

Comparing the Effect of Different Anti-Inflammatory Treatment Regimens on the incidence of pseudophakic cystoid Macular Edema after Uneventful Phacoemulsification Surgery

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Abstract

Aim: To compare the effects of different topical anti-inflammatory regimens on the incidence of macular edema after uneventful phacoemulsification surgery

Methods: Randomized clinical trial. 65 eyes with no evident risk factor of post operative CME did phacoemulsification were assigned to 3 groups according to the type of postoperative anti-inflammatory treatment regimen used, group A received postoperative topical NSAIDs with topical steroid eye drops, group B received only postoperative steroid eye drops and group C received single immediately postoperative subconjunctival injection of 0.5 mL (20 mg) triamcinolone acetonide. Patients were evaluated preoperatively, at 2 week and 6 weeks postoperatively as regard central macular thickness by OCT, decimal BCVA and IOP.

Results: Changes of central macular thickness on OCT in the 3 studied periods were lower in group A than in group B and C, however they are not statistically significant. During the study, 4 patients (6.15%) developed PCME according to cutoff value of 315 μ m central macular thickness. Additionally, correlations between central macular thickness changes and different preoperative and operative parameters including age, sex, relevant systemic diseases, cataract density, surgeon factor and phaco machine used, were assessed during the 6-weeks follow-up period and found to be not statistically significant. Also, there were no statistically significant differences between the 3 groups as regards improvement of BCVA or reduction of IOP.

Conclusion: A single subconjunctival triamcinolone depot injection at the end of uncomplicated cataract surgery is a safe and effective alternative to topical steroid eye drops in preventing postoperative intraocular inflammation.

Keywords:

Pseudophakic cystoid macular edema (PCME), central subfield thickness, subconjunctival triamcinolone acetonide

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Introduction

Pseudophakic cystoid macular edema (PCME), also known as Irvine–Gass syndrome, is the most common cause of unexpected visual loss after cataract surgery.⁽¹⁾ The advent of phacoemulsification and small incision cataract surgery has reduced the incidence of PCME, but the sheer volume of cataract surgery still makes PCME a prevalent morbidity. Substantial advances in the treatment and prophylaxis of PCME have not been made during the past two decades, but encouraging investigational treatments are emerging.⁽²⁾ PCME is defined as angiographic (seen on fluorescein angiography) or clinical (associated with decreased visual acuity), and acute (within 6 months) or chronic (over 6 months). Optical coherence tomography (OCT) definitions have also been proposed.⁽³⁾ The incidence of angiographic PCME is as high as 60% after intracapsular cataract extraction, compared with 15–30% after extracapsular extraction.⁽¹⁾ PCME after modern phacoemulsification as detected on OCT has ranged from 4⁽⁴⁾ to 11%⁽⁵⁾, but as high as 41%⁽²⁾. The incidence of clinical PCME is much lower, and ranges from 0.1 to 2.35%.⁽⁶⁻⁷⁾ Up to 80% of these symptomatic patients will experience spontaneous improvement by 3–12 months.⁽²⁾ PCME pathogenesis is likely

multifactorial, but inflammation caused by surgical manipulation appears to be the major cause. Inflammatory mediators break down the blood–aqueous and blood–retinal barriers, leading to increased vascular permeability⁽⁸⁾. Transudate accumulates in the outer plexiform and inner nuclear layers of the retina and microcysts coalesce into cysts. Lamellar holes and subretinal fluid accumulation may also occur.⁽¹⁾

The proposed factors for aphakic or pseudophakic CME include hypotony⁽⁹⁾, inflammation⁽¹⁰⁾, phototoxicity⁽¹¹⁾, and vitreous traction⁽¹⁰⁾. Prostaglandins have been studied as a potential causative factor for CME following cataract/intraocular lens surgery.⁽¹²⁻¹³⁾ Surgical complications that predispose eyes to PCME include vitreous loss, vitreous traction at incision sites, vitrectomy for retained lens fragments, iris trauma, posterior capsule rupture, intraocular lens (IOL) dislocation, early postoperative capsulotomy, and the use of iris-fixated or anterior chamber IOLs.^(1, 14) Eyes with diabetic maculopathy have a higher risk of

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developing PCME⁽¹⁵⁻¹⁶⁾. It may be difficult to distinguish PCME from progression of diabetic macular edema (DME). Uveitis predisposes eyes to premature cataract formation, and cataract extraction in these patients carries a higher risk for complications⁽¹⁷⁾. Retinal vein occlusion (RVO), epiretinal membrane, and prostaglandin analogs are also risk factors for PCME.⁽⁷⁾

The incidence of clinical PCME peaks at approximately 4–6 weeks postoperatively. Most patients with clinical PCME will present with blurry vision, and biomicroscopy will show retinal thickening and loss of the foveal depression. Findings are best observed using a fundus contact lens, and red-free light may allow better visualization of cystic changes.⁽¹⁸⁾ Fluorescein angiography findings include retinal telangiectasis, capillary dilatation, and leakage from perifoveal capillaries in the early frames developing into the classic ‘petalloid’ pattern in late frames. Optic nerve staining may also be seen and aids to distinguish pseudophakic PCME from other causes of CME.⁽¹⁹⁾ Optical Coherence Tomography (OCT) has become widely adopted and allows convenient monitoring of disease activity. A central subfield thickness (CSF) of 315 μm is described as the upper limit for macular thickness measurements by Spectralis Spectral Domain-OCT (Heidelberg Engineering, Vista, California, USA) for the normal population, the mean central point thickness (CPT) was $227.3 \pm 23.2 \mu\text{m}$, and mean CSF was $270.2 \pm 22.5 \mu\text{m}$.⁽²⁰⁾

