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ORIGINAL ARTICLE

Comparative assessment of the endothelial toxicity of intracameral cefuroxime after phacoemulsification

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Abstract

Purpose: The aim of the study was to investigate the possible adverse effect of intracameral cefuroxime (ICC) on corneal endothelium by comparing it with subconjunctival gentamycin (SCG) injection.

Methods: Patients were divided in two groups; ICC (1 mg/0.1 ml) and SCG (40 mg/ml). Corrected distance visual acuity, anterior segment examination, intraocular pressure measurement, specular microscopy (endothelial cell density, coefficient of variation (CV), hexagonality, and central corneal thickness (CCT) were performed before surgery and at postoperative controls on week 1, month 1, and month 3.

Results: Fifty-one eyes received ICC, 37 eyes SCG, and the mean ages of the patients were 70.0±5.5 and 69.2±6.6 (p=0.644). Endothelial cell loss at month 1 was 17.07% in ICC and 16.75% in SCG group (p=0.899). CCT returned to pre-operative values in SCG group at month 1 (p=0.483). Whereas in ICC eyes, a statistically significantly higher CCT still persisted at month 1 (p=0.015). CV showed no statistically significant difference at three post-operative visits compared to baseline in SCG group. Whereas in ICC group, a statistically significant increase was observed in CV at week 1 (p=0.000) and month 1 (p=0.012). At month 3 visit, a statistically significantly lower hexagonality was observed in ICC when compared with SCG (p=0.019).

Conclusion: Results of our study showed that the licensed ICC use after phacoemulsification is safe as SCG in clinical point of view. However, abnormalities in CCT, CV, and hexagonality suggest subclinical endothelial toxicity of cefuroxime.

Keywords: Corneal endothelium; intracameral cefuroxime; toxicity.

Prophylactic antibiotic use at the end of phacoemulsification and intraocular lens implantation is a common practice among cataract surgeons worldwide. Subconjunctival injections have been supplanted by intraocular antibiotics in recent years.[1] Cefuroxime, moxifloxacin, and vancomycin are commonly used for this purpose.[2] However, intraocular antibiotics may cause toxicity. In a review study, 503 eyes were analyzed for safety and toxicity of intracameral cefuroxime (ICC). Toxic effects were observed in 14% including corneal edema, endothel loss, toxic anterior segment syndrome (TASS), macular edema, and loss of vision. Incorrect dilution of cefuroxime, intended for systemic ad-

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ministration, was the main cause in most of the cases.[3] Three-fold the recommended dose ICC was administered to 6 patients by mistake and no adverse effect has been reported. However, 40–50 fold dose can cause severe inflammation, macular edema, and vision loss. Higher doses (10–100 mg) may lead to permanent vision loss.

Efficacy of ICC in preventing endophthalmitis after cataract surgery has been shown previously.[4] This study was conducted to investigate the safety and toxicity of ICC 1 mg/0.1 ml. Although its efficacy has been demonstrated in earlier studies, subconjunctival gentamycin (SCG) may be considered a historical method of prophylaxis in the modern era. [5] However, it is relatively safe having no endothelial toxicity unless accidentally given intracamerally.[6–8]

Materials and Methods

In this prospective study, 88 eyes of 87 patients who underwent uneventful phacoemulsification surgery between May 2017 and May 2019 at University of Health Sciences, Izmir Bozyaka Teaching Hospital, Department of Ophthalmology were analyzed. Ethical committee approval was obtained from our institution and the study was conducted under the tenets of the Helsinki Declaration (date: 12/02/2020,decision no: 11). All operations were performed with Centurion Vision System (Alcon Surgical, Fort Worth, Texas, USA) by two surgeons (TK, BY). Patients with senile cataract were divided in two groups; ICC (1 mg/0.1 ml) and SCG (40 mg/ml). Fifty-one eyes received ICC and 37 eyes received SCG.

Patients who had senile cataracts with soft to medium hardness nucleus (Grade 2–3 according to Oxford Nucleus Grading System) aged 65–80 years were included in the study. Patients who had pseudoexfoliation, small pupil, corneal (dystrophic or degenerative such as Fuchs endothelial dystrophy or trachoma) or retinal disease, glaucoma, uveitis, previous trauma or ocular surgery, any complication during phacosurgery, and diabetes mellitus were excluded from the study. Patients whose surgery was completed in more than 20 min were also not included in the study.

