Perioperative Intracameral Cocktail Combination Vs Topical Treatment in Cataract Surgery

Katarakt Cerrahisinde Perioperatif İntrakameral Kokteyl ile Topikal Tedavinin Karşılaştırılması

Katarakt Cerrahisinde Kokteyl Kombinasyonu / Cocktail Combination in Cataract Surgery

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Özet

Amaç: Fakoemulsifikasyon cerrahisi sonrası ön kamaraya verilen ilaç karışımı kokteyl ile konvansiyonel postoperatif topikal antibiyotik ve steroid kullanımının karşılaştırılması amaçlandı. Gereç ve Yöntem: Retrospektif olarak yapılan çalışmada topikal anestezi ile ameliyat edilen 60 hastanın 60 gözü dahil edildi. Kokteylin içinde vancomycin, ceftazidime, diclofenac, dexamethasone, triamcinolone acetonide ve dengeli tuz solüsyonu bulunuyordu. Ameliyat öncesi ve ameliyattan sonraki 1, 4, 8, 15 ve 29. günlerde tashihli görme keskinliği ve göz içi basıncı ölçülen hastalar çalışmaya dahil edildi. Bulgular: Yapılan takiplerde iki grup arasında tashihli görme keskinliği ve göz içi basıncı ölçümleri arasında istatistiksel olarak anlamlı fark saptanmadı. Kokteyl grubunda postoperatif 1. günde 5mmHg veya daha fazla yükselme 9(%30) gözde, Topikal grubunda 3(%10) gözde görülmüştür. Ancak fark istatistiksel olarak anlamlı değildir (p=0,053). Tartışma: Fakoemulsifikasyon sonrası ön kamaraya verilen kokteyl, postoperatif topikal ilaç kullanımı kadar etkin ve güvenlidir. Aynı günde üç veya daha fazla ameliyat yapıldığında kokteyl kullanımı daha ekonomiktir.

Anahtar Kelimeler

Fakoemülsifikasyon; Antibiyotik; Antienflamatuar Ajanlar; Görme Keskinliği

Abstract

Aim: To compare intracameral drug mixture cocktail with postoperative conventional topical antibiotic-steroid following phacoemulsification. Material and Method: This retrospective study comprised 60 eyes of 60 patients having phacoemulsification under topical anesthesia. The cocktail comprised of vancomycin, ceftazidime, diclofenac, dexamethasone, triamcinolone acetonide and balanced salt solution. Best corrected visual acuity and intraocular pressure were measured preoperatively and at 1, 4, 8, 15 and 29th days postoperatively. Results: Best corrected visual acuity and intraocular pressure measurements did not show significant difference at any time points. More than or equal to 5mmHg rise in intraocular pressure was observed on postoperative day 1 in 9(30%) eyes of Cocktail group and 3(10%) eyes of Topical group. The difference was not significant (p=0,053).Discussion: Intracameral cocktail following phacoemulsification is as safe and effective as topical drops. If there are more than or equal to 3 surgeries in an operating day, then the use of cocktail is more economical compared to topical drops.

Keywords

Phacoemulsification; Antibiotic; Antiinflammatory Agents; Visual Acuity

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Introduction

The first known description of cataract surgery is found in Susruta who performed couching dating back to 2000 B.C. [1]. The foundation of modern cataract surgery was laid down by the introduction of intraocular lenses (IOL) by Harold Ridley [2]. State of the art small incision cataract surgery was made possible by the invention of phacoemulsification, continuous curvilinear capsulorhexis, and foldable IOLs [3-5].

The uses of anesthesia and antibiotics have also evolved. Topical and intracameral anesthesia are increasingly employed due to low side effect profile [6]. Intracameral antibiotics are also used more often [6-11]. Gills is currently injecting a mixture of antibiotic and antiinflammatory agents, shortly called cocktail, into the anterior chamber and/or vitreus at the end of each phacoemulsification case [12-14]. (Gills JP: Using intraocular medication to improve safety and comfort of cataract surgery – Course #2202. Presented at the Annual Meeting of the American Society Cataract and Refractive Surgery. San Diego, CA, May, 2004).

