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The effect of topical non-steroidal anti-inflammatory drugs in prevention of post- operative macular edema after cataract surgery

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Abstract
Objective: to compare the effect of topical non-steroidal anti-inflammatory drugs versus steroidal drugs in prevention of post-operative macular edema after cataract surgery.
Materials and Methods: the study was conducted on 40 eyes of 40 patients who had cataract extraction using conventional uncomplicated phacoemulsification performed by the same surgeon. Study included fourty patients divided into two groups according to the treatment with topical drugs for 2 weeks, after phacoemulsification surgery with foldable IOL implantation**.**
Results: The macular thickness results revealed statistically significant (p-value: 0.035) in the difference between postoperative and preoperative macular thickness in two groups.
Conclusion: topical NSAID (nepefenac) is more effective for reducing the incidences of CME, macular thickness and improving the visual acuity outcome after uncomplicated cataract surgery than topical steroids.

Keywords: steroid, cataract, topical, inflammatory

Introduction

Cataract surgery with foldable lens implantation is the most challenging ophthalmic surgery in developed countries. Quick recovery of visual acuity and uneventful surgery can be achieved by an effective technical approach and appropriate therapy. Macular edema is one of the most important complications of cataract surgery. It is the main cause of postoperative visual impairment, even in patients without risk factors and in cases of uneventful surgery (Miyake *et al*., 2011) [5]. Cystoid macular edema (CME) following cataract surgery, also known as Irvine–Gass syndrome, is a well-known cause of poor vision following uneventful cataract surgery (Shields *et al*., 2015) [6]. The condition is usually self-limiting, and the resolution of symptoms usually occurs within 3–12 months; it may occasionally persist and lead to permanent vision loss (Shields *et al*., 2015) [6]. Traditionally, topical corticosteroids have been used in ophthalmology to control postoperative inflammation after cataract surgery. Although effective, these drugs may interfere with wound healing, aggravate infections, or increase intraocular pressure (IOP) (Waterbury *et al*., 1987) [7]. For this reason, during the last decade several topical ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) have been developed, and their use in the treatment of postoperative inflammation has progressively increased, All commercially available NSAIDs generally have good ocular penetration with minimal systemic absorption and are widely used in the pre- and postoperative management of cataract surgery (Flach *et al*., 2002) [2]. Many studies examined NSAIDs' effects on prevention of postoperative inflammation and macular edema included the concomitant administration of corticosteroids.

Patients and Methods

This is experimental study in which we compared the effect of topical non-steroidal anti-inflammatory drugs versus steroidal drugs in prevention of post-operative macular edema after cataract surgery. Our study was conducted on 40 eyes of 40 patients who had cataract extraction using conventional uncomplicated phacoemulsification performed by the same surgeon between May 2018 and September 2018.Patients divided randomized into two groups according to the treatment with topical drugs for 2 weeks postoperative.
Group A: Was treated with a combination of prednisolone 1% six times/day for 2 weeks and gatifloxacin 0.3% six times / day for 2 weeks.
Group B: Was treated with a combination of nepefenac 0.1 % six times/day for 2 weeks and gatifloxacin 0.3% six times / day for 2 weeks.

b. Ophthalmic examination including:

- Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) preoperative and 14 days post-operative
- Examination of ocular adnexa including the eye lids, conjunctiva, lacrimal system and orbit.
- Anterior segment detailed slit lamp examination.
- Fundus examination by indirect ophthalmoscopy.
- Biometry by: (Sonomed Escalon FB, PacScan model 300A+, New York, USA), Keratometry by: (NIDEK CO., LTD., auto ref/keratometer ARK-510A, Gamagori, Japan).

c. Retinal macular thickness by OCT (Carl Zeiss Meditec AG, Cirrus 5000 HD-OCT, Germany)
Macular thickness maps were produced for every patient preoperatively and at 2 weeks postoperatively by OCT.

Results

In this study we compared the effect of topical nonsteroidal anti-inflammatory drugs versus steroidal drugs in prevention of post-operative macular edema after cataract surgery. Our study included fourty patients divided into two groups according to the treatment with topical drugs for 2 weeks, after phacoemulsification surgery with foldable IOL implantation.

Group A: Was treated with a combination of prednisolone 1% six times/day and gatifloxacin 0.3% six times / day for 2 weeks.