PCME is characterized by loss of the foveal depression, retinal thickening, and cystic hyporeflective lesions, Fig (3). OCT also allows the detection of vitreoretinal traction and lamellar holes. However, despite OCT’s superior sensitivity and convenience, fluorescein angiography remains the gold standard because it can rule out other causes of CME.⁽¹⁸⁾ There is currently no standardized treatment or prophylactic protocol for PCME, because well designed large RCTs with long-term follow-up are lacking. Topical NSAIDs and topical corticosteroids are nevertheless first-line modalities.⁽²⁾

NSAIDs have beneficial effects over corticosteroids including reduction of the risk of secondary infections, analgesia effect, and stabilization of IOP.⁽²¹⁾ NSAIDs have relative potency against Cox 1 and Cox 2. Cox -2 specific activity in postcataract surgery is important as it’s believed that Cox -2 enzyme is a primary mediator of ocular inflammation.⁽²²⁾ Topical NSAIDs have become the mainstay of perioperative PCME prophylaxis. Ketorolac 0.4% (Acular; Allergan, Irvine, California, USA), diclofenac 0.1% (Voltaren; Bausch and Lomb, Tampa, Florida, USA), bromfenac 0.09% (Xibrom/Bromday; Ista Pharmaceuticals, Irvine, California, USA), and the relatively new nepafenac 0.1% (Nevanac; Alcon, Fort Worth, Texas, USA) are US Food and Drug Administration (FDA) approved for postoperative inflammation (not for PCME).⁽²³⁻²⁴⁾ In spite of using corticosteroids as gold standard for

treatment of ocular inflammation, it is associated with adverse effects that warrant their judicious use.⁽²⁵⁾ Corticosteroids side effects include suppression of host immune response which increases susceptibility to microbial infections, retardation of corneal epithelium and stromal wound healing, and rise in intraocular pressure (IOP). These multiple side effects make steroids not safe for extended periods.⁽²⁵⁾ Topical corticosteroids are commonly used in prophylaxis and treatment of PCME, but the evidence is surprisingly limited. The true efficacy of steroids appears to be confounded by concomitant use of NSAIDs in most studies⁽²⁾, although NSAIDs and corticosteroids may work synergistically, at least in the short-term.⁽²⁶⁾ Sub-Tenon’s and retrobulbar corticosteroids have been shown to be effective for PCME refractory to topical treatments⁽⁶⁾. Other treatment options include intravitreal anti-VEGF agents, oral carbonic anhydrase inhibitors, also pars plana vitrectomy which may be considered when PCME is complicated by vitreoretinal traction, and/or if the PCME is unresponsive to medical treatment for more than 1 year and less than 2 years⁽⁶⁾. Finally, there remains a lack of well-designed RCTs to evaluate the medical and surgical treatment and prophylaxis of PCME. Formulating the optimum regimen for prophylaxis and treatment of macular edema following cataract surgery needs comparative studies between different treatment modalities. In this study, we aim compare the effects of different topical anti-inflammatory regimens on the incidence of macular edema after uneventful phacoemulsification surgery.

Subjects and methods

The study included 65 eyes of 52 patients without any known risk factors of PCME undergoing phacoemulsification cataract surgery assigned to 3 groups according to the type of postoperative anti-inflammatory treatment regimen used. Group A received postoperative topical NSAIDs (nepafenac 0.1% (NevanacTM, Alcon, Fort Worth, Texas, USA)) ophthalmic solution four times daily for 1 day before the procedure and for 5 weeks after) with topical steroid eye (prednisolone acetate 1% (PredforteTM, Allergan Ltd, UK)) drops (hourly for 2 days postoperatively, and then 5 times daily to be tapered over 5 weeks), another received only postoperative steroid eye drops and the last one received single immediately postoperative subconjunctival injection of 0.5 mL (20 mg) triamcinolone acetonide (Kenacort-A 40 mg/mL).

All patients were also treated with moxifloxacin ophthalmic solution 0.5% (vigamox; Alcon) four times daily for 1 day before the procedure and four times daily postoperatively for 10 days. Patients were evaluated at 1 day, 2 week and 6 weeks postoperatively.

The primary outcome measured was retinal thickness through OCT. OCT scans were obtained using a single Spectralis Spectral-Domain OCT instrument (Hiedelberg SD-OCT, Germany) preoperatively and at

2 and 6 weeks postoperatively using a fast macular line scan that covered 20° centred on the fovea through a dilated pupil. CME was defined as the presence of well-defined cystic fluid pockets, which present as hyporeflexive lacunae with well-defined boundaries observed in the retina layers⁽¹⁷⁾ or a central macular thickness above 315 µm.⁽²²⁾

The secondary outcomes were BCVA, clinical CME incidence and intraocular pressure (IOP).

Results

Preoperative and operative parameters:

Different preoperative and operative parameters that were thought to possibly have an effect on study results were assessed, including age, gender, related systemic diseases, cataract density, surgeon factor and phaco machine used.

There were no statistically significant differences between the 3 studied groups. (tables 1-5)

Table (1): Comparison between the three studied groups according to demographic data

	Group A (n = 22)		Group B (n = 21)		Group C (n = 22)		Test of Sig.	p
	No.	%	No.	%	No.	%		
Sex								
Male	11	50.0	7	33.3	8	36.4	$\chi^2=$ 1.427	0.490
Female	11	50.0	14	66.7	14	63.6		
Age (years)								
Min. – Max.	51.0 – 82.0		50.0 – 78.0		50.0 – 84.0		F= 1.314	0.276
Mean ± SD.	65.27 ± 8.52		62.29 ± 6.87		66.05 ± 8.46			
Median	65.0		62.0		66.50			

χ^2 : Chi square test

F: F for ANOVA test

p: p value for comparing between the three groups

Table (2): Comparison between the three studied groups according to systemic disease

