ORIGINAL ARTICLE

To Compare The Safety & Efficacy of Loteprednol Etabonate 0.5% & Prednisolone Acetate 1% in the Post-operative Inflammation Following Cataract Extraction with Intraocular Lens Implantation

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Abstract

To compare the mean rise in intraocular pressure and post-operative inflammation between loteprednol etabonate 0.5% and prednisolone acetatae1%. Out Patient Department of Ophthalmology Department, Government Medical College, Jammu. Comparative case series. Patients aged 18 years and older undergoing cataract surgery were divided into two groups: Group A (n=100) was prescribed loteprednol etabonate 0.5% (LE) four times a day; Group B (n=100) was prescribed prednisolone acetate 1% (PA) four times a day. Patients with pre-existing medical conditions like raised intraocular pressure, maculopathy, uveitis, retinopathy were excluded. Intraocular pressure and post-operative inflammation were assessed over 42 days after cataract surgery. Loteprednol etabonate 0.5% (LE) and prednisolone acetate 1% (PA) were equally efficacious in decreasing Anterior Chamber cells (0.08±0.27 vs 0.05±0.22 respectively; p=0.39) and Anterior Chamber flare (0.06±0.24 vs 0.05±0.22 respectively; p=0.76) at 42 days. There was statistically significant difference in intraocular pressure at 42nd days with LE as compare to PA(16.21±3.34 vs 18.62±2.36 respectively; p<0.001). The equivalent control of inflammation can be obtained through treatment with LE and PA after cataract surgery but the mean rise in intraocular pressure in patients treated with loteprednol etabonate is less than in patients treated with prednisolone acetate.

Keywords

Prednisolone Acetate, Loteprednol Etabonate, Postoperative Inflammation, Intraocular Pressure

Introduction

Cataract surgery has advanced dramatically in the past several decades, leading to improved visual outcome and less tissue damage. However some degree of post-operative inflammation remains an unavoidable complication of cataract surgery.(1)

Corticosteroids remains the mainstay for treatment of post-operative inflammation in cataract surgery.(2,3) However, most topical steroids are associated with increased intraocular pressure, increase risk of infection, increase risk of cataract formation (in phakic patients), decreased wound healing and suppression of hypothalamic-pituitary axis after long-term use.(1,4-6) Loteprednol etabonate, a unique ester based steroid, works on the principal of "site active concept". This concept is used to design the drugs that can be deactivated in the body after their therapeutic effects have been achieved. It reduces the side effects.(7) Structurally, loteprednol etabonate differs from prednisolone in that the ketone at the carbon -20 position is replaced with a chloromethyl ester and 17-alpha hydroxyl group is replaced with a carbonate moiety (8). After exerting its effects, loteprednol is rapidly metabolised. Due to rapid metabolism of loteprednol, the incidence of rise in intraocular pressure is less in comparison to C-20 steroids, even in known steroid responders.(5,9)

There have been few studies comparing efficacy and safety of loteprednol etabonate with prednisolone acetate in patients with ocular inflammation after cataract surgery. Hence, it was considered to undertake a study to answer this question.

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Material and Method

The comparative case series was conducted at outpatient department of Ophthalmology, Government Medical College Jammu from 1st November 2011 to 30th November 2012.

The present study was designed to evaluate the efficacy and safety of loteptednol etabonate 0.5% and prednisolone acetate 1% in post-operative inflammation at 42nd day after cataract surgery. This study was conducted on patients who underwent cataract extraction surgery with intraocular lens implantation during their follow-up in the Out Patient Department of Ophthalmology, Government Medical College, Jammu. The study was approved by institutional ethical committee.

The patients more than 18 years old, who were planned for cataract extraction with intraocular lens implantation enrolled prior to surgery. Exclusion criteria: Patients with elevated intraocular pressure, known sensitivity to steroids, retinopathy, maculopathy, uveitis, cornea or vitreous opacities that would interfere with the visual acuity, history of ocular surgery, ocular trauma or had a visual potential in the fellow eye of worse than 6/18, expected to require the use of concurrent ocular or systemic non-steroidal anti-inflammatory drugs, mast cell stabilizers, antihistamine, or decongestants within 2 days before or 21 days after surgery, require ocular or systemic steroids or immunosuppressants within 14 days prior to or 21 days following surgery.

The written informed consent was taken prior to enrollment. Patients with intraoperative complications during surgery including posterior capsule rupture and vitreous loss were excluded from analysis.

Following cataract extraction with Intraocular lens implantation, patients were divided serially in either Group A and B. Group A received loteprednol etabonate 0.5% four times a day and Group B prednisolone acetate 1% four times day, beginning 24 hours after the cataract surgery till 42 days. Patients were followed on 1st, 3rd, 8th, 15th, 30th and 42nd day post-operative day for measurement of intraocular pressure using Goldman applanation tonometer mounted on slit-lamp (Topcon) and post-operative inflammation using slitlamp examination. Post operative inflammation was assessed by Anterior chamber cells and flare which were measured and graded by counting within the field visible with a slit lamp keeping the beam measuring (2X1) mm at maximum intensity with maximum magnification. (SUN Working Group Classification).(10)

Statistical Analysis

The analysis was conducted using computer software MS Excel (2013) and SPSS 12.0 for windows. Quantitative variables were represented as %age and mean (SD) was reported for quantitative variable. Student t-test was employed to assess statistical significance between the two groups. A p-value of <0.05 was considered as statistically significant.

Results

Mean (± sd) age (in years) in Group A and B were 63±12 and 60±12 respectively. Comparison of intraocular pressure and inflammation prior to surgery as well as at on 1st, 3rd, 8th, 15th, 30th and 42nd days is depicted in table 1.

There was a statistically significant mean difference in intraocular pressure (in mmHg) at baseline and 42nd day; in Group A was 4.00 ± 2.04 and Group B was 6.50 ± 2.02 ($p < 0.001$). However, no statistically significant difference was observed in anterior chamber cells (Group A: 0.08 ± 0.27 and in Group B: 0.05 ± 0.22 $p = 0.39$), and anterior chamber flare (Group A: 0.06 ± 0.24 and Group B: 0.05 ± 0.22. $p = 0.76$) at 42nd post-operative day.

Discussion

Use of topical steroids in various ocular surgeries has been well established. They reduce the post-operative inflammation as well as the associated symptoms like pain, swelling and photophobia. Early generation corticosteroids like prednisolone acetate have been used in post-operative inflammation after cataract surgery for many years. Smerdon et al conducted a study to compare the efficacy of prednisolone acetate with vehicle in post-operative inflammation after cataract surgery and found prednisolone acetate to be an effective drug for resolution of post-operative inflammation when compared to vehicle.(11) Lorenz *et al* also found the similar results (12). Newer generation steroid loteprednol etabonate is different from other steroids in having ester group at C-20 position rather than ketone group due to which it undergoes rapid de-esterification. Comstock TL *et al* in 2011conducted a study to compare the safety and efficacy of loteprednol etabonate ophthalmic ointment 0.5% with