Group B: Was treated with a combination of nepefenac 0.1 % six times/day and gatifloxacin 0.3% six times / day for 2 weeks

- We measure the best corrected visual acuity (BCVA) preoperative and 14 days post-operative.
- Retinal macular thickness using spectral domain optical coherence topography pre-operative and 14 days post-operative.

Table 1: Personal data

		Group A	Group B	Test value	P-value	Sig.
		No. = 20	No. = 20			
Age	Mean±SD	62.30 ± 5.56	60.50 ± 5.49	1.030•	0.310	NS
	Range	53 – 70	51 – 68			
Gender	Male	4 (20.0%)	4 (20.0%)	0.000*	1.000	NS
	Female	16 (80.0%)	16 (80.0%)			

P-value >0.05: Non significant; P-value <0.05: Significant; P-value< 0.01: highly significant, NS: Non significant; S: Significant; HS: Highly significant, *:Chi-square test; •: Independent t-test

Table 2: The best corrected visual acuity preoperative and at 2 weeks postoperative

		Group A	Group B	Test value•	P-value	Sig.
		No. = 20	No. = 20			
Best corrected visual acuity preoperative	Mean±SD	0.26 ± 0.16	0.22 ± 0.13	0.904	0.372	NS
	Range	0.05 – 0.5	0.05 – 0.4			
Best corrected visual acuity postoperative	Mean±SD	0.54 ± 0.23	0.70 ± 0.22	-2.346	0.024	S
	Range	0.05 – 0.8	0.1 – 0.9			
Difference	Mean±SD	0.28 ± 0.21	0.48 ± 0.20	-3.166	0.003	HS
	Range	0 – 0.55	0.05 – 0.85			

P-value >0.05: Non significant; P-value <0.05: Significant; P-value< 0.01: highly significant, There was statistically highly significant increase in BCVA values after phacoemulsification in two groups (p-value: 0.003) the improvement in group B is better than group A.

Table 3: The macular thickness measurement preoperative and at 2 weeks postoperative

		Group A	Group B	Test value	P-value	Sig.
		No. = 20	No. = 20			
Macular thickness preoperative	Mean±SD	236.00 ± 22.19	229.80 ± 33.20	0.694•	0.492	NS
	Range	197 – 277	180 – 275			
Macular thickness postoperative	Mean±SD	277.20 ± 48.54	260.50 ± 42.03	1.163•	0.252	NS
	Range	220 – 390	210 – 370			
Difference	Median(IQR)	40 (16 – 63.5)	11.00 (0 - 38)	-2.114‡	0.035	S
	Range	2.00 – 139.00	-10.00 –180.00			

P-value >0.05: Non significant; P-value <0.05: Significant; P-value< 0.01: highly significant

The macular thickness results revealed statistically significant (p-value: 0.035) in the difference between postoperative and preoperative macular thickness in two groups.

The group A showed increasing in the macular thickness than the group B.

Cases

Case 1

Male patient in group B aged 51 years old having right immature cataract with preoperative BCVA: 0.3.

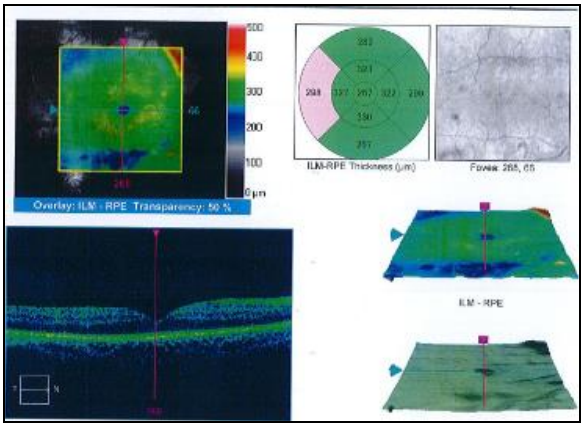

Fig 1: Preoperative OCT of case 1, central macular thickness: 267.