	Group A (n = 22)		Group B (n = 21)		Group C (n = 22)		χ^2	MCp
	No.	%	No.	%	No.	%		
Systemic disease								
No DM - No HTN	11	50.0	14	66.7	12	54.5	8.381	0.370
DM - No HTN	1	4.5	3	14.3	1	4.5		
HTN - No DM	7	31.8	3	14.3	3	13.6		
DM - HTN	2	9.1	0	0.0	4	18.2		
Others	1	4.5	1	4.8	2	9.1		

Table (3): Comparison between the three studied groups according to cataract density

	Group A (n = 22)		Group B (n = 21)		Group C (n = 22)		χ^2	MCp
	No.	%	No.	%	No.	%		
Cataract density								
N 1/2 ± PSC ± cortical	4	18.2	3	14.3	2	9.1	1.155	0.971
N +2 ± PSC ± cortical	16	72.7	16	76.2	17	77.3		
N 2/3, N3 ± PSC ± cortical	2	9.1	2	9.5	3	13.6		

Table (4): Comparison between the three studied groups according to surgeon

	Group A (n = 22)		Group B (n = 21)		Group C (n = 22)		χ^2	MCp
	No.	%	No.	%	No.	%		
Surgeon								
Surgeon 1	6	27.3	10	47.6	14	63.6	9.833	0.411
Surgeon 2	6	27.3	3	14.3	2	9.1		
Surgeon 3	4	18.2	3	14.3	2	9.1		
Surgeon 4	4	18.2	5	23.8	4	18.2		
Surgeon 5	1	4.5	0	0.0	0	0.0		
Surgeon 6	1	4.5	0	0.0	0	0.0		

Table (5): Comparison between the three studied groups according to phaco machine

	Group A (n = 22)		Group B (n = 21)		Group C (n = 22)		χ^2	p
	No.	%	No.	%	No.	%		
Phaco machine								
Oerteli	8	36.4	8	38.1	7	31.8	0.199	0.905
Signature	14	63.6	13	61.9	15	68.2		

 χ^2 : Chi square test

p: p value for comparing between the three groups

Preoperative central macular thickness by OCT:

Pre-operative central macular thickness in group A ranged from 187-300 μm , group B from 225-312 μm and group C from 202-298 μm , there were no statistically significant differences in preoperative central macular thickness in the 3 groups (table 6).

Preoperative BCVA:

Pre-operative decimal BCVA in group A ranged from 0.01-0.5, group B from 0.01-0.5 and group C from 0.1-0.5, there were no statistically significant differences in preoperative BCVA in the 3 groups (table 7).

Preoperative IOP:

Pre-operative IOP in group A ranged from 10-22 mmHg, group B from 11-22 mmHg and group C from 8-22 mmHg, there were no statistically significant differences in preoperative IOP in the 3 groups (table 8).

Primary outcome; change of central macular thickness on OCT:

Changes of central macular thickness on OCT in 3 periods (from preoperatively to 2 weeks postoperatively, from 2 to 6 weeks postoperatively and from preoperatively to 6 weeks postoperatively) were lower in group A than in group B and C, however they are not statistically significant (table 9).

Table (6): Comparison between the three studied groups according to preoperative OCT

OCT	Group A (n = 22)	Group B (n = 21)	Group C (n = 22)	F	p
Preoperative					
Min. – Max.	187.0 – 300.0	225.0 – 312.0	202.0 – 298.0		
Mean \pm SD.	259.6 \pm 28.85	259.6 \pm 19.53	259.9 \pm 26.11	0.001	0.999
Median	264.5	260.0	265.0		

F: F for ANOVA test

p: p value for comparing between the three groups

Table (7): Comparison between the three studied groups according to preoperative decimal BCVA

BCVA decimal	Group A (n = 22)	Group B (n = 21)	Group C (n = 22)	H	p
Preoperative					
Min. – Max.	0.01 – 0.50	0.01 – 0.50	0.1 – 0.50		
Mean \pm SD.	0.14 \pm 0.11	0.13 \pm 0.13	0.19 \pm 0.14	2.514	0.284
Median	0.10	0.10	0.17		

H: Kruskal Wallis test

p: p value for comparing between the three groups

Table (8): Comparison between the three studied groups according to preoperative IOP

IOP	Group A (n = 22)	Group B (n = 20)	Group C (n = 21)	F	p
Preoperative					
Min. – Max.	10.0 – 22.0	11.0 – 22.0	8.0 – 20.0		
Mean ± SD.	15.18 ± 3.25	15.80 ± 2.42	14.52 ± 2.56	1.081	0.346
Median	14.50	16.0	14.0		

F: F for ANOVA test p: p value for comparing between the three groups *: Statistically significant at p ≤ 0.05

Table (9): Comparison between the three studied groups according to OCT changes

OCT Changes from	Group A (n = 21)	Group B (n = 18)	Group C (n = 19)	H	p
Pre to 2 weeks					
Min. – Max.	-29.0 – 66.0	-12.0 – 21.0	-28.0 – 24.0		
Mean ± SD.	7.32±24.76	2.35±8.0	2.32±11.29	0.021	0.990
Median	2.0	2.50	3.0		
2 weeks to 6 weeks					
Min. – Max.	-43.0 – 27.0	-7.0 – 62.0	-3.0 – 90.0		
Mean ± SD.	3.43±12.77	9.17±14.65	12.26±20.64	1.540	0.463
Median	5.0	7.0	6.0		
Pre to 6 weeks					
Min. – Max.	-25.0 – 77.0	-8.0 – 51.0	-3.0 – 82.0		
Mean ± SD.	9.76±24.01	10.83±13.02	14.0±19.76	0.961	0.618
Median	6.0	7.50	8.0		

H: Kruskal Wallis test p: p value for comparing between the three groups

However, changes of central macular thickness on OCT in each group among different periods (from preoperatively to 2 weeks postoperatively, from 2 to 6 weeks postoperatively and from preoperatively to 6 weeks postoperatively) showed statistically significant

difference, where the increase in CSF thickness was higher at 6-week follow-up than at 2-week follow-up from the preoperative base line OCT measurements, this was most marked in group C (subconjunctival triamcinolone acetonide), with no significant clinical effects (table 10).

