rare, the present study is too small to allow any conclusions to be drawn about the efficacy of the antimicrobial regimens used. Some of the limitations of the present study include the small sample size, the short follow-up time and the lack of physician and patient masking. The presence of TA crystals in the anterior chamber through at least 1 week postoperatively prevented physician masking. Moreover, grading of the anterior chamber cells was a highly subjective measurement and could potentially be influenced by investigator bias. Another limitation is the lack of corneal pachymetry and specular microscopy measurements to identify possible latent corneal adverse effects. The instruments for these measurements were unavailable. The use of topical tobramycin in the IC TA group also limits the interpretation of the antimicrobial effects of intracameral gentamicin in the present study.

In conclusion, the present study suggests that intracameral injections of 2 mg TA and 0.2 mg gentamicin following cataract surgery may be an appropriate treatment option for the management of postoperative inflammation following uncomplicated cataract surgery. It may be particularly valuable for those patients with anticipated poor compliance with eye drop administration or at risk of developing ocular surface problems following topical dosing. Further studies with a larger sample size, objective technique for more reliable and reproducible documentation of the anterior chamber inflammation, and longer follow-up are warranted to establish the clinical efficacy and safety of intracameral TA and gentamicin in cataract surgery patients.

Potential conflicts of interest

None.

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การฉีดยา triamcinolone acetonide และ gentamicin เข้าช่องหน้าม่านตาในการลดการอักเสบหลังการผ่าตัดต้อกระจก

พรชัย สิมะโรจน์, พรรณลักษณ์ สินสวัสดิ์, เกวลิน เลขานนท์

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของการฉีดยา triamcinolone acetonide และ gentamicin เข้าช่องหน้าม่านตาในการลดการอักเสบ หลังการผ่าตัดต้อกระจก เปรียบเทียบกับยาหยอดตาชนิดรวม dexamethasone และ tobramycin*

วัสดุและวิธีการ: *เป็นการเก็บรวบรวมข้อมูลแบบไปข้างหน้า ศึกษาในผู้ป่วย 60 คน ที่มารับการทำผ่าตัดต้อกระจกชนิด phacoemulsification โดยเมื่อสิ้นสุดการผ่าตัดผู้ป่วยแต่ละรายจะได้รับการสุ่มให้ได้รับการฉีดยา triamcinolone acetonide และ gentacimin เข้าช่องหน้าม่านตา 1 ครั้ง ทันทีหลังผ่าตัด แล้วตามด้วยยาหยอดตา tobramycin วันละ 4 ครั้ง เป็นเวลาเพียง 1 สัปดาห์ (กลุ่ม 1 = 30 คน) หรือได้รับยาหยอดตาชนิดรวม dexamethasone และ tobramycin วันละ 4 ครั้ง จนกว่าการอักเสบจะหายไป (กลุ่ม 2 = 30 คน) หลังจากนั้นผู้ป่วยจะได้รับการตรวจติดตามหลังผ่าตัด ซึ่งได้แก่ การวัดระดับการมองเห็น การตรวจ slit lamp biomicroscopy เพื่อประเมินการอักเสบที่เกิดขึ้นในช่องหน้าม่านตาหลังผ่าตัด การวัดความดันลูกตา และการตรวจหาภาวะแทรกซ้อนอื่น ๆ ทั้งที่เกิดจากการผ่าตัด หรือจากยาที่ใช้ในช่วงหลังผ่าตัด*

ผลการศึกษา: *จากการศึกษานี้พบว่า ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของการอักเสบที่เกิดขึ้นในช่องหน้าม่านตาที่ 1 วัน และ 1 สัปดาห์หลังผ่าตัด ระหว่างกลุ่มที่ 1 และกลุ่มที่ 2 (p = 0.50 และ 0.328 ตามลำดับ) อย่างไรก็ตามพบว่าที่ 1 เดือนหลังผ่าตัดกลุ่มที่ 1 มีระดับการอักเสบน้อยกว่าอย่างมีนัยสำคัญทางสถิติ ส่วนค่าเฉลี่ยของระดับการมองเห็นและความดันลูกตาพบว่าไม่มีความแตกต่างกันในระหว่าง 2 กลุ่ม ทั้งที่ 1 วัน, 1 สัปดาห์ และ 1 เดือนหลังผ่าตัดนอกจากนี้ไม่พบภาวะแทรกซ้อนใด ๆ หรือ ภาวะลูกตาติดเชื้อหลังผ่าตัดในทั้ง 2 กลุ่ม*

สรุป: *การฉีดยา triamcinolone acetonide และ gentamicin เข้าช่องหน้าม่านตาทันทีหลังผ่าตัดเป็นวิธีการรักษาที่ได้ผลดีอีกทางเลือกหนึ่งที่ใช้ช่วยลดอาการอักเสบที่เกิดขึ้นหลังการผ่าตัดต้อกระจก*