Postoperative BCVA: 0.8

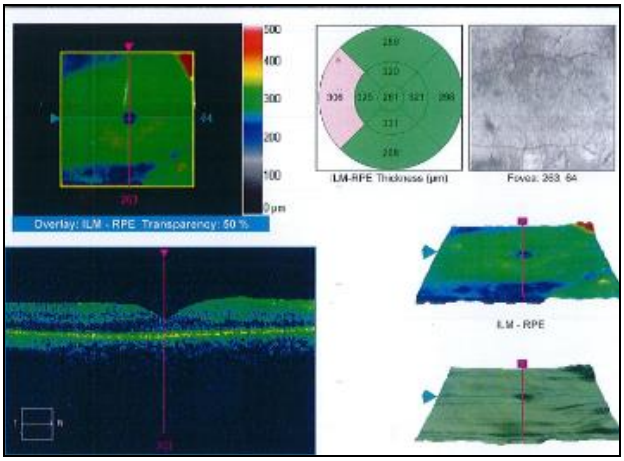

Fig 2: Postoperative OCT of case 1, central macular thickness: 261.

Case 2

Female patient in group B aged 61 years old having right immature cataract with preoperative BCVA: 0.3.

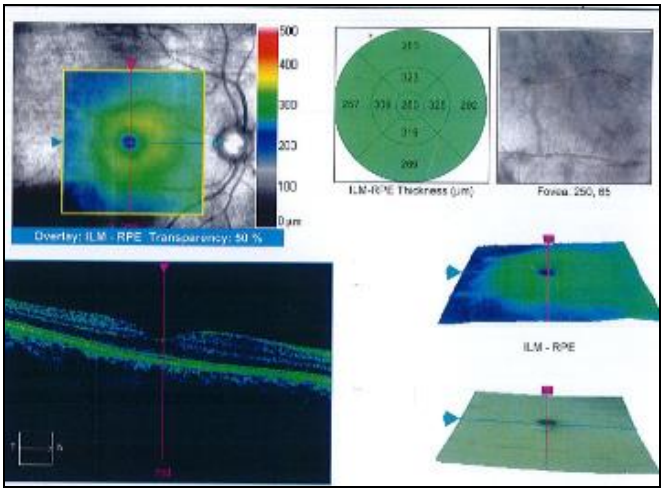

Fig 3: Preoperative OCT of case 2 central macular thickness: 260.

Postoperative BCVA: 0.7

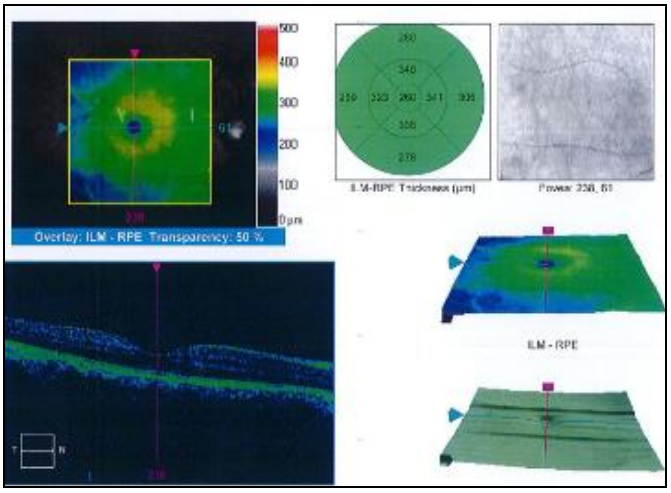

Fig 4: Postoperative OCT of case 2 central macular thickness: 260.

Case 3

Male patient in group B aged 62 years old having right immature cataract with preoperative BCVA: 0. 05.

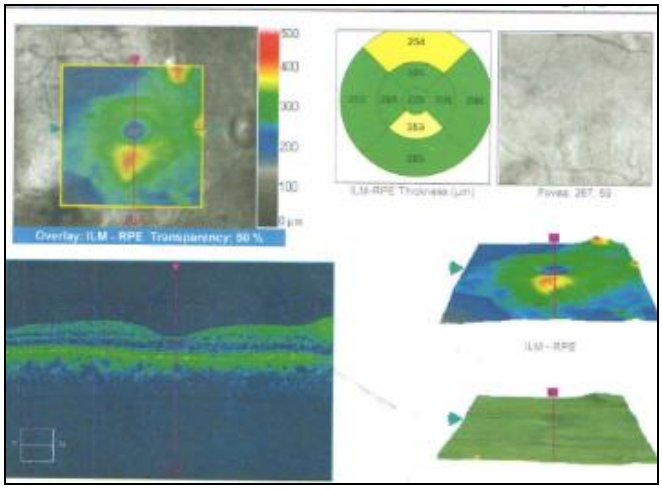

Fig 5: Preoperative OCT of case 3, central macular thickness: 228.