Table (10): Comparison between OCT Changes in each group

	OCT Changes from			Fr	p
	Pre to 2 weeks (n = 22)	2 weeks to 6 weeks (n = 21)	Pre to 6 weeks (n = 21)		
Group A					
Min. – Max.	-29.0 – 66.0	-43.0 – 27.0	-25.0 – 77.0		
Mean ± SD.	7.32±24.76	3.43±12.77	9.76±24.01	6.321*	0.042
Median	2.0	5.0	6.0		
Sig. bet. periods	p ₁ =0.217, p ₂ =0.014*, p ₃ =0.217				
Group B					
Min. – Max.	-12.0 – 21.0	-7.0 – 62.0	-8.0 – 51.0		
Mean ± SD.	2.35±8.0	9.17±14.65	10.83±13.02	11.681*	0.003*
Median	2.50	7.0	7.50		
Sig. bet. periods	p ₁ =0.055, p ₂ =0.001*, p ₃ =0.157				
Group C					
Min. – Max.	-28.0 – 24.0	-3.0 – 90.0	-3.0 – 82.0		
Mean ± SD.	2.32±11.29	12.26±20.64	14.0±19.76	7.547*	0.023*
Median	3.0	6.0	8.0		
Sig. bet. periods	p ₁ =0.043*, p ₂ =0.009*, p ₃ =0.570				

Fr: Friedman test, Sig. bet. periods was done using Post Hoc Test (Dunn's)

p: p value for comparison between different periods

p₁: p value for comparing between Changes from Pre to 2 weeks and 2 weeks to 6 weeks

p₂: p value for comparing between Changes from Pre to 2 weeks and Pre to 6 weeks

p₃: p value for comparing between Changes from 2 weeks to 6 weeks and Pre to 6 weeks

*: Statistically significant at p ≤ 0.05

Manifest PCME cases:

During the study, 4 patients (6.15%) developed PCME according to cutoff value of 315 μm central macular thickness, Patient 1 in group A detected at the 2-week follow-up, with CSF thickness of 350 μm and BCVA of 0.33, Patient 2 in group B detected at the 6-week follow-up, with CSF thickness of 330 μm and BCVA of 0.5 and Patients 3 and 4 in group C, one detected at the 6-week follow-up, with CSF thickness of 337 μm and

BCVA of 1.0 and another detected at the 2-week follow-up, with CSF thickness of 321 μm and BCVA of 0.1 respectively.

Those patients were given topical NSAIDs, if not added to their regimen with short course of oral CAI in addition to topical steroid eyedrops, and followed up clinically and by OCT, all of them showed marked improvement, as shown for example in follow-up OCTs of Patient 1 (figures 1-4)

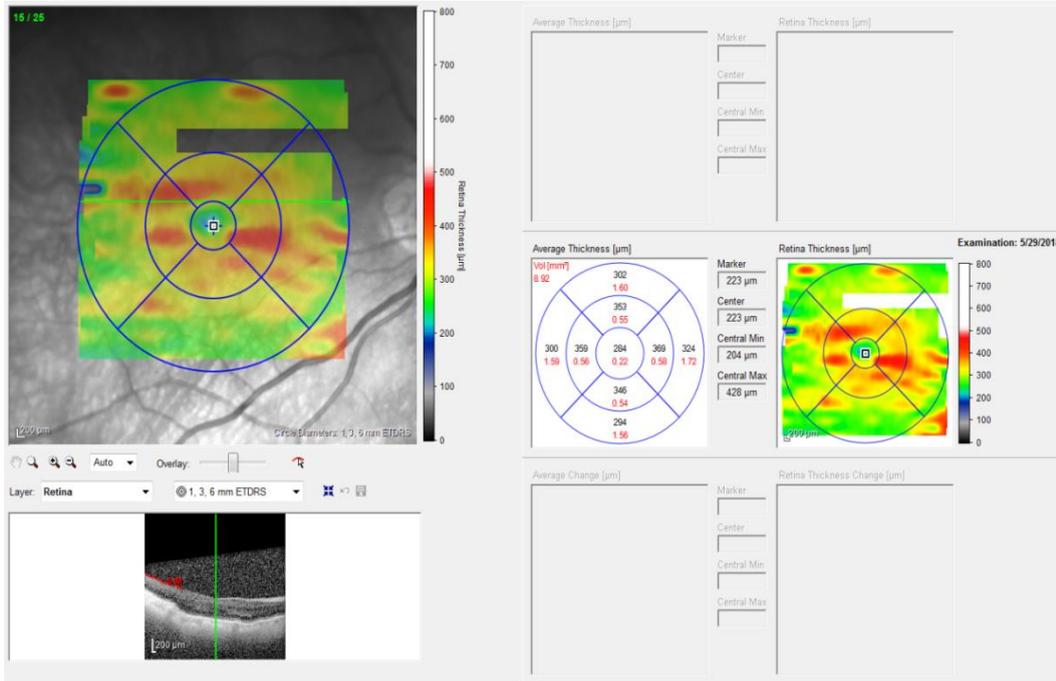


Figure (1): Preoperative OCT of patient 1.

