Original Article

Compare the safety and efficacy of loteprendol etabonate 0.5% and prednisolone acetate 1% in the post operative inflammation following cataract extraction with intra ocular lens implant.

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Keywords: *Inflammation, Steroids, Intraocular Pressure, Loteprednol, Prednisolone*

Abstract

Background: Inflammatory conditions represent one of the most common encountered clinical challenges in the ophthalmology. Topical steroids remain the cornerstone of ocular therapy. Loteprednol etabonate is a site-specific agent, approximates the efficacy of prednisolone acetate and has minimal effect on intraocular pressure (IOP). Limited studies have compared these two drugs, hence, it was considered worthwhile to compare loteprendol etabonate and prednisolone acetate in post operative inflammation following cataract extraction with IOL implant.

Methodology: 30 patients operated for cataract extraction surgery with IOL implantation were studied for post operative inflammation and IOP changes, were divided into two groups. Group A received loteprednol etabonate and group B received prednisolone acetate. Cells in the anterior chamber (AC), flare were graded Signs of post operative inflammation including cells in anterior chamber (AC) and flare score were observed on day 1, 3, 8, 15 and 30. IOP was measured in each of these visits.

Results: Both loteprdnol and prednisolone were equally efficacious in decreasing AC cells and flare but there was a statistically significant difference in the increase of IOP caused by both drugs. IOP increase of ≥10mm Hg was observed in patients receiving prednisolone.

Conclusion: Both drugs were found to be highly effective in controlling post cataract extract inflammation with favourable safety profile. Loteprednol etabonate was found to have lesser propensity as compared to prednisolone acetate to increase IOP.

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Introduction

Cataract surgery is one of the most frequently performed elective surgical procedures with significantly improved visual outcome and lowering the risk of complications (1). Surgical removal of cataracts combined with intraocular lens (IOL) implantation might lead to ocular inflammation (2). This inflammatory response includes the release of prostaglandins and leukotirenes with migration of neutrophils and macrophages to the site of surgical trauma (2, 3). This post operative inflammatory response might manifest as mild iritis, corneal edema, increased cells and flare in anterior chamber with accompanying hyperalgesia (2, 3). If left untreated it could lead to suboptimal vision and even cystoids macular edema (CME) (2).

Ocular inflammation associated with cataract surgery can be managed by topical anti-inflammatory drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) with/without corticosteroids. Both these groups are effective in resolving postoperative inflammation and pain, thereby, increasing patient comfort, and decreasing the risk of complications (2). Non-steroidal anti-inflammatory drugs are safe and effective in the treatment of postoperative inflammation and pain, but, have been linked to a varying degree of potential reduction in corneal sensitivity, associated with an increased risk of superficial punctate keratitis and subjective symptoms of discomfort after instillation into the cul-de-sac (4).

Corticosteroids inhibit phospholipase A2, thereby inhibiting the cyclooxygenase and lipoxygenase pathways and the formation of all eicosanoids and increase the synthesis of anti-inflammatory lipocortins (2, 3). Corticosteroids mediate their anti-inflammatory effects through the glucocorticoid receptor by direct and indirect actions at the genomic level (3). These drugs suppress both the early (capillary dilation, increased vascular permeability, recruitment of leukocytes) and late (deposition of fibrin, proliferation of inflammatory cells and chemokines) phases of inflammation (2). Thereby reducing intraocular inflammation and also alleviate associated symptoms, such as photophobia, swelling, pain, and tenderness (3). Corticosteroids are also associated with side-effects, including steroid induced intraocular pressure (IOP) elevation, lowered resistance to infection, risk of cataract formation, and decreased wound healing (2).

Loteprednol etabonate is a novel corticosteroid produced by retrometabolic design and differs from prednisolone in that the ketone at the carbon-20 (C-20) position is replaced with a chloromethyl ester and the 17α-hydroxyl group is replaced with a carbonate moiety. Clinical Studeis have demonstrated that loteprednol etabonate has minimal effect on IOP with long term use and a much lower propensity to increase IOP relative to prednisolone acetate (2).

Thorough literature search revealed limited study comparing the efficacy and safety of prednisolone acetate and loteprendol etabonate hence, it was considered worthwhile to compare the efficacy and safety of prednisone acetate and loteprendol etabonate in post operative inflammation following cataract extraction with IOL implantation in our set-up.

Materials and Methods

The present study was done to evaluate:

- The efficacy of loteprendol etabonate 0.5% and prednisolone acetate 1% in post operative inflammation following cataract extraction with IOL implantation
- The safety of loteprendol etabonate 0.5% and prednisolone acetate 1% in post operative inflammation following cataract extraction with IOL implantation

This prospective, randomized, parallel group study was conducted at Rajindra Hospital, Government Medical College, Patiala in patients visiting the ophthalmological department. The study was approved by the Institutional Ethics Committee and only those patients who were willing to give written informed consent were enrolled in the study. All patients operated for cataract surgery with IOL implantation were screened and those patients who fulfilled the inclusion and exclusion criteria were enrolled in the study.

