

Role of Bromfenac in the Prevention of Pseudophakic Cystoid Macular Edema

P. Sreenivasulu¹, C.Hari Hara Prasad²

ABSTRACT

Introduction: Pseudophakic Cystoid Macular Edema (CME) remains a common cause of reduced vision after cataract surgery. The aim of the present study was to assess the significance of Bromfenac along with corticosteroids which is used routinely for post operative cataract surgeries.

Material and Methods: Among 1270 studied population, Group 1 - 600 cases were treated with corticosteroids eye drops only for the period of 6 weeks in tapering dose. Group 2 - 600 cases were treated with corticosteroids eye drops for the period of 6 weeks in tapering dose and bromfenac eye drops twice daily preoperatively for 2 days and 4 weeks post operatively along with corticosteroids for 6 weeks in tapering dose. Group 3 - 70 cases were treated with both corticosteroids and Bromfenac for 8 weeks.

Results: In patients not at risk were treated with corticosteroids only develop Pseudophakic CME in 15 (2.5%) patients out of 600 patients. The patients not at risk were treated with corticosteroids with bromfenac combination, develop Pseudophakic CME in 2 (0.33%) patients out of 600 patients. The patients at risk were treated with combination of corticosteroids and bromfenac, develop Pseudophakic CME in 20 (28.5%) patients out of 70 patients.

Conclusion: Bromfenac along with corticosteroids more effectively reduce the incidence of Pseudophakic Cystoid macular edema than either of the drugs alone.

Keywords: Corticosteroid, Bromfenac, Pseudophakic Cystoid Macular Edema

INTRODUCTION

Pseudophakic Cystoid Macular Edema (CME) remains a common cause of reduced vision after cataract surgery. Pseudophakic CME was first described by A. Ray Irvine and Donald Gass described that peak incidence occur at 6 weeks postoperatively.^{1,2} Pseudophakic CME is also called as Irvine-Gass Syndrome.

Pseudophakic CME is the accumulation of extracellular fluid in the outer plexiform and inner nuclear layer of the macula that occurs as a result of disruption of blood retinal barrier. They were of three types: Angiographic Pseudophakic CME seen on fluorescein angiography, which may be or may not be associated with reduced vision.³ Clinical pseudophakic CME associated with decreased visual acuity.⁴ Optical coherence tomography(OCT) definition is also proposed.⁵

Angiographic CME incidence is 15-30% worldwide.⁶ Clinical CME is 0.12-0.25%,⁷ OCT CME is 41%.⁸ Risk factors for Pseudophakic CME are Capsular tear leads to vitreous loss,⁹ vitreous traction at incision site, retained lens fragments¹⁰, uveitis¹¹, diabetes¹², vascular diseases like Hypertension, CRVO etc., Type of IOL - ACIOL, Iris fixated IOL.¹³

Various methods are available to know the different types of Pseudophakic CME. Clinical CME is diagnosed with Ophthalmoscopic examination which shows honey comb pattern. Angiographic pseudophakic CME diagnosed with Fluorescein angiography which shows petaloid pattern. OCT CME diagnosis by OCT which shows loss of foveal depression, retinal thickening and cystic hyporeflective area within macula. Corticosteroids reduces the inflammation by inhibiting the phospholipase A2 and Non steroidal Anti-inflammatory drugs (NSAIDs) inhibit the COX, which is the major isoform.¹⁴ Corticosteroids is the routinely used for treatment of post operative cataract surgeries. Side effects of Corticosteroids and NSAIDs are glaucoma, conjunctival hyperaemia, toxic to the cornea in the form of punctate epithelial erosions on prolonged usage.

Corticosteroids and NSAIDs are used to prevent the CME, few studies suggest that they act synergistically.¹⁵ Hence this study has selected use of corticosteroids and Bromfenac to reduce the incidence of Pseudophakic CME.

The aim of the present study was to assess the significance of Bromfenac along with corticosteroids which is used routinely for post operative cataract surgeries

MATERIAL AND METHODS

This was a prospective study done for two years (2014 -2015) at Department of Ophthalmology, Government General Hospital, Ananthapuramu. Ethical Committee was taken for doing this study and informed consent was taken from all the studied population before the start of the study.