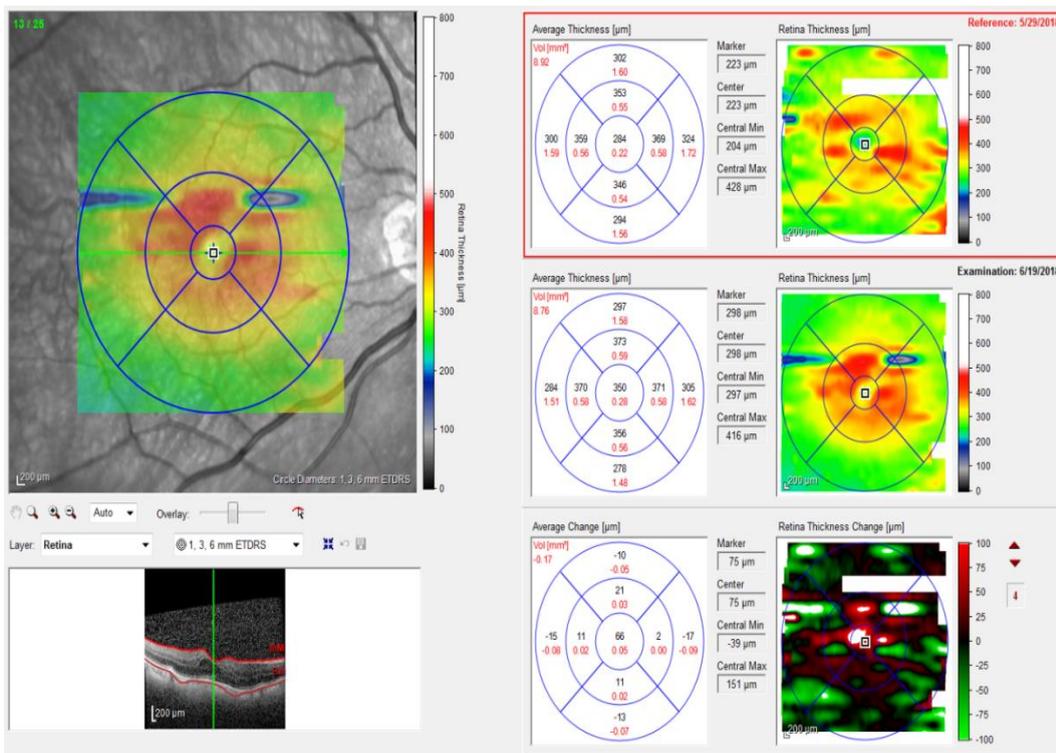


Figure (2): 2-week follow up OCT of patient 1.

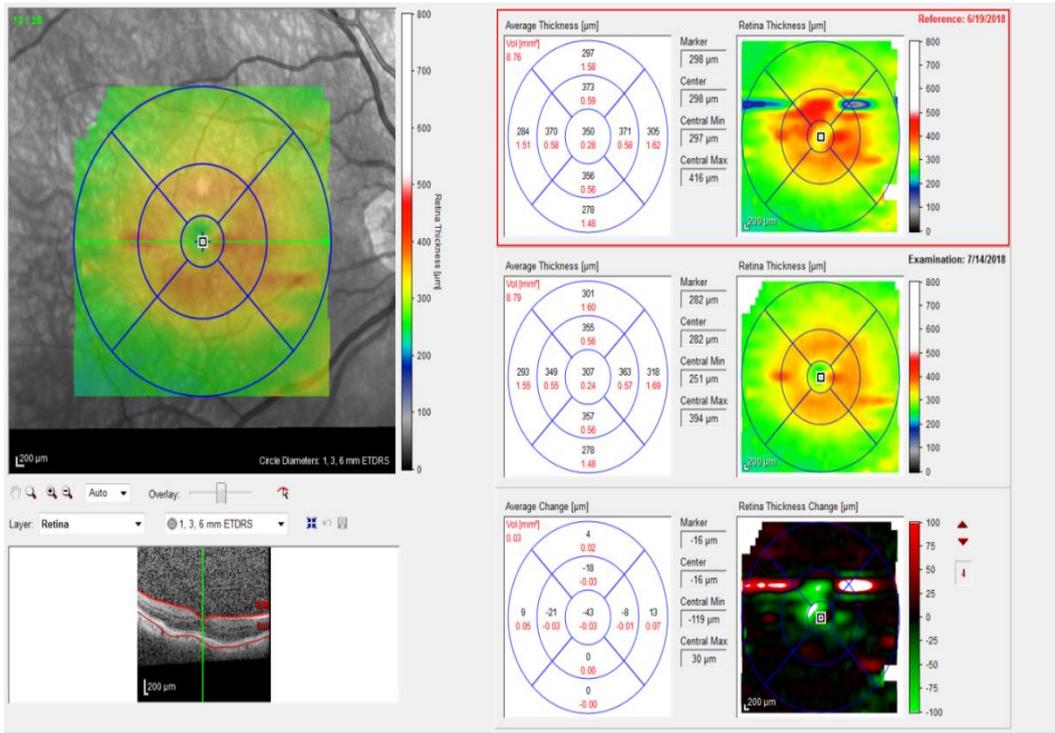


Figure (3): 6-week follow up OCT of patient 1.

