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ORIGINAL ARTICLE

Topical Bromfenac Combined with Prednisolone Versus Topical Prednisolone in The Management of Pseudophakic Cystoid Macular OedemaHani A. Albialy^{1*}, Doaa. M.Guda², Mostafa.M.Wagih³¹Ophthalmology Department, Zagazig University, Zagazig, Egypt²Zagazig ophthalmic hospital, Zagazig, Egypt³Ophthalmology Department, Zagazig University, Zagazig, Egypt***Corresponding author:**Hani A. Albialy
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Submit Date 2019-12-03**Revise Date** 2019-12-09**Accept Date** 2019-12-13**ABSTRACT****Purpose:** To compare the efficacy of topical Bromfenac 0.09% combined with topical Prednisone acetate 1% versus topical Prednisolone alone in the management of pseudophakic cystoid macular oedema.**Methods:** Randomized simple comparative study included 20 eyes of 20 patients diagnosed with cystoid macular oedema (CMO) following uncomplicated phacoemulsification . Ten eyes were received topical Bromfenac 0.09% combined with topical Prednisone acetate 1% while the other 10 eyes received only topical Prednisone acetate 1% . Outcomes were measured at the baseline, one month, two months and three months after treatment by visual acuity assessment, slit lamp biomicroscopic examination and OCT macular thickness scan.**Results:** Mean baseline BCVA in Group 1 was 0.65 ± 0.23 , and after 3 months was 0.35 ± 0.21 . Group 2 showed baseline mean visual acuity 0.75 ± 0.19 , at the end of study mean values were 0.35 ± 0.21 . Mean macular thickness of Group 1 at baseline were $381.3 \pm 72.3 \mu$, while the mean macular thickness of group 2 were $382 \pm 115.7 \mu$. At the end of study macular thickness group 1 mean values were $307.2 \pm 67.5 \mu$, while group 2 mean values were $356.1 \pm 108.82 \mu$. There was statistically significant difference in central macular thickness and visual acuity between baseline values and at two and three months visits .**Conclusion:** Bromfenac 0.09% combined with topical Prednisone acetate 1% significantly decreased macular thickness and improved visual acuity in cases with postoperative pseudophakic macular oedema compared to patients received topical Prednisone acetate 1% only.**Keywords:** Pseudophakic cystoid macular oedema , Irvin gas syndrome, Bromfenac 0.09%, Prednisone acetate 1%, cataract surgery.**INTRODUCTION**

Pseudophakic cystoid macular edema (PCME) is one of the common causes of visual impairment following cataract extraction [1]. It's also named Irvine Gass syndrome as it is initially reported by S. Rodman Irvine in 1953 [2] and it's fluorescein angiography (FA) pattern described by Donald and Gass later on [3]. The incidence of the disease was with very high percentage (20 to 60%) with old-fashioned techniques of cataract extraction and diminished greatly with modern surgery techniques (0% to 2.35%) [4, 5]. Many theories had described the pathogenesis of Irvine Gass syndrome . The main factor is an inflammatory process which lead to paramacular vascular dilatation and breakdown of blood retinal

barrier which ensue the oedema leading to eosinophilic transudation which accumulate in the outer plexiform and inner nuclear layer of the retina leading to the cystic changes, side-by-side with subretinal fluid which may also present [6]. Surgical manipulation may lead to the release of arachidonic acid from uveal tissue with subsequent release of leukotrienes via lipooxygenase pathway or prostaglandins via cyclooxygenase (COX) pathway which diffuse posteriorly to disturb blood retinal barrier with subsequent leakage and edema. It's not well understood why leakage is only confined to macula , but this may be partially explained by the vascularity of the macula with subsequent lack in fluid absorption [7,8].

Diagnosis of pseudophakic cystoid macular oedema (CMO) can be achieved clinically, by fluorescein angiography, and with optical coherence tomography (OCT). Several risk factors preclude and aggravate incidence of pseudophakic cystoid macular edema as uveitis, glaucoma medication, complicated surgery with excessive trauma leading to post-operative inflammation or vitreous loss, and less commonly retinal vein occlusion or retinal membrane which present before surgery [9]. Different treatment modalities were reported for (PCME) management but none of them is standardized [10]. They include non steroidal anti-inflammatory drugs NSAIDs (ketorolac 0.4%, bromofenac 0.09%, nepafenac 0.1% and diclofenac 0.1%) which topically applied to inhibit cyclooxygenase (COX1&COX2) enzymes by reducing prostaglandins production [11]. Corticosteroids are used in the prophylaxis and treatment of different ocular disease due to its long-term anti-inflammatory effect as it prevent prostaglandins and leukotrienes production [12], prevention of prostaglandins production is achieved by inhibitions of phospholipase A2 In arachidonic acid Cascade it also inhibits macrophages and neutrophils migration and decreased capillary permeability and vasodilatation [11]. Anti-vascular endothelial growth factor has been shown to be effective in refractory pseudophakic cystoid macular edema [13]. Carbonic anhydrase inhibitor like oral acetazolamide is thought to improve macular edema in retinitis pigmentosa but the rule in pseudophakic cystoid macular oedema still uncertain but it is thought to increase pumping activity of retinal pigment epithelium [14]. Surgical intervention by vitreolysis or vitrectomy may play a role in treatment [15].