CDVA, anterior segment examination, intraocular pressure measurement (IOP), fundus examination, and endothelial cell count including corneal thickness measurement were performed before surgery and at post-operative controls on week 1, month 1, and month 3. Endothelial cell density (ECD), hexagonality, coefficient of variation (CV), and central corneal thickness (CCT) were recorded before and after surgery with a non-contact specular microscope (Nidek CEM-350; Nidek Inc, Fremont, CA) by a masked eye bank technician. Endothelial imaging was acquired automatically using Center Method in the primary position. Optical pachymetry was in accuracy of±10 µm performed at the same time. A printout was taken and kept in patient file. IOP measurements were performed with Goldmann applanation tonometer. Dilated fundus examination was performed with a 90D lens on a biomicroscope. Cornea examination, pupil dilatation, and nucleus density were evaluated on a slit lamp. Nucleus hardness was graded according to Oxford Classification between 0 and 5. Nucleus hardness, axial length, surgery time, cumulated dissipated energy (CDE), and used balanced salt solution (BSS Ocrosol, Polifarma, Türkiye) volume were also recorded. CDVA was measured with a projected Snellen chart and LogMAR equivalents were used for statistical analysis.

The main outcome measures were the post-operative changes in visual acuity, ECD, and CCT. Secondary outcome measures were post-operative endothelial cell parameters including CV and hexagonality as well as adverse events. Two groups were statistically compared in terms of both clinical and corneal endothelial parameters.

All operations were performed under topical anesthesia with 0.5% proparacaine HCl (Alcaine®, Alcone Couvreur Belgium) by two experienced surgeons (BY and TK). After superior clear corneal incision with a 2.8 mm phaco knife anterior chamber was filled with 1.8% Na hyaluronate (Bio-Hyalur, Biotech Ophthalmics, Hertfordshire, United Kingdom). Capsulorhexis and nucleus removal by Divide and Conquer technique followed by hydrophilic intraocular lens implantation. Torsional energy (Ozil) was used for nucleus emulsification in all cases. At the end of the surgery, a licensed cefuroxime 1 mg/0.1ml (Aprokam 50 mg, Laboratoires Thea, France) was injected through the side port with a 27G cannula. In SCG group, including patients with penicillin allergy, a subconjunctival preservative-free aqueous solution of gentamycin (Genta 40 mg ampule, IE Ulagay, Türkiye) was injected under the inferior fornix of the conjunctiva. After surgery; CDE, surgery time, and BSS volume were recorded.

Statistical Analysis

Data were analyzed using IBM SPSS StaticsVersion 24 software. Comparison of the categoric data between groups was performed with Pearson Chi-square test. Continuous values were analyzed according to normal distribution characteristics using t-test or Mann–Whitney U test. Comparison of pre- and post-operative endothelial cell analysis values was performed with Wilcoxon Signed Ranks test. The correlation between endothelial cell parameters with CDE and axial length was analyzed with Pearson correla-

tion analysis. A p-value under 0.05 was considered statistically significant.

Results

Eighty-eight eyes were included in the study. Pre-operative characteristics of SCG and ICC groups are shown in Table 1. There was no statistically significant difference between two groups in terms of age, gender, axial length, nucleus grade, CDVA, and IOP (p values 0.64, 0.16, 0.71, 0.47, 0.71, and 0.17). Parameters during and after phacoemulsification surgery are shown in Table 2. There was no statistically significant difference between two groups in terms of CDVA, IOP, CDE, operation time, and BSS volüme (p values 0.65, 0.07, 0.46, 0.76, and 0.56). A statistically significant improvement in CDVA was observed in both groups after surgery: From 0.66±0.3 to 0.07±0.09 LogMAR in SCG group (p=0.000) and from 0.66±0.27 to 0.07±0.07 LogMAR in ICC group (p=0.000, Wilcoxon Signed Ranks Test).

Pre-operative ECD was 2352.49±213.82 cells/mm^2 in SCG group and 2395.98±287.04 cells/mm^2 in ICC group. There was no statistically significant difference in terms of pre-operative ECD (p=0.418). Post-operative ECD changes of both groups are shown in Table 3. An overall decrease in ECD was observed in both groups after surgery. ECD at week 1, month 1, and month 3 was all statistically significantly lower compared to pre-operative values as expected (p=0.000 for both groups in all three post-operative visits, Wilcoxon Signed Ranks test). While lower ECD was detected in all three post-operative controls in the ICC group compared to the previous control, in SCG group ECD decreased through week 1 and month 1 but an increase occurred at month 3. However, there was no statistically significant difference between two groups in ECD at post-operative week 1, month 1, and month 3 visits. Interestingly, none of the eyes in ICC group has shown a post-operative ECD under 1100 cells/mm^2 whereas there were some eyes with an ECD under 1000 cells/mm^2 in SCG group at three post-operative visits. A statistically similar percentage of ECD loss was observed in both groups through three post-operative visits. The mean percentage of post-operative endothe-