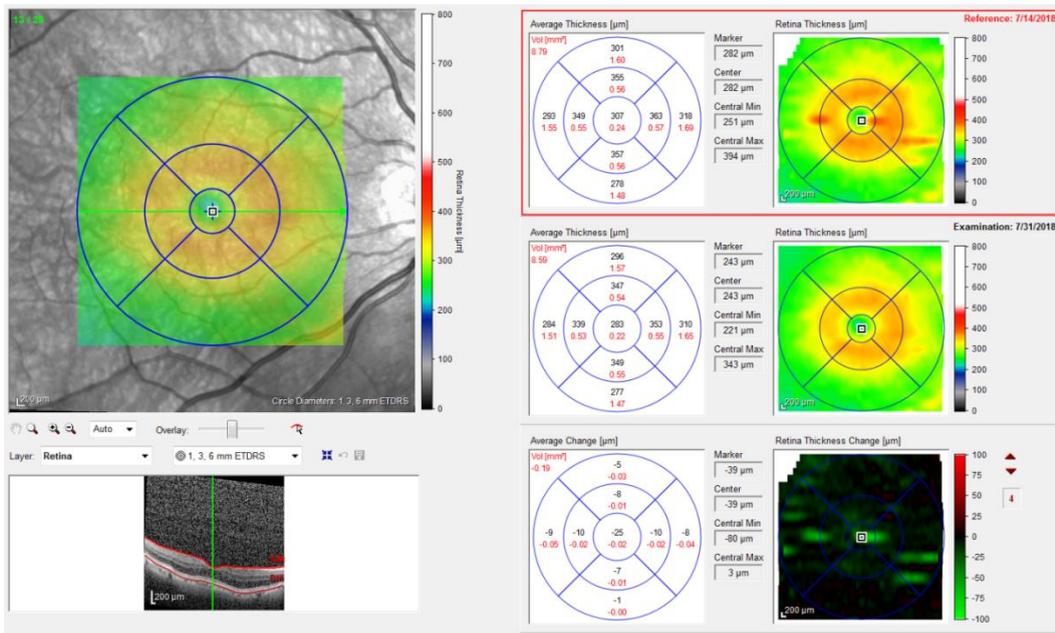


Figure (4): 8-week follow up OCT of patient 1.

Secondary outcomes:

Change of decimal BCVA:

Changes of decimal BCVA in 3 periods (from preoperatively to 2 weeks postoperatively, from 2 to 6 weeks postoperatively and from preoperatively to 6 weeks postoperatively) were lower in group C than in group A and B, however these are not statistically significant (table 11).

H: Kruskal Wallis test

p: p value for comparing between the three groups

Change of IOP:

Changes of IOP in 3 periods (from preoperatively to 2 weeks postoperatively, from 2 to 6 weeks postoperatively and from preoperatively to 6 weeks postoperatively) were lower in group C than in group A and B, however these are not statistically significant (table 12), Fig (11).

Table (11): Comparison between the three studied groups according to BCVA decimal changes

BCVA decimal Changes from	Group A (n = 21)	Group B (n = 18)	Group C (n = 19)	H	p
Pre to 2 weeks					
Min. – Max.	0.16 – 0.75	0.17 – 0.65	0.09 – 0.75		
Mean ± SD.	0.43 ± 0.15	0.43 ± 0.13	0.42 ± 0.16	0.446	0.800
Median	0.45	0.48	0.41		
2 weeks to 6 weeks					
Min. – Max.	0.0 – 0.34	0.0 – 0.17	0.0 – 0.33		
Mean ± SD.	0.07 ± 0.14	0.03 ± 0.06	0.08 ± 0.13	1.139	0.566
Median	0.0	0.0	0.0		
Pre to 6 weeks					
Min. – Max.	0.40 – 0.83	0.17 – 0.65	0.0 – 0.97		
Mean ± SD.	0.52 ± 0.12	0.46 ± 0.13	0.47 ± 0.22	0.887	0.642
Median	0.50	0.49	0.42		

Table (12): Comparison between the three studied groups according to IOP changes

IOP Changes from	Group A (n = 21)	Group B (n = 15)	Group C (n = 19)	H	p
Pre to 2 weeks					
Min. – Max.	-10.0 – 4.0	-6.0 – 3.0	-7.0 – 6.0		
Mean ± SD.	-1.62 ± 3.26	-1.47 ± 2.07	-0.32 ± 2.69	2.905	0.234
Median	-1.0	-2.0	-1.0		
2 weeks to 6 weeks					
Min. – Max.	-3.0 – 9.0	-3.0 – 2.0	-9.0 – 4.0		
Mean ± SD.	0.28 ± 3.16	-0.42 ± 1.78	-0.60 ± 2.95	0.004	0.998
Median	-0.50	0.0	0.0		
Pre to 6 weeks					
Min. – Max.	-7.0 – 6.0	-6.0 – 0.0	-6.0 – 6.0		
Mean ± SD.	-1.47 ± 2.89	-2.57 ± 1.83	-0.93 ± 3.32	1.725	0.422
Median	-2.0	-2.50	-1.50		

H: Kruskal Wallis test

p: p value for comparing between the three groups

Discussion

A lot of studies compared different PCME anti-inflammatory prophylaxis regimens including different topical NSAIDs either with each other or with topical steroids. Nevertheless, the current medical literature suggests that a consensus has not been reached regarding the appropriate methods for preventing acute pseudophakic CME.⁽²⁷⁾ In the current study no statistically significant difference was found in postoperative CSF thickness changes at 2 and 6 weeks after uneventful phacoemulsification among topical

NSAID and steroid, topical steroid only and subconjunctival triamcinolone groups, with similar results in decimal BCVA and IOP changes. Additionally, all three groups had varying statistically significant intraocular differences between baseline and 2 and 6 weeks. This statistically significant increases in postoperative retinal thickness measurements were maintained up to 6 week follow-up visit in all groups studied.

Similar results were shown by Tzelikis PF, et al.⁽²⁸⁾ in a comparative study of ketorolac 0.4% and nepafenac

0.1% for the prevention of cystoid macular oedema after phacoemulsification in a prospective placebo-controlled randomised study. In addition, Ticly FG, et al. (29) through a randomized trial of 81 patients to study the prophylactic use of ketorolac tromethamine after cataract surgery for up to 5 weeks, with 44 in the placebo group and 37 in the ketorolac group, showed that the incidence of angiographic CME was 2/44 (4.5%) in the control group and 2/37 (5.4%) in the ketorolac group, there was no evidence of CME in these patients on OCT analysis. A comparative study by Stock RA, et al. (30) of macular thickness by optical coherence tomography measurements after uneventful phacoemulsification using ketorolac tromethamine, nepafenac, vs a control group, preoperatively and postoperatively concluded that there is no significant differences in macular thickness were observed between the patient groups using two types of NSAIDs or between those groups and the control group that used propylene glycol, indicating that neither drug was superior to the other or the placebo. However, a slight macular thickening, without reduction of visual acuity, was observed in all groups.