Postoperative BCVA: 0.1

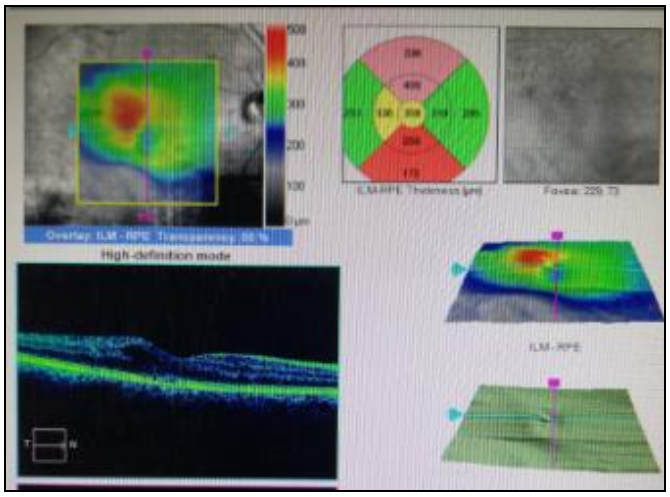

Fig 6: Postoperative OCT of case 3, central macular thickness: 308

Discussion

Cataract surgery is one of the most frequently performed elective surgical procedures in developed countries. The surgical methods have improved significantly over the years, thus lowering the risk of complications and raising patients' and surgeons' expectations of a successful visual outcome. In patients without other eye diseases, 20/20 visual outcome is a realistic expectation (Gulkilik *et al*., 2006) [3]. Pseudophakic cystoid macular edema (PCME, also termed "IrvineeGass syndrome") is a swelling of the fovea due to fluid accumulation occurring a few weeks to months after cataract surgery. It is the most common cause of visual decline after cataract surgery. The prevalence of PCME varies from study to study depending on how PCME is defined. By using fluorescein angiography, a prevalence of PCME of up to 20% has been reported (Gulkilik *et al*., 2006) [3]. Deciding which anti-inflammatory agent to use in patients undergoing cataract surgery is important to ensure a favourable outcome. Currently, 2 drug groups are available to control ocular inflammation steroids and nonsteroidal anti-inflammatory drugs (NSAIDs).Steroids are potent anti-inflammatory agents that work by acting on a number of intercellular inflammatory mediators, and NSAIDs work by inhibiting the cyclooxygenase enzymes. The cyclooxygenase enzymes catalyze the formation of prostaglandins. Preventing the formation of prostaglandins