We had modified Gills' cocktail and had used it in our study. To our knowledge, there are no published reports of the effectiveness of intracameral cocktail in phacoemulsification surgery. This study compared the effectiveness of intracameral cocktail and conventional topical antibiotic and steroid combination following phacoemulsification.

Material and Method

The study included 60 eyes of 60 patients scheduled for phacoemulsification at Adnan Menderes University Department of Ophthalmology. Inclusion criteria were the presence of cataract that was suitable for phacoemulsification with topical anesthesia. Exclusion criteria included history of glaucoma or intraocular surgery, presence of corneal scar that might cause a misreading of intraocular pressure (IOP) and central corneal thickness (CCT), or chronic use of topical drops for any reason. The research followed the tenets of the Declaration of Helsinki, and all patients gave written informed consent after they received an explanation of the nature and possible consequences of the procedures.

Eyes were randomized with block randomization to 2 groups of 30 each. The Cocktail group received intracameral 0.15cc of the drug mixture prepared in the morning of each operating day (Table 1). The dosages of drugs within the 0.15cc are given in Table 2. The Cocktail group did not receive any topical medications postoperatively. The Topical group received conventional postoperative topical antibiotic and steroid combination following phacoemulsification (Table 1). Neither of the groups received postoperative ocular hypotensive medication.

Three surgeons operated on 10 eyes from each group through a 3.0mm clear corneal incision using a peristaltic phacoemulsification machine (Diplomax®). Sodium hyaluronate 2% (Oculocrom®) and sodium hyaluronate 1.4% (Neocrom®) were used during capsulorhexis creation and IOL implantation respectively. Implanted IOLs were either one-piece acrylic (ANU6, Polymer Technologies International EOU®) or three-piece silicone (AQ2010V, STAAR Surgical Company®). The only intraocular medication used was 0.5mg epinephrine added into 500ml of irrigating balanced salt solution. Total phacoemulsification time (TPT), and effective phacoemulsification time (EPT) were noted. Both the surgeons and patients were unaware of the group assignments. Surgeons were only informed of individual patients' group status immediately before wound closure, at the conclusion of surgery, when intracameral cocktail injection was required. Since cocktail receiving eyes are evident from outside due to the white color of triamcinolone acetonide, masking was not possible at the postoperative follow-up (Figure 1ABC).

Best corrected visual acuity (BCVA, converted to logMAR from decimal notation), biomicroscopic examination, non contact tonometry (Xpert NCT Plus Advanced Logic Tonometer), ultrasonic pachymetry (Advent), and dilated fundus examination and classification of the lens opacity with Lens Opacities Classification System III (LOCS III) were done on preoperative examination [15]. Ultrasonic pachymetry measurements were repeated three times asking the patient to blink voluntarily between the measurements as restraining from blinking has been shown to thin the cornea artificially [16]. The angle between the pachymeter probe tip and the corneal surface will determine the thickness of the corneal slice that the instrument measures. Hence, the thinnest reading would represent the closest alignment to perpendicular. Higher readings would point to a slight tilt of the probe. The lowest of the 3 CCT readings was used for analysis as it was thought to most likely reflect a perpendicular alignment of the pachymeter probe and, therefore, to be the most accurate measurement. Postoperative examinations were done on days 1, 4, 8, 15, and 29.