All patients diagnosed with cataract, more than 18years of age, willing to undergo cataract surgery with IOL implantation and able to comply with the visiting schedule were included in the study. Any patient with proliferative diabetic retinopathy, shallow anterior chamber, macular edema, retinal detachment, aniridia or iris atrophy, uveitis, history of iritis, iris neovascularization, medically uncontrolled glaucoma, and advanced glaucomatous damage; uncontrolled diabetes; with concurrent infectious/non infectious conjunctivitis, keratitis or uveitis were excluded from the study. Even pregnant and lactating mother were excluded from the study.

A total of 30 patients operated for cataract extraction surgery with IOL implantation were studied for post operative inflammation and IOP changes. These patients were divided into two groups of 15 patients each: Group A received loteprednol etabonate 0.5% four times a day, whereas Group B received prednisolone acetate 1% four times a day. Patients were asked to instil 1 drop of study drug depending into the conjunctival sac of the operated eye four times daily beginning 24 hours after surgery

and continue throughout first month of the post-operative period. The patients were followed on 1st, 3rd, 8th, 15th and 30th post operative days. All observations were made by the same specialist and recorded by an assistant to avoid inter examiner variability.

The following parameters were assessed in the patients: The signs of post operative inflammation including cells in anterior chamber (AC) and flare score were observed on the following post operative days: 1st, 3rd, 8th, 15th and 30th days. Cells in the AC and flare were graded as per annexure 1 (5).

The IOP was measured in the operated eye with the help of Goldmann Applanation Tonometry on each visit. All observations were done with a Carl Zeiss Slit Lamp also mounted with a Goldmann Applanation Tonometer.

Statistical Analysis: All the data assembled was presented as mean ± SD. Results were analyzed with the help of appropriate parametric and non parametric tests like students t-test. Results with p value <0.05 was considered as statistically significant.

Table1. Means of various parameters in Group A and Group B on each visit

Time Interval	Group A			Group B		
	AC Cells	Flare	IOP	AC Cells	Flare	IOP
Baseline			14.86±1.92			15.66± 1.91
1st day	2.13±0.74	2.13±0.83	15.60±1.45	2.06±0.79	2.13±0.83	17.93±2.31
3rd day	1.66±0.61	1.53±0.63	17.0±1.64	1.46±0.63	1.53±0.63	20.13±2.06
8th day	1.13±0.63	0.93±0.79	18.0±1.69	0.93±0.70	0.93±0.70	22.26±2.05
15th day	0.66±0.61	0.60±0.63	19.86±1.50	0.53±0.63	0.66±0.61	24.13±2.03
30th day	0.40±0.50	0.33±0.45	21.73±1.45	0.26±0.45	0.26±0.45	25.66±2.12

Table 2. Changes in various parameters studied in patients of Group A

Parameters	Time	Mean±SD	Change	"t" value	"p" value	Significance
AC Cells	1st day	2.13±0.74	1.73±0.59	11.30	<0.001	Highly Significant
	30th day	0.40±0.50				
Flare	1st day	2.13±0.83	1.80±0.56	12.43	<0.001	Highly Significant
	30th day	0.33±0.45				
IOP	1st day	15.60±1.45	6.86±0.99	26.85	<0.001	Highly Significant
	30th day	21.73±1.45				

T**able 3. Changes in various parameters studied in patients of Group B**

Parameters	Time	Mean±SD	Change	"t" value	"p" value	Significance
AC Cells	1st day	2.06±0.79	1.80±0.67	10.31	<0.001	Highly Significant
	30th day	0.26±0.45				
Flare	1st day	2.13±0.83	1.86±0.63	11.29	<0.001	Highly Significant
	30th day	0.26±0.45				
IOP	1st day	15.66±1.91	10.0±0.75	51.23	<0.001	Highly Significant
	30th day	25.66±2.12				

Table 4. Comparison of changes in various parameters studied in both groups

Parameters	Group	Mean change from 1st to 30th day	"t" value	"p" value	Significance
AC Cells	A	1.73±0.59	0.28	>0.05	Non Significant
	B	1.80±0.67			
Flare	A	1.80±0.56	0.30	>0.05	Non Significant
	B	1.86±0.63			
IOP	A	6.86±0.99	9.73	<0.001	Highly Significant
	B	10.0±0.75			

Result

A total of 30 patients operated for cataract extraction surgery with IOL implantation were studied for post operative inflammation and IOP changes were divided into two groups of 15 patients each: Group A received loteprednol etabonate 0.5% four times a day, whereas Group B received prednisolone acetate 1% four times a day. The characteristic of patients in both groups have been elaborated in table1. The IOP was comparable at baseline in both groups (14.86±1.92 vs. 15.66±1.91 mm of Hg). The response in both groups have been elaborated, there was a decrease in AC cells and Flare at the end of 30 days and Group A had statistically significantly ($p<0.05$) lower IOP changes as compared to Group B (21.73±1.45 vs. 25.66±2.12 mm of Hg). (Table 1)

Changes in Group A: The change in various parameters in group A has been highlighted in Table 2. There was a statistically significant decrease in number of AC cells and flare on day 30 and a statistically significant increase in IOP at day 30 as compared to day 1.