Table 1. Pre-operative characteristics of SC gentamycin and IC cefuroxime

	IC Cefuroxime (n=51), Mean±SD	SC Gentamycine (n=37), Mean±SD	p-value
Mean age	70.0±5.5 (60–79)	69.2±6.6 (60–80)	0.644
Sex (Male/Female)	31/20	17/20	0.168
Mean Axial Length (mm)	23.38±0.78	23.32±0.84	0.711
Grading of Nucleus Hardness	2.25±0.4	2.19±0.4	0.470
CDVA (LogMAR)	0.66±0.27	0.66±0.3	0.715
Intraocular Pressure (mmHg)	13.29±2.01	12.73±2.42	0.175

CDVA: Corrected distance visual acuity; IC: Intracameral; SC: Subconjunctival; SD: Standard deviation.

Table 2. Surgical and post-operative parameters of SC gentamycin and IC cefuroxime groups

	IC Cefuroxime, Mean±SD	SC Gentamycine, Mean±SD	p-value
CDVA	0.07±0.07	0.07±0.09	0.653
Intraocular Pressure (mmHg)	15.00±2.11	13.95±2.78	0.078
Cumulated Dissipated Energy (%-Seconds)	13.19±5.87	12.17±4.21	0.465
Operation Time (min)	13.75±3.97	13.68±3.01	0.764
Infusion Volume (ml)	71.31±23.51	67.81±18.75	0.565

CDVA: Corrected distance visual acuity; IC: Intracameral; SC: Subconjunctival; SD: Standard deviation.

Table 3. Pre- and post-operative endothelial cell densities (ECD) of SC Gentamycin and IC Ceforoxime groups

	ECD (cells/mm^2)				
	IC Cefuroxime, Mean±SD	p[a]	SC Gentamycine, Mean±SD	p[a]	p[b]
Pre-operative	2395.98±287.04		2352.49±213.82		0.418
Post-operative week 1	2026.47±427.71	0.000	1989.39±383.3	0.000	0.852
Post-operative month 1	1977.31±426.43	0.000	1952.59±351.66	0.000	0.916
Post-operative month 3	1968.9±407.99	0.000	1971.78±306.78	0.000	0.669

ECD: Endothelial cell densities; IC: Intracameral; SC: Subconjunctival; SD: Standard deviation. [a](in-group analysis) [b](inter-group analysis).

lial cell loss (ECL) was 15.24±15.67% in SCG group and 15.05±15.83 % in ICC at week 1 (p=0.823; Mann–Whitney U test). It was 16.75±14.79% and 17.07±16.12% at month 1 (p=0.899) as well as 16.11±11.71% and 17.55±14.41% (p=0.939) at month 3, respectively.

The mean pre-operative CV value was 31.38±3.93 in SCG group and 28.88±4.74 in ICC group. The difference was statistically significant (p=0.002). That means a higher variation in endothelial cell size was present at baseline in SCG group. Although that disadvantage at the beginning, no statistically significant difference was observed between two groups through the three post-operative visits. Inter-group statistical analysis of CV values through 3-time points revealed similar changes in two groups (Independent sample t-test, Mann–Whitney U test). Mean CV values were 31.95±5.5 in SCG group and 33.65±8.12 in ICC group at post-operative week 1 (p=0.773). It was 31.27±6.2 and 30.37±3.26 at month 1 (p=0.425) as well as 30.11±4.51 to 29.65±5.19 at month 3 (p=0.367), respectively. Post-operative "in-group" changes of CV were analyzed in two groups. In SCG group; no statistically significant difference was found at all three post-operative visits compared to baseline (p values 0.875, 0.851, and 0.138; Wilcoxon Signed Ranks test). Whereas in ICC group, a statistically significant increase was observed in CV at week 1 as well as month 1 compare to pre-operative CV values (p values 0.000, 0.012, and 0.232) (Table 4).