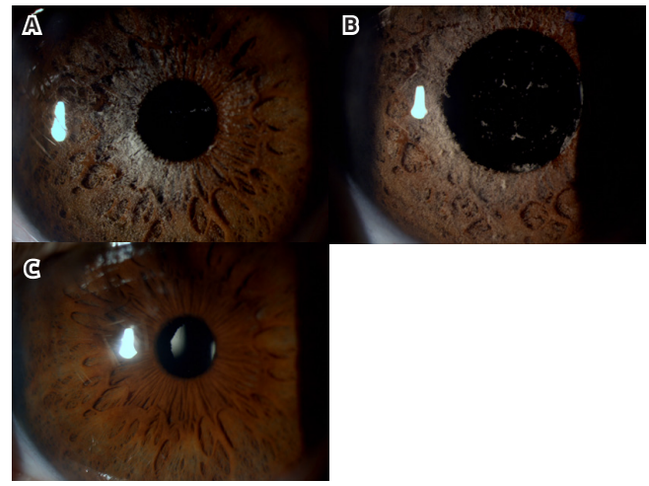


Figure 1. Anterior segment photographs of an eye at postoperative days 1 (A), 4 (B), and 15 (C) after receiving 0.15ml of cocktail following phacoemulsification. Notice abundant triamcinolone acetonide on the intraocular lens at postoperative day 1 (A) that completely disappears at postoperative day 15 (C).

Results for age, LOCS III scores, TPT, and EPT are given as mean ± standard deviation. Independent samples t test was used for independent variables. For proportions, Chi-square test was used for statistical significance. SPSS 9.0 for Windows software was used for statistical analyses. $P<0.05$ was considered as statistically significant.

Results

Table 3 shows the demographic data of the patients. There was no significant difference between the groups. No eye had a capsule break or vitreous loss intraoperatively.

Table 4 shows the results and intergroup comparisons for pseudoexfoliation, phacodonesis, LOCS III scores, TPT, EPT, and implanted IOL type. There was no statistical significance between the groups with respect to any of the parameters.

Mean BCVA was lower in the Cocktail group in the first 8 days of follow-up and slightly better on days 15, and 29. The difference was significant only on postoperative day 4 (p=0.047) (Figure 2). Figure 3 shows the mean IOP changes on preoperative and postoperative follow-up. Although the mean IOP on postoperative days 1, and 4 was higher in the Cocktail group the difference was not significant. Mean IOP on days 8, 15 and 29 were about the same. Table 5 shows number of eyes with an IOP of 30mmHg or higher and eyes with an increase of 5 mm Hg or more on postoperative day 1. One eye (3%) in the Cocktail group that had an IOP reading of 30mmHg has not received any ocular hypotensives. The same eye had an IOP of 18mmHg on postoperative day 4. IOP rise more than or equal to 5mmHg was seen in 9 (30%) eyes in the Cocktail group, and 3 (10%) eyes in the Topical group (p=0,053). None of the eyes except one in the Cocktail group had the same increase in IOP on postoperative day 4.

Mean postoperative CCT was lower in the Cocktail group at all time points. However the difference was not statistically significant (Figure 4).

Discussion

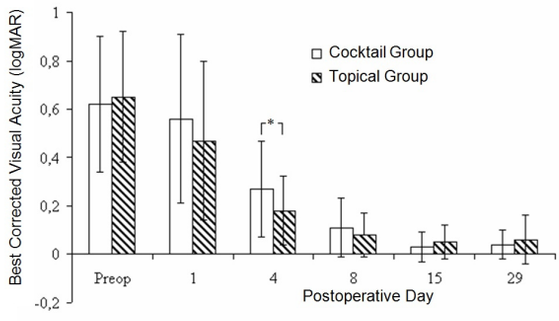


Figure 2. Group comparison of the mean best corrected visual acuity at preoperative, and postoperative follow-up was not significant at any time point except postoperative day 4 (preoperative, p=0.673; day 1, p=0.329; day 4, p=0.047; day 8, p=0.424; day 15, p=0.495; day 29, p=0.305). Bars represent standard deviations. (* = P<0.05).