Changes in Group B: The change in various parameters in group B has been highlighted in Table 3. There was a statistically significant decrease in number of AC cells and flare on day 30 and a statistically significant increase in IOP at day 30 as compared to day 1.

Comparison of Group A vs. Group B: The comparison of mean change from day 1st to day 30th has been highlighted in table 4. The mean change in AC cells and flare was almost comparable in both the groups, There was a statistically significant change in IOP in both groups, the patients in group A and a significantly lower rise in IOP as compared to Group B.

Discussion

Several studies have established the safety and efficacy of loteprednol etaboante 0.5% and prednisolone acetate 1% in the treatment of postoperative inflammation and pain. The objective of our study was to compare the efficacy and safety of loteprendol etabonate 0.5% and prednisolone acetate 1% in post operative inflammation following cataract extraction with IOL implantation. The results of our study suggest that both loteprednol etabonate 0.5% and prednisolone acetate 1% are equally efficacious in decreasing AC cells and flare but there is significant difference in the increase of IOP caused by both drugs. IOP increase of ≥10mm Hg was observed only in patients receiving prednisolone acetate 1% (11 out of 15 patients).

Topical corticosteroids are routinely used to reduce intraocular post-operative inflammation following cataract surgery, which is measured by anterior segment cell and flare reaction. They also alleviate associated symptoms of pain swelling and tenderness (3).

Loteprednol etabonate was designed starting with Δ^1 cortienic acid which is an inactive metabolite of prednisolone, it is metabolized rapidly metabolized by tissue esterases to Δ^1 cortienic acid etabonate and then to Δ^1cortienic acid, thereby limiting any potential adverse effects associated with it (6, 7).

A study done by Grigorian et al. to compare the efficacy and safety of loteprednol etabonate and prednisolone acetate 1 %, in the treatment of postoperative inflammation following cataract surgery showed that patients from both groups achieved a similar resolution of postoperative inflammation (conjunctival hyperemia, corneal edema, aqueous cells, flare), and treatment with loteprednol etabonate had less effect on IOP elevation than prednisolone is similar to the result obtained in our study (8).

Another study by Ching JinWei et.al., in 2002 (a meta analysis of 8 randomized trial) had shown that increase in IOP of ≥10 mm of Hg is not seen in patients treated with loteprednol etabonate. We observed similar results with none of the 15 patients on loteprednol etabonate having a rise in IOP≥ 10 mm of Hg, whereas, 11 out of 15 patients on prednisolone acetate had a rise of ≥10 mm of Hg in the IOP readings. As per clinical efficacy of both drugs in reducing signs of inflammation i.e. AC cells and flare, as noted in our study both were found to be equally efficacious (9).

Another study done by Coban and Kocak also compared the safety of loteprednol etabonate 0.5 % and prednisolone acetate 1 % in patients after uncomplicated phacoemulsification surgery. At all postoperative visits, the mean IOP was lower in the loteprednol etabonate group than in the prednisolone group are quite similar to the results obtained in our study (10).

Another study done by Stewart compared the efficacy and safety of loteprednol etabonate 0.5 % and fluorometholone acetate 0.1 % in the treatment of postoperative inflammation demonstrated no statistically significant differences in flare, anterior segment cell, or conjunctival hyperemia as well as no significant adverse events were observed in both group. However the results of our study differ from this study as we had a significant change in IOP in patients with prednisolone group (11).

There are certain limitations to our study, firstly the sample size is small and secondly the study duration is less may be a longer study duration could have a different result.

Conclusion

Both Loteprednol etabonate and prednisolone acetate were found to e highly effective agents for control of post cataract extract inflammation with favourable safety profile but loteprednol etabonate was found to have lesser propensity as compared to prednisolone acetate to increase IOP, which is one of the most important side effect associated with topical corticosteroid use. This loteprednol etabonate, which is newer drug, has the properties which make it a more favourable choice over prednisolone. This addition of loteprednol has further widened the window of safety in topical corticosteroid therapy.

Acknowledgements

None.

Funding

None.

Competing Interests

None declared.

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Annexure 1.

Aqueous flare and cells are measured by counting within the field visible with a slit-lamp keeping the beam at maximum intensity with maximum magnification (Modification of the technique originally described by Hogan et.al.)

Grade	Flare (beam 2 mm height, 1m width)	Cells per field (2mm height, 1mm width)
0	Absent	0
1+	Faint, barely detectable	5-10
2+	Moderate, iris and lens details clear	10-20
3+	Marked, iris and lens detail hazy	20-50
4+	Intense flare, fibrinous aqueous	>50
Hogan MJ, Kimura SJ, Thygeson P. Signs and symptoms of uveitis. Anterior uveitis. Am J Ophthalmol 1959; 47: 155-70		