METHODS

This prospective simple randomized comparative study was designed to study the efficacy of using topical bromfenac 0.09% combined with topical Prednisone acetate 1% versus topical prednisolone alone in the management of pseudophakic cystoid macular oedema. Inclusion criteria were patients with uncomplicated cataract surgery complicated with postoperative cystoid macular edema diagnosed clinically and furtherly confirmed by optical coherence tomography (OCT) with increase in central macular thickness. Exclusion criteria included any case that received preoperative prophylactic medications (such as NSAID), patients with diseases that can ensue CMO such as diabetes mellitus, retinal vein occlusion, intraoperative capsular tear and patient receiving anti- glaucoma treatment.

A detailed ophthalmological examination including slit-lamp examination, visual acuity assessment (BCVA) using Snellen chart converted to logMAR, intraocular pressure measurement, and OCT to measure baseline central thickness was done prior to starting medication. Written informed consent was obtained from all participants and the study was performed and approved by the research ethical committee of Alfath eye hospital, Zagazig. The work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. A total of 20 eyes of 20 patients with pseudophakic cystoid macular edema were enrolled in this study from January 2019 to June 2019 which further divided into two groups. Group 1 received topical bromfenac 0.09% drops twice daily combined with prednisolone acetate four times daily then tapered off by one drop per day weekly for four weeks. Group 2 received topical Prednisolone drops four times daily for one week then tapered off by one drop per day weekly for four weeks with 1:1 ratio bromofenac and prednisolone : prednisolone ratio. Follow-up was done weekly for the first month and monthly for the next two months. Visual acuity and macular oedema clinically assessed on slit lamp biomicroscopy, and OCT for the central thickness was done monthly and the result recorded and further analysed statistically using SPSS software (Statistical Package for the Social Sciences, version 23, SPSS Inc., Chicago, III, USA).

RESULTS

This study included 20 eyes of 20 patients (9) were males & (11) were females, the mean age group were (56.9) years ranging from (52) to (79). The mean visual acuity at starting of the study in group 1 were $(0.65) \pm 0.23$ ranging from (0.3) to (1) and for group 2 were $(0.75) \pm 0.19$ Ranging from (0.5) to (1). At the end of study visual acuity mean values were $(0.35) \pm 0.21$ Ranging from (0.2) to (0.8). (Table1). OCT macular thickness mean values at the start of the study were $(381.3) \pm 72.2\mu$ Ranging from (305μ) to (511μ) For group 1 & group 2 were $(382) \pm 115.7\mu$ ranging from (297μ) to (570μ) . At the end of study macular thickness group 1 mean values were $(307.2) \pm 67.5\mu$ Ranging from (251μ) to (413μ) , while group 2 mean values were $(356.1) \pm 108.82\mu$ Ranging from (251μ) to (570μ) .

Statistical analysis of this study revealed significant values between both groups concerning visual acuity and macular central thickness (Table. 2).

Table (2) Macular thickness Values in both groups

Drugs		Baseline	One month	Two months	Three months
Bromfenac 0.09	N	10	10	10	10
	Mean	.6500	.5700	.4700	.3500
	Std. Deviation	.23214	.22136	.17029	.21213
	Minimum	.30	.20	.30	.20
	Maximum	1.00	.80	.80	.80
Control	N	10	10	10	10
	Mean	.7500	.6900	.6600	.5900
	Std. Deviation	.19003	.21318	.19551	.31429
	Minimum	.50	.30	.30	.20
	Maximum	1.00	1.00	1.00	1.00
Total	N	20	20	20	20
	Mean	.7000	.6300	.5650	.4700
	Std. Deviation	.21275	.22029	.20333	.28855
	Minimum	.30	.20	.30	.20
	Maximum	1.00	1.00	1.00	1.00

Table (2) Macular thickness Values in both groups

Drugs		Baseline	One month	Two months	Three months
Bromfenac 0.09	N	10	10	10	10
	Mean	381.3000	362.2000	335.7000	307.2000
	Std. Deviation	72.26656	74.08074	48.10648	67.47477
	Minimum	305.00	283.00	272.00	251.00
	Maximum	511.00	473.00	410.00	413.00
Control	N	10	10	10	10
	Mean	382.9000	380.8000	369.0000	356.1000
	Std. Deviation	115.70120	99.13717	93.64116	108.82141
	Minimum	297.00	297.00	271.00	251.00
	Maximum	570.00	571.00	532.00	570.00
Total	N	20	20	20	20
	Mean	382.1000	371.5000	352.3500	331.6500
	Std. Deviation	93.89126	85.70912	74.44198	91.62583
	Minimum	297.00	283.00	271.00	251.00
	Maximum	570.00	571.00	532.00	570.00