Pre-operative hexagonality was comparable in either group (p=0.585) (Table 5). Mean hexagonality showed a statistically significant decrease in both groups at post-operative week 1 due to the surgical trauma. However, it was a similar rate of decrease, and week 1 hexagonality values of the two groups did not show any statistically significant difference (p=0.332, Mann-Whitney U test). The mean hexagonality value at post-operative week 1 was 65.7±4.99% in SCG group and 66.47±6.91% in ICC. Furthermore, a statistically similar rate of recovery in hexagonality was observed toward the normal in both groups at month 1 (p=0.290). However, the statistical comparison of month 3 hexagonality values of the two groups revealed a significantly lower hexagonality value in ICC group compared to SCG (p=0.019). The mean percentage of hexagonality at month 3 was 70.84±4.1 in SCG group and 69.0±4.04 in ICC.

Mean pre-operative CCT was 558.22±36.54 µm in SCG group and 548.61±32.41 µm in ICC group. The difference was not statistically significant (p=0.197). CCT significantly increased due to post-operative corneal edema in both groups at week 1 (p-value was 0.000 in both groups) (Table 6). Comparison of the two groups in terms of CCT changes through three post-operative visits did not reveal any statistically significant difference between the two groups at any time point. However, "in-group" analysis revealed a statistically significant difference in the speed of the resolution of corneal edema between the two groups. Corneal edema resolved and CCT returned to pre-operative values in SCG group at month 1 (p=0.483). Whereas in ICC eyes, a statistically significantly higher CCT (edema) persisted at month 1 compared to pre-operative values (p=0.015). However, in month 3, CCT returned to normal, even thinner than pre-operative values, in both groups (p=0.001 in SCG and p=0.000 in ICC, Wilcoxon Signed Ranks test).

Table 4. Pre- and post-operative mean Coefficient of Variation (CV) values of SC Gentamycin and IC Cefuroxime groups

	CV (%)				
	IC Cefuroxime, Mean±SD	p[a]	SC Gentamycin, Mean±SD	p[a]	p[b]
Pre-operative	28.88±4.74		31.38±3.93		0.002
Post-operative week 1	33.65±8.12	0.000	31.95±5.5	0.875	0.773
Post-operative month 1	30.37±3.26	0.012	31.27±6.2	0.851	0.425
Post-operative month 3	29.65±5.19	0.232	30.11±4.51	0.138	0.367

CV: Coefficient of variation; IC: Intracameral; SC: Subconjunctival; SD: Standard deviation. [a](in-group analysis) [b](inter-group analysis).

Table 5. Pre- and post-operative mean hexagonality values of SC Gentamycin and IC Cefuroxime groups

	Hexagonality (%)				
	IC Cefuroxime, Mean±SD	p[a]	SC Gentamycin, Mean±SD	p[a]	p[b]
Pre-operative	68.71±10.05		69.00±5.42		0.585
Post-operative week 1	66.47±6.91	0.001	65.70±4.99	0.004	0.332
Post-operative month 1	68.90±5.27	0.417	67.65±6.15	0.687	0.290
Post-operative month 3	69.00±4.04	0.303	70.84±4.17	0.064	0.019

IC: Intracameral; SC: Subconjunctival; SD: Standard deviation. [a](in-group analysis) [b](inter-group analysis).

Table 6. Mean pre- and post-operative central corneal thickness (CCT) values of SC Gentamycin and IC Cefuroxime groups

	CCT (µm)				
	IC Cefuroxime, Mean±SD	p[a]	SC Gentamycin, Mean±SD	p[a]	p[b]
Pre-operative	548.61±32.41		558.22±36.54		0.197
Post-operative week 1	569.25±41.36	0.000	573.49±40.48	0.000	0.634
Post-operative month 1	554.47±35.42	0.015	559.51±37.39	0.483	0.521
Post-operative month 3	544.29±32.54	0.000	553.41±36.86	0.000	0.224

CCT: Central corneal thickness; IC: Intracameral; SC: Subconjunctival; SD: Standard deviation. [a](in-group analysis) [b](inter-group analysis).

All eyes of the study were analyzed in terms of the impact of CDE on post-operative changes in ECD, CCT, and CV as well as hexagonality values (Pearson Correlation Analysis). Only a statistically significant correlation was found between CDE and ECD. High total energy used during surgery (CDE) was associated with higher ECL in all three post-operative visits at week 1, month 1, and month 3 (p values were 0.002 for all). No statistically significant correlation was found between CDE and CCT, CV, and hexagonality parameters in any of the 3-time points (P>0.05).