reduces the inflammatory process (Gulkilik *et al*., 2006) [3]. Our study compares the efficacy of topical steroids with that of topical NSAIDs in preventing PCME. We compared by the difference between preoperative and postoperative BCVA, the difference between preoperative and postoperative macular thickness and the percentage of CME. We found that There was no statistically significant (p-value: 0.114) in the percentage of CME in two groups, in group A, there were 14 persons (70.0%) hadn't CME while 6 persons (30.0%) had CME,in group B there were 18 persons (90.0%) hadn't CME and 2 persons (10.0%) only had CME,so the percentage of CME in group A is more than in group B. The macular thickness results revealed statistically significant (p-value: 0.035) in the difference between postoperative and preoperative macular thickness in two groups, the difference of macular thickness increased more in group A than in group B. The best corrected results revealed highly significant statistics (p-value: 0.003) in the difference between postoperative and preoperative BCVA values in two groups, the improvement in group B is better than group A. This results mean that the topical NSAID (nepefenac) reduces the incidences of CME, macular thickness and improve the visual acuity outcome after cataract surgery. Similar to our study, Kessel *et al*. (2014) [4] found that topical NSAIDs are more effective in preventing PCME than topical steroids. Pseudophakic cystoid macular edema was 6 to 7 times more prevalent in patients randomized to topical steroids compared with topical NSAIDs when evaluated by fluorescein angiography or OCT at 4 to 5 weeks after cataract surgery. The prevalence of PCME was significantly higher in the steroid group than in the NSAID group: 3.8% versus 25.3% of patients in contrast to our study in which the percentage of CME shows no statistical significant between two groups. They used different types of steroids, betamethasone, dexamethasone, fluorometholone and rimexolone. They grouped their meta-analyses according to the strength of the steroids but did not find that the most potent steroids were significantly more effective in controlling inflammation or reducing PCME than the weak steroids. Five different NSAIDs were used. Diclofenac, ketorolac bromfenac, nepafenac, and indomethacin their meta-analyses were not designed to determine which NSAID is most effective. It also compared between the NSAIDs and steroids in prevention of inflammation post cataract surgery and they found that postoperative inflammation was less in patients randomized to NSAIDs. Other study which coincide with our study Miyake *et al*. (2011) [5] also compared between NSAIDs and steroids but they used fluorometholone and nepefenac they found that Nepafenac was more effective than fluorometholone in preventing angiographic CME and BAB disruption, and results indicate nepafenac leads to more rapid visual recovery. In their study patients were randomized to receive nepafenac 0.1% eyedrops or fluorometholone 0.1% eyedrops for 5 weeks after phacoemulsification with foldable IOL implantation. The incidence and severity of CME were evaluated by fluorescein angiography, retinal foveal thickness on optical coherence tomography, and BAB disruption on laser flare-cell photometry. Five weeks postoperative they found that the incidence of fluorescein angiographic CME was significantly lower in the nepafenac group (14.3%) than in the fluorometholone group (81.5%) (P<.0001), the fovea was thinner in the nepafenac group than in the fluorometholone group at 2 weeks (P=.0266) and 5 weeks (P=.0055) and the visual acuity recovery from baseline was significantly greater in the nepafenac group (80.0%) than in the fluorometholone group (55.2%) (P=.0395). They also assessed the effect of steroid and NSAIDs of inflammation At 1, 2, and 5 weeks, anterior chamber flare was significantly less in the nepafenac group than in the fluorometholone group (P<.0001, P<.0001, and P=.0304, respectively). Other studies assessed the adjuvant treatment with NSAIDs in addition to steroidal treatment. Wittpenn *et al*. (2008) [8] compared topical ketorolac 0.4% plus steroid vs steroid alone in low-risk cataract surgery. Patients were randomized to receive either prednisolone acetate 1% 4 times daily alone (steroid group; n = 278) or prednisolone 1% 4 times daily plus ketorolac 0.4% 4 times daily (ketorolac/steroid group; n = 268) for approximately four weeks postoperatively, in the ketorolac/steroid group patients also received topical ketorolac 0.4% 4 times daily for three days preoperatively, in both groups patients received four doses of ketorolac 0.4% one hour before surgery. Outcome measures included CME incidence, retinal thickness as measured by optical coherence tomography (OCT) and best-corrected visual acuity. No patients in the ketorolac/steroid group and five patients in the steroid group had clinically apparent CME (P =. 032). Based on OCT, in the ketorolac/steroid group mean retinal thickening was less (3.9 microm vs 9.6 microm; P =. 003), and fewer patients had retinal thickening of more than 10 microm as compared with the steroid group (26% vs 51%; P <. 001). Other study supported, Cardascia *et al*. (2016) [1] reported that topical treatment with NSAIDs enhanced the efficacy of steroids to reduce postoperative macular edema. In this study they compared between different types of NSAIDs (nepafenac, bromfenac, indomethacin and Diclofenac) in addition to dexamethasone. 14 patients were treated with bromfenac, 15 with nepafenac, 12 with indomethacin, and 14 with diclofenac; 10 patients were treated with dexamethasone and netilmicin alone.The efficacy of each treatment was determined by comparing the changes in macular thickness 1 week after surgery which was reduced only in the group treated with nepafenac (−1.3 %, $p = 0.048$), was increased in the group treated with dexamethasone and netilmicin alone (+4.3 %, $p = 0.04$), and did not change in the groups treated with bromfenac (−1.1 %, $p = 0.3$), indomethacin (+0.1 %, $p = 0.19$), or diclofenac (+1.2 %, $p = 0.74$).

Conclusion

In conclusion, topical NSAID (nepefenac) is more effective for reducing the incidences of CME, macular thickness and improving the visual acuity outcome after uncomplicated cataract surgery than topical steroids (prednisolone).

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