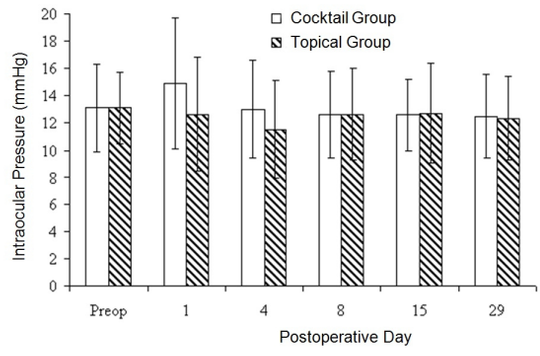


Figure 3. Group comparison of the mean intraocular pressure at preoperative, and postoperative follow-up was not significant at any time point (preoperative, p=1.000; day 1, p=0.059; day 4, p=0.118; day 8, p=1.000; day 15, p=0.935; day 29, p=0.771). Bars represent standard deviations.

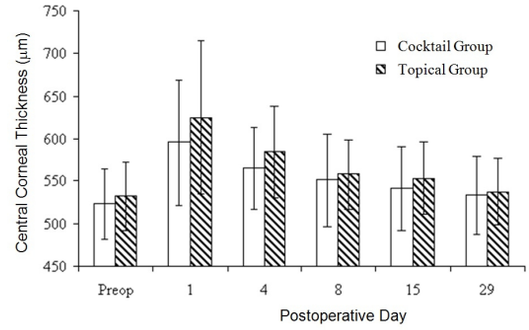


Figure 4. Group comparison of the mean central corneal thickness at preoperative and postoperative follow-up was not significant at any time point (preoperative, p=0.377; day 1, p=0.174; day 4, p=0.169; day 8, p=0.627; day 15, p=0.310; day 29, p=0.695). Bars represent standard deviations.

This study is the first report in the literature showing the effectiveness and safety of intracameral antibiotic and anti-inflammatory combination following phacoemulsification.

Anesthetics and antibiotics are being used intracamerally for some time [7-11]. Gills has reported injecting a combination of antibiotic and antiinflammatory agents, shortly called cocktail, into the anterior chamber and/or vitreus at the end of each phacoemulsification case [12-14]. Gills JP: Using intraocular medication to improve safety and comfort of cataract surgery – Course #2202. Presented at the Annual Meeting of the American Society Cataract and Refractive Surgery. San Diego, CA, May, 2004). The only modification we made to the cocktail was substitution of indomethacin with diclofenac sodium. This was done simply because injectable indomethacin was not available in Turkey at the time of the study.

Vancomycin within the anterior chamber was 112.5 µg with each injection of 0.15ml of the cocktail. A lower rate of positive cultures was reported when 0.01-0.02mg/ml vancomycin was added to the irrigating fluid [17,18]. Vancomycin inhibited the growth of methicillin-resistant Staphylococcus aureus in vitro when used at a dose of 0.05mg/ml [19]. Anterior chamber dose of the other antibiotic, ceftazidime, in the cocktail was 67.5 µg. Results of microbiologic culture and in vitro susceptibility done on records of 497 consecutive endophthalmitis patients following cataract surgery showed 99% efficacy for vancomycin against gram-positive bacteria, and 100% efficacy for ceftazidime against gram-negative bacteria [20].

An argument that might arise from the judicious use of intraocular use of antibiotics is the development of resistant strains. Anterior chamber is a closed space and any bacteria trapped inside after the surgery either dies or causes endophthalmitis. It is very unlikely for an organism to produce a resistant strain and pass into the venous system, or for antibiotics to reach to colonized areas of the body at high enough concentration to promote resistance [21].

Steroid following cataract surgery are used for suppressing inflammation. The dose of dexamethasone, and triamcinolone acetonide given into the anterior chamber with each cocktail injection is 13.5µg, and 3mg respectively. In a 1 year study there was significantly better inflammation control and no significant endothelial cell loss when patients receiving intracameral slow release pellets containing 120µg dexamethasone compared to topical dexamethasone following extracapsular cataract extrac-

tion [22].