Bromfenac (0.09%) eye drops was selected for doing this study among various NSAIDs because of many reasons such as reaches peak concentration in aqueous humor in 2-3 hours after administration, remain affectively for more than 12 hours and can be found in retinal tissue 24 hours¹⁶, rapidly penetrates to produce early and sustain drug levels in all ocular tissues¹⁷, no reports of systemic toxicity have been published and bromfenac has good topical tolerance effect with no incidence of adverse effects¹⁸, improves the visual acuity less retinal thickening¹⁹, more stable macular volume, used twice daily whereas other NSAIDs used four times a day.²⁰

A total of 1270 cases were selected to do this study. For ease of

¹Associate Professor, ²Assistant Professor, Government Medical College and General Hospital, Ananthapuramu, India

Corresponding author: Dr. P. Sreenivasulu M.D., Associate Professor, Department of Ophthalmology, Government General Hospital, Ananthapuramu - 515001, Andhra Pradesh, India

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the study, the studied population were divided into three groups.

Group 1 - Persons attending to Ophthal OPD for follow-up after cataract surgery without any risk factors related to Pseudophakic CME

Group 2 - Persons attending to Ophthal OPD for follow-up after cataract surgery without any risk factors related to Pseudophakic CME

Group 3 - Persons attending to Ophthal OPD for follow-up after cataract surgery with any risk factors related to Pseudophakic CME

Among 1270 studied population, Group 1 - 600 cases were treated with corticosteroids eye drops only for the period of 6 weeks in tapering dose. Group 2 - 600 cases were treated with corticosteroids eye drops for the period of 6 weeks in tapering dose and bromfenac eye drops twice daily preoperatively for 2 days and 4 weeks post operatively along with corticosteroids for 6 weeks in tapering dose. Group 3 - 70 cases were treated with both corticosteroids and Bromfenac for 8 weeks.

All groups were advised to come for follow-up monthly once, and those patients were observed for 6 months or more for vision and ophthalmoscopic examination.

STATISTICAL ANALYSIS

All the results were entered and analyzed. Statistical analysis was done using Graph pad software by Fischer's exact test. The p value <0.05 is considered significant

RESULTS

A total of 1270 cataract surgery operated patients were selected to do this study. Post operative patients who were came for follow up, divided into 3 groups. Among 1270 most of the cataract surgeries were done by Posterior chamber IOL (Intraocular Lens) methods. 1250 (98.4%) surgeries by PC IOL and 20 (1.5%) were operated by AC IOL.

Out of 1270 patients, 70 (5.51%) were presented with risk factors for Pseudophakic cystoid macular edema. Among 70 patients, most of them were Diabetics and hypertensives.

A total of 37 (2.91%) patients out of 1270 were developed Pseudophakic cystoid macular edema. Pseudophakic CME was observed most commonly in postoperative patients with risk factors (Group 3).

In patients not at risk were treated with corticosteroids only develop Pseudophakic CME in 15 patients out of 600 patients (Table-1). The patients not at risk were treated with corticosteroids with bromfenac combination, develop Pseudophakic CME in 2 patients out of 600 patients. The patients at risk were treated

with combination of corticosteroids and bromfenac, develop Pseudophakic CME in 20 patients out of 70 patients.

On statistical analysis, p value was calculated. There is a significant association between groups (Table-2).

DISCUSSION

Pseudophakic cystoid macular edema is a potentially serious vision threatening complication of cataract surgery. Diagnosis of Pseudophakic clinically by presenting complaints of decreased vision, which is known as "Clinical Cystoid Macular Edema". Acute Pseudophakic CME is defined as CME which occurs within 6 months of cataract surgery. Chronic Pseudophakic CME is defined when CME occurs after 6 months of cataract surgery.