Discussion

Post-operative endophthalmitis is one of the most devastating complications of intraocular surgery.[9] European Society of Cataract and Refractive Surgeons multicenter study revealed that the use of ICC at the end of surgery provided almost 5-fold decrease in the occurrence of post-operative endophthalmitis.[10] Since corneal endothelial cells are very sensitive to any form of toxic exposure, the safety concern of ICC is still under investigation.[2] In Montan et al's. [11] clinical study comprising 45 eyes of prophylactic ICC (1 mg/0.1 ml) and 45 controls; a high anterior chamber concentration of ICC was reported even 1 h after surgery and ICC was found safe in terms of local toxicity. However, in vitro study by Yoeruek et al.[12] revealed dose-dependant toxicity of cefuroxime. They reported that endothelial cell viability decreases after exposure to cefuroxime concentrations starting from 0.275 mg/0.1 ml which is much lower than the usual dose of 1.0 mg/0.1 ml and accelerated cell death occurs after the dose of 1.5 mg/0.1 ml. That means that the safety range of cefuroxime is rather narrow. TASS is characterized by sterile post-operative inflammation and corneal edema after surgery. In severe cases, permanent damage can occur in the corneal endothelium, trabecular meshwork, and macula. In addition to antibiotics, intraocular lenses, intracameral anesthetics, and capsule dyes may lead to toxicity.[13] TASS has been reported after uncomplicated cataract surgery with ICC prophylaxis.[14] However, Gardner et al.[15] suggested that the axetil form of cefuroxime, which is not indented for intraocular use, was responsible for the TASS cases in that report. Although no TASS case was observed in our study, certain clues were found suggesting subclinical endothelial toxicity due to ICC.

In the present study, the equal post-operative visual improvement and ECL outcomes in ICC compared with SCG suggest that ICC prophylaxis are safe and have no clinically discernible toxic effect. Likewise, Montan et al.[11] reported no endothelial toxicity with ICC. In their study, ICC did not have a statistically significant effect on post-operative visual acuity, induced laser flare intensity, or ECL compared with non-administration of intracameral antibiotic prophylaxis. The median aqueous humor concentration of cefuroxime at 30 s was found 2742 mg/L, declining to 756 mg/L 1 h after drug instillation.[11] Shahraki et al.[16] reported a 8.4% of ECL and no post-operative change in hexagonality with ICC (1 mg/0.1 ml). They concluded ICC was a safe method for endophthalmitis prophylaxis. Ozlem et al.[2] reported no endothelial toxicity in the animal model either. ICC with usual doses (1 mg/0.1 ml) resulted in 12.05% ECL after cataract surgery.[17] ECL after uncomplicated phacosurgery has been reported as 11.6%[18] and 15.5%.[19] In our study, the mean ECL was 16.1% in SCG and 17.6% in ICC eyes at month 3 (p=0.939). The higher ECL compared to the previous reports may be due to the use of Divide and conquer technique instead of Chop in our cases. Since latter is associated with less endothelial cell damage.[20] However, Storr-Paulsen et al.[21] reported the same ECL, CV, and hexagonality values after phacoemulsification with both techniques.

By definition, CV value is the ratio of the standard deviation of the cell area to the mean cell area. It is an indicator of endothelial cell polymegethism. Its normal value is ≤30% in adults. The CV increases after any trauma or toxicity to the corneal endothelium.[22] In our study, the CV value showed a significant + 4.77 points increase in ICC group of eyes (p=0.000) at post-operative week 1 whereas only a + 0.57 increase in SCG eyes (p=0.875). At post-operative month 1; the mean CV was still 1.49 points higher in ICC group (p=0.012), but it was −0.11 points lower in SCG eyes

(p=0.851) compare to pre-operative values. In ICC group eyes, the CV value hardly returned to normal at month 3. This finding suggests the possible toxicity of ICC on the corneal endothelium. Likewise, Pérez-Canales et al.[17] compared intracameral vancomycin with cefuroxime 1 mg/0.1 ml in their study including 30 eyes in each group and observed a statistically significant change in CV at post-operative 3 month in ICC group.