However, a similar study by Shorstein NH, et al. (31) compared effectiveness of 3 prophylactic strategies to prevent clinical macular edema after phacoemulsification surgery, The drug regimens consisted of postoperative topical prednisolone acetate (PA) alone or with a nonsteroidal anti-inflammatory drug (NSAID) or intraoperative subconjunctival injection of 2 mg triamcinolone acetonide (TA) alone. The study concluded that adding a prophylactic NSAID to PA treatment was associated with a reduced risk of macular edema with visual acuity of 20/40 or worse also that the risk and safety of TA injection were similar to those of PA alone (31) McCafferty S, et al. (32) performed a prospective study for PCME prevention and risk factors in 1000 eyes with adjunctive once daily topical nepafenac 0.3% (503) versus placebo (497) where correlation of PCME to NSAID use and the presence of pre-operative risk factors for PCME were assessed including, contralateral PCME, diabetic retinopathy, retinal vein occlusion, macular hole, epiretinal membrane, macular degeneration, retinal detachment repair, and prostaglandin use, this study concluded that topical nepafenac 0.3% reduces PCME in patients with pre-operative risk factors for PCME compared to placebo but shows no benefit in patients without pre-operative risk factors. (32) Dieleman M, et al. (33) conducted a study of 400 eyes to compare single perioperative subconjunctival steroid depot versus postoperative steroid eyedrops in the prevention of intraocular inflammation and macular edema after cataract surgery, this study concluded that a single subconjunctival betamethasone acetonide injection appears to be a useful alternative to prolonged postoperative administration of dexamethasone eyedrops in controlling intraocular

inflammation and development of macular edema after phacoemulsification. (33)

Although, steroid exposure in any form or dosage can cause intraocular hypertension as a side effect and may present with delayed onset of several months. (34) no significant increase in IOP in either group was observed during the follow up; however, patients with glaucoma and other ocular pathology were excluded from this study. (33) Another study by Merkoudis N, et al. (35) compared peroperative subconjunctival injection of methylprednisolone (20 mg) and standard postoperative steroid drops (dexamethasone 1 mg/ml) after uneventful cataract surgery, this study concluded that a single subconjunctival injection of methylprednisolone depot at the end of uncomplicated cataract surgery is a safe and effective alternative to dexamethasone eye drops in preventing postoperative intraocular inflammation, and it might therefore be considered for treatment of individuals with compliance issues especially in elderly patients or in people with disabilities. However, the effect of subconjunctival depot steroids in glaucoma patients and in challenging cases with possibly high phacoemulsification times and/or iris manipulation remains to be investigated. (35)

In low risk patients, routine use of topical NSAIDs after uneventful cataract surgery is not necessary and puts an additional economic burden on our patients. Injection of 0.5 ml (20mg) triamcinolone acetonide posteriorly sub-tenon at the conclusion of surgery is as safe and effective in terms of prevention of intraocular inflammation and might therefore be considered for treatment of individuals with compliance issues especially in elderly patients or in people with disabilities. Further studies with longer follow up periods are recommended to get full picture of the changes of central macular thickness after uneventful cataract surgery and whether these are reversible or not.

Conclusion

Single subconjunctival triamcinolone depot injection at the end of uncomplicated cataract surgery is a safe and effective alternative to topical steroid eye drops in preventing postoperative intraocular inflammation.

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Conflicts of interest

There are no conflicts of interest.

References

1. Flach AJ. The incidence, pathogenesis and treatment of cystoid macular edema following cataract surgery. Transactions of the American Ophthalmological Society. 1998;96:557.
2. Shelsta HN, Jampol LM. Pharmacologic therapy of pseudophakic cystoid macular edema: 2010 update. Retina. 2011;31(1):4-12.
3. Kim SJ, Belair M-L, Bressler NM, Dunn JP, Thorne JE, Kedhar SR, et al. A method of reporting macular edema after cataract surgery using optical coherence tomography. Retina. 2008;28(6):870-6.
4. Bélair M-L, Kim SJ, Thorne JE, Dunn JP, Kedhar SR, Brown DM, et al. Incidence of cystoid macular edema after cataract surgery in patients with and without uveitis