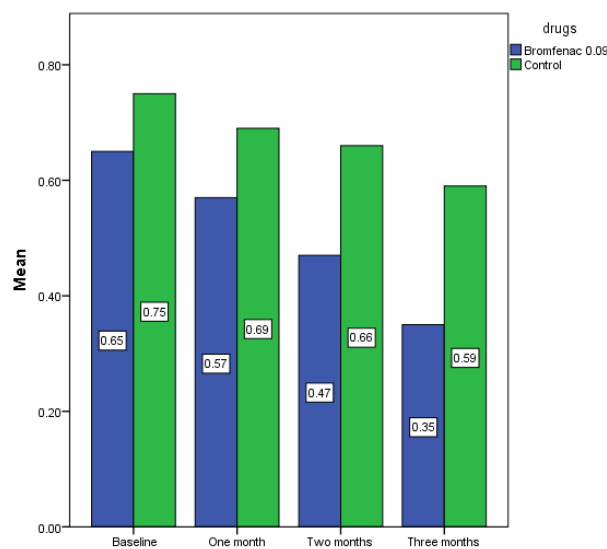


Figure 1: visual acuity values in both groups

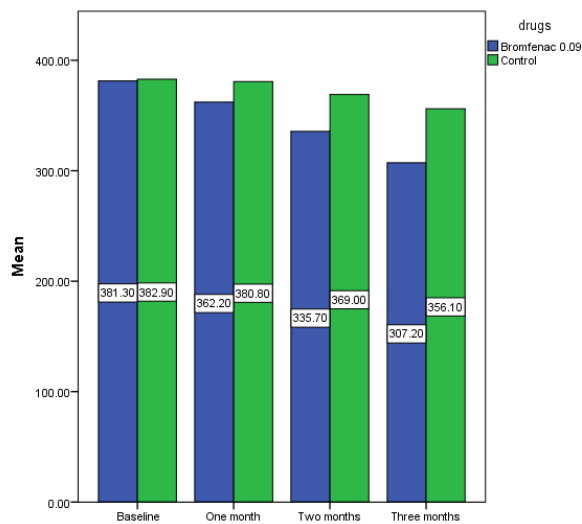


Figure 2: Comparison of macular thickness between both groups

DISCUSSION

We evaluated the safety and efficacy of the topical application of Bromfenac 0.09% combined with topical Prednisone acetate 1% versus topical Prednisone alone in the management of pseudophakic cystoid macular oedema. We assessed the central macular thickness and visual acuity in both groups. In group 1 there was significant decrease of foveal thickness between baseline (on one side) and one month, two months and 3 months (on the other side) as P value was ≤ 0.05 . Group 1 visual acuity showed significant improvement in visual acuity in two months and 3 months (P value ≤ 0.05), while group 2 showed insignificant improvement of visual acuity in all visits, (P value ≥ 0.05).

Based on the above results, we conclude that Bromfenac 0.09% combined with topical Prednisone acetate 1% is better than topical Prednisone acetate 1% alone improved visual acuity and decreased the foveal thickness more than topical Prednisone.

Rho compared bromfenac 0.09, diclofenac 0.1 and ketorolac 0.5% in patients exhibiting CME within one year after uncomplicated cataract surgery and revealed that there is improvement of visual acuity in all treatments with a significant difference in favor of bromfenac [16]. Kadrmas showed that 11 cases have cystoid macular edema treated with ketorolac 0.4 after cataract surgery but was unresponsive and switched to treatment with bromfenac 0.09%, all cases showed complete resolution of cystoid macular edema after treatment of bromfenac as well as an improvement in visual acuity [17].

Warren compared five groups of pseudophakic cystoid macular edema, diclofenac 0.1%, ketorolac 0.4%, nepafenac 0.1%, bromfenac 0.09% and

placebo and revealed that bromfenac and nepafenac produced significantly greater reduction in macular thickness and visual acuity than placebo group [18].

Wang compared bromfenac 0.1%, fluorometholone 0.1% and dexamethasone 0.1% and reported decreased foveal thickness in bromfenac group than fluoremethasone and dexamethasone groups [19].

Li did retrospective study between two groups group one received bromfenac three days preoperatively and two weeks postoperatively and control group with no bromfenac and both groups received dexamethasone reported that mean foveal thickness didn't change significantly in bromfenac group but increased significantly in control group (steroid only) and cystoid macular edema was statistically similar for both groups [20].

The comparative study done by Jung reported that there is no significant change between bromfenac 0.1% and ketorolac 0.45 in foveal thickness or visual acuity effect, while higher effects were obtained in steroid control group [21]. Walters and Hoy compared bromfenac 0.07% and placebo and reported that incidence of cystoid macular edema over 22 day follow up was in bromfenac group was 0.5%, while placebo group was 1.5% [22, 23]. Henderson reported that macular edema in bromfenac 0.09 group was 0.7% while placebo group was 1.4% [24]. Although this clinical trial study has some limitations as small sample size and we didn't compare bromfenac with other non-steroidal drugs, we recommend bromfenac 0.09 for prophylaxis and treatment of pseudophakic cystoid macular edema.

Conflict of Interest: no conflict of interest

Financial closure: Non

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