The etiology of Pseudophakic CME is multifactorial including hypotony, surgical trauma. Major cause is in aqueous or vitreous humor there is up regulation of inflammatory mediators like prostaglandins, cytokines, histamines after surgery. Inflammatory mediators are responsible for increase in vascular permeability by breaking down the blood aqueous and blood retinal barrier.²¹ In Outer plexiform and inner nuclear layer of the retina, accumulation of eosinophils occurs which creates cystic spaces and in turn coalesce of all spaces to form a large pocket of fluid in macular area.

In the present study, total of 37 (2.91%) patients out of 1270 were developed Pseudophakic cystoid macular edema. Pseudophakic CME was observed most commonly in postoperative patients with risk factors (Group 3).

In patients not at risk were treated with corticosteroids only develop Pseudophakic CME in 15 (2.5%) patients out of 600 patients. The patients not at risk were treated with corticosteroids with bromfenac combination, develop Pseudophakic CME in 2 (0.33%) patients out of 600 patients. The patients at risk were treated with combination of corticosteroids and bromfenac, develop Pseudophakic CME in 20 (28.5%) patients out of 70 patients as per this study.

Wittpenn et al¹⁵ observed none of the Clinical/OCT CME was reported from ketorolac patients, whereas 5 out of 278 patients who received perioperative prednisolone developed CME. Yavas et al²² reported that 15% of patients who received indomethacin only and 0% of patients who received perioperative and post operative topical indomethacin developed angiographic PCME. Many other studies supported that Pseudophakic CME incidence decreases with topical administration of NSAIDS²³⁻²⁵ Studies also documented that there is decrease in total macular volume and macular swelling on administration of NSAIDS.²⁶ Bromfenac is an excellent drug with good pharmacokinetic

	Group 1	Group 2	Group 3
Total number of patients	600	600	70
Pseudophakic CME	15	2	20
Percentage of Pseudophakic CME	2.5%	0.33%	28.5%

Table-1: Incidence of Pseudophakic CME in 3 groups.

	Group 1 Vs Group 2	Group 2 Vs Group 3	Group 1 Vs Group 3
p value	0.0022	0.0001	0.0001
Significance	SS	ESS	ESS

ESS - Extremely Statistically Significant; SS - Statistically Significant

Table-2: Showing significance of Pseudophakic CME incidence

properties and have efficacy on clinical trials by topical administration. Bromfenac for prevention of pseudophakic CME was supported George Voyatzis et al²⁷ who was documented by observing 4 case studies, combination of corticosteroids and bromfenac more effectively decrease CME than either class of agents alone.

Predominantly Pseudophakic CME is observed in patients with risk factors, 28.5% when compared with post operative patients without risk factors. Patients who were diagnosed with CME were referred to higher specialty hospitals to consult retina specialist for further evaluation and management, as our institute is not having specialty clinic for retina.

In this study there is a significant decrease in incidence of Pseudophakic CME by preoperative and post operative instillation of both corticosteroids and bromfenac ophthalmic solutions. Incidence is more in patients with risk factors for Pseudophakic CME significantly when compared with patients without any risk factors

Use of corticosteroid with NSAID eye drops is more effective in reducing cystoid macular edema than corticosteroid monotherapy. Prolonged use of corticosteroids can cause raised intraocular pressure. It suggested that NSAIDs and corticosteroids may work effectively for prevention of Pseudophakic CME appearing after surgery.

There are many recent advances has come now-a-days for the treatment of Pseudophakic Cystoid macular edema such as Intravitreal injection of triamcinolone, NSAIDs - Diclofenac²⁸, Anti-VEGF, Infliximab²⁹, Subcutaneous injection os INF-a³⁰, surgical treatments like Laser vitreolysis, Parsplana vitrectomy.⁷ All the treatmnet are still undergoing various trials and pathogenetic mechanism of Pseudophakic CME is not clearly known, which is not giving enough chances to find the targeted drug for prevention of Pseudophakic CME.

Conclusion:

The Bromfenac 0.09% is preferred drug in reducing pain, post surgical inflammation and to prevent treat the cystoid macular edema after cataract surgery with no significant adverse effects. Bromfenac along with corticosteroids effectively reduce the incidence of Pseudophakic Cystoid macular edema.

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