- using optical coherence tomography. *American journal of ophthalmology*. 2009;148(1):128-35. e2.
5. Perente I, Utine CA, Ozturker C, Cakir M, Kaya V, Eren H, et al. Evaluation of macular changes after uncomplicated phacoemulsification surgery by optical coherence tomography. *Current eye research*. 2007;32(3):241-7.
 6. Loewenstein A, Zur D. Postsurgical cystoid macular edema. *Macular Edema*. 47: Karger Publishers; 2010. p. 148-59.
 7. Henderson BA, Kim JY, Ament CS, Ferrufino-Ponce ZK, Grabowska A, Cremers SL. Clinical pseudophakic cystoid macular edema: risk factors for development and duration after treatment. *Journal of Cataract & Refractive Surgery*. 2007;33(9):1550-8.
 8. Falavarjani KG, Parvareh M-M, Modarres M, Hashemi M, Samiy N. Intravitreal bevacizumab for pseudophakic cystoid macular edema; a systematic review. *Journal of ophthalmic & vision research*. 2012;7(3):235.
 9. Dellaporta A. Fundus changes in postoperative hypotony. *American journal of ophthalmology*. 1955;40(6):781-5.
 10. Irvine SR. A Newly Defined Vitreous Syndrome Following Cataract Surgery*: Interpreted According to Recent Concepts of the Structure of the Vitreous, The Seventh Francis I. Proctor Lecture. *American journal of ophthalmology*. 1953;36(5):600b.
 11. Gass J, Norton E. Cystoid macular edema and papilledema following cataract extraction: a fluorescein fundoscopic and angiographic study. *Archives of Ophthalmology*. 1966;76(5):646-61.
 12. Miyake K, Ibaraki N. Prostaglandins and cystoid macular edema. *Survey of ophthalmology*. 2002;47:S203-S18.
 13. Miyake K, Masuda K, Shirato S, Oshika T, Eguchi K, Hoshi H, et al. Comparison of diclofenac and fluorometholone in preventing cystoid macular edema after small incision cataract surgery: a multicentered prospective trial. *Japanese journal of ophthalmology*. 2000;44(1):58-67.
 14. Cohen SM, Davis A, Cukrowski C. Cystoid macular edema after pars plana vitrectomy for retained lens fragments. *Journal of Cataract & Refractive Surgery*. 2006;32(9):1521-6.
 15. Hayashi K, Igarashi C, Hirata A, Hayashi H. Changes in diabetic macular oedema after phacoemulsification surgery. *Eye*. 2009;23(2):389.
 16. Schmier JK, Halpern MT, Covert DW, Matthews GP. Evaluation of costs for cystoid macular edema among patients after cataract surgery. *Retina*. 2007;27(5):621-8.
 17. Ram J, Gupta A, Kumar S, Kaushik S, Gupta N, Severia S. Phacoemulsification with intraocular lens implantation in patients with uveitis. *Journal of Cataract & Refractive Surgery*. 2010;36(8):1283-8.
 18. Yonekawa Y, Kim IK. Pseudophakic cystoid macular edema. *Current opinion in ophthalmology*. 2012;23(1):26-32.
 19. Heier JS, Topping TM, Baumann W, Dirks MS, Chern S. Ketorolac versus prednisolone versus combination therapy in the treatment of acute pseudophakic cystoid macular edema. *Ophthalmology*. 2000;107(11):2034-8.
 20. Grover S, Murthy RK, Brar VS, Chalam KV. Normative data for macular thickness by high-definition spectral-domain optical coherence tomography (Spectralis). *American journal of ophthalmology*. 2009;148(2):266-71.
 21. Colin J. The role of NSAIDs in the management of postoperative ophthalmic inflammation. *Drugs*. 2007;67(9):1291-308.
 22. Cho H, Wolf KJ, Wolf EJ. Management of ocular inflammation and pain following cataract surgery: focus on bromfenac ophthalmic solution. *Clinical ophthalmology (Auckland, NZ)*. 2009;3:199.
 23. Baklayan GA, Patterson HM, Song CK, Gow JA, McNamara TR. 24-Hour evaluation of the ocular distribution of 14C-labeled bromfenac following topical instillation into the eyes of New Zealand white rabbits. *Journal of Ocular Pharmacology and Therapeutics*. 2008;24(4):392-8.
 24. Hariprasad SM, Callanan D, Gainey S, He Y-G, Warren K. Cystoid and diabetic macular edema treated with nepafenac 0.1%. *Journal of Ocular Pharmacology and Therapeutics*. 2007;23(6):585-90.
 25. McGhee CN, Dean S, Danesh-Meyer H. Locally administered ocular corticosteroids. *Drug Safety*. 2002;25(1):33-55.
 26. Flach AJ, Dolan BJ, Donahue ME, Faktorovich EG, Gonzalez GA. Comparative effects of ketorolac 0.5% or diclofenac 0.1% ophthalmic solutions on inflammation after cataract surgery. *Ophthalmology*. 1998;105(9):1775-9.
 27. Yilmaz T, Cordero-Coma M, Gallagher M. Ketorolac therapy for the prevention of acute pseudophakic cystoid macular edema: a systematic review. *Eye*. 2012;26(2):252.
 28. Tzelikis PF, Vieira M, Hida WT, Motta AF, Nakano CT, Nakano EM, et al. Comparison of ketorolac 0.4% and nepafenac 0.1% for the prevention of cystoid macular oedema after phacoemulsification: prospective placebo-controlled randomised study. *British journal of ophthalmology*. 2015;99(5):654-8.
 29. Ticyl FG, Lira RP, Zanetti FR, Machado MC, Rodrigues GB, Arieta CEL. Prophylactic use of ketorolac tromethamine in cataract surgery: a randomized trial. *Journal of Ocular Pharmacology and Therapeutics*. 2014;30(6):495-501.
 30. Stock RA, Galvan DK, Godoy R, Bonamigo EL. Comparison of macular thickness by optical coherence tomography measurements after uneventful phacoemulsification using ketorolac tromethamine, nepafenac, vs a control group, preoperatively and postoperatively. *Clinical Ophthalmology (Auckland, NZ)*. 2018;12:607.
 31. Shorstein NH, Liu L, Waxman MD, Herrinton LJ. Comparative effectiveness of three prophylactic strategies to prevent clinical macular edema after phacoemulsification surgery. *Ophthalmology*. 2015;122(12):2450-6.
 32. McCafferty S, Harris A, Kew C, Kassam T, Lane L, Levine J, et al. Pseudophakic cystoid macular edema prevention and risk factors; prospective study with adjunctive once daily topical nepafenac 0.3% versus placebo. *BMC ophthalmology*. 2017;17(1):16.
 33. Dieleman M, Wubbels RJ, van Kooten-Noordzij M, de Waard PW. Single perioperative subconjunctival steroid depot versus postoperative steroid eyedrops to prevent intraocular inflammation and macular edema after cataract surgery. *Journal of Cataract & Refractive Surgery*. 2011;37(9):1589-97.
 34. Kalina RE. Increased intraocular pressure following subconjunctival corticosteroid administration. *Archives of Ophthalmology*. 1969;81(6):788-90.
 35. Merkoudis N, Wikberg Matsson A, Granstam E. Comparison of perioperative subconjunctival injection of methylprednisolone and standard postoperative steroid drops after uneventful cataract surgery. *Acta ophthalmologica*. 2014;92(7):623-8.