No corneal toxicity was noted when triamcinolone acetonide up to 4mg had been injected into the anterior chamber [14]. Intravitreal triamcinolone acetonide can increase IOP in the first 3 months [22-24]. In these studies, higher doses of 4 to 25 mg of triamcinolone acetonide were administered. In our study, mean postoperative IOP on days 1, and 4 were higher in the Cocktail group. However the difference between the groups did not reach a statistically significant level at any time point. One patient in the Cocktail group and none in the Topical group had an IOP of 30 mm Hg or higher on postoperative day 1. The number of patients with an IOP increase of 5 mm Hg or more on postoperatively day 1 was relatively high in the Cocktail group (30%) compared with the number in the Topical group (10%) but the difference was not significantly different (p=0.053). Only one patient in the Cocktail group still had IOP increase of 5 mm Hg or more on postoperative day 4 that was normalized on postoperative day 15. The rise in IOP can either be due to high IOP response to topical ophthalmic steroids [25], or clogging of the trabecular meshwork by triamcinolone acetonide particles. According to our clinical observation, triamcinolone acetonide clears from the anterior chamber at most within two weeks. Whatever the reason is for the rise in IOP, it seems unlikely to be stationery.

Some studies using intravitreal triamcinolone acetonide had reported non-infectious endophthalmitis or pseudoendophthalmitis [26,27]. An acute reaction to the vehicle of the drug is thought to be a theoretical possibility. Intravitreal injections by retinal surgeons use a higher dose (up to 25 mg) and a different technique, which may account for the endophthalmitis like picture. We did not observe an endophthalmitis like picture in any of our cases. Intracameral triamcinolone acetonide sticks on the capsule, IOL, iris, and especially sinks to the inferior angle. This may be mistaken as a hypopyon; however, the patient is asymptomatic.

With modern cataract surgical technique, the incidence of cystoid macular edema has diminished; however, clinical cystoid macular edema is seen in 0.3% to 3%, and angiographic cystoid macular edema is evident in 20% to 30% of pseudophakic eyes [28,29]. Topical diclofenac results in significant reduction in clinical cystoid macular edema [30]. We had administered intracameral 5.625µg diclofenac with the cocktail injection. The use of intracameral diclofenac has not been mentioned in the literature. However, intravitreal injection of 540 µg or higher doses of diclofenac resulted in ocular toxicity in the rabbit, demonstrated as cataract, vitreous haze and retinal damage [31].

The most dreadful side effect of intracameral injections is corneal endothelial damage. Following CCT after cataract surgery would give an idea about endothelial function. In our study, use of intracameral cocktail was as effective and safe as conventional topical steroid and antibiotic in recovery of CCT following phacoemulsification. Mean CCT values were lower in the Cocktail group compared to the Topical group especially on postoperative days 1, and 4 although the difference was not significant.

Visual acuity might be lower in the early postoperative days due to the sticking of white triamcinolone acetonide precipitates on the IOL. Mean best corrected visual acuity was better in the Topical group on postoperative days 1, 4, and 8; the only significant difference being on postoperative day 4. Mean visual acuities were very close to each other beginning from the second postoperative week corresponding to the time when triamcinolone acetonide becomes clinically unrecognizable within the anterior chamber.

An investigation into the causes of non-compliance by patients using eye drops has revealed high prevalence [32]. About half the patients had difficulty aiming the drop, and other problems including squeezing the bottle, blinking, and seeing the tip of the bottle. Intracameral cocktail following phacoemulsification can be a useful solution for non-compliance, and an alternative for those reluctant to use topical drops.

In conclusion, administration of intracameral cocktail had no significant side effect on IOP, CCT, and best corrected visual acuity compared to conventional topical steroid, and antibiotic following phacoemulsification. We recommend the use of intracameral cocktail because it is effective, safe, inexpensive, and resolves non-compliance.

Competing interests

The authors declare that they have no competing interests.

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