Hexagonality is the percentage of endothelial cells with six faces. Its normal value is between 60% and 70% in adults.[22] Polymegethism and pleomorphism are the earlier indicators of corneal endothelial stress compared to ECD.[22] Pérez-Canales et al.[17] reported no statistically significant change in hexagonality with ICC after cataract surgery. Whereas, in our study, statistically significant decreases in hexagonality were observed in both SCG and ICC groups one week after surgery. At month 3 visit, a statistically significantly lower hexagonality was observed in ICC compared to SCG (p=0.019). Mean hexagonality was 69.0±4.04% in ICC and 70.84±4.17% in SCG group. Although both percentages are within the normal range, this finding may indicate that the endothelium was less healthy and still under stress at month 3 after ICC injection compare to SCG. That may be considered another clue for the subclinical toxicity of cefuroxime.

Normal CCT is mean 522–574 μ and an important indicator of the endothelial pump function.[23] Perone et al.[24] reported that post-operative CCT was a reliable marker of endothelial damage after phacoemulsification. They found early thickening after surgery returning to the pre-operative level within 15 days after surgery. In our study, another clue for toxicity was observed at month 1 CCT records. Corneal edema resolved and CCT returned to baseline in SCG group eyes (p=0.483) whereas in ICC eyes, a statistically significantly higher CCT (edema) still persisted at month 1 when compared to baseline (p=0.015). This finding suggests that corneal edema recovery is slower in ICC than SCG indicating a low level of endothelial toxicity after ICC injection. At month 3, CCT returned to pre-operative levels even statistically significantly thinner values in both groups (p=0.001 in SCG and 0.000 in ICC group). Late corneal thinning may be a result of post-operative use of topical steroids.

In our study, ICC was compared with SCG since latter is of an extraocular procedure with no reported toxicity. Nevertheless, inadvertent injection of undiluted gentamycin into the anterior chamber can cause endothelial toxicity.[6] High-frequency vibrations of the phaco tip and the heat energy can be harmful to the corneal endothelium and may result in post-operative corneal edema. In torsional (Ozil, Alcon) technology, ultrasound energy is produced by 32-kilohertz rotational oscillations of the phaco tip. It is reported to be more effective in cataract removal with less damage to the endothelium.[25] Torsional energy has been preferred in our study. Posterior capsule rupture and harder nuclei are associated with a higher ECL. Thus, eyes with PCR were excluded from the study. Bamdad et al.[26] reported an overall 11.4% ECL after phacoemulsification which is significantly higher in diabetic eyes (14.6% versus 8.7%). Thus, diabetic patients were excluded from our study. ECD at post-operative month 1 was 1952.59±351.66 cells/mm^2 in SCG and 1977.31±426.43 cells/mm^2 in ICC group of our study. ECL at month 1 was 16.75% in SCG and 17.07%. Differences were not statistically significant. Longer surgery time, higher cataract density,[18] greater infusion volume, and a greater amount of total emitted ultrasound energy were significantly associated with higher ECL.[27] These parameters were statistically equal in either group of our study. Standardization of the patient's age, nucleus hardness, pre-operative ECD as well as operative variables such as CDE, infusion volume, and surgery time make our results more reliable. Torsional phaco mode was reported with a significantly less ECL compare to conventional phacoemulsification.[28] Thus, the torsional mode was utilized in our study. Diabetes mellitus damages the corneal endothelium and causes structural and functional impairments that decrease cellular reserve in response to stress. Thus, diabetic patients were excluded from our study.[29] Since phacoemulsification has been reported to be a significantly higher ECL in eyes with pseudoexfoliation,[30] these eyes were also excluded from the study. Restrictions of our study are as follows; the anterior chamber depth was not taken into consideration and the present study has no control group with a sham injection of intracameral BSS.

Conclusion

Our results suggest that the licensed ICC use after phacoemulsification is safe as SCG prophylaxis in clinical point of view. However, abnormalities in CCT, CV, and hexagonality suggest subclinical endothelial toxicity of the cefuroxime that tends to resolve within 3 months. The ICC prophylaxis decreases the endophthalmitis rate 5-fold so that the minimal endothelial toxicity observed in the present study may be considered as a little burden for avoiding such a devastating complication of cataract surgery. To inject cefuroxime slowly toward the capsular bag to give time for it to dilute in the humor aqueous may be prudent to avoid toxicity.

Ethics Committee Approval: This study was approved by University of Health Sciences Izmir Bozyaka Training and Research Hospital Medicine Ethics Committee (date: 12.02.202; number: 11).

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Authorship Contributions: Concept: S.T.; Design: F.B.; Supervision: T.K.; Resource: T.K.; Materials: B.Y.; Data Collection and/or Processing: F.B.; Analysis and/or Interpretation: F.B., T.K.; Literature Search: S.T.; Writing: B.Y.; Critical Reviews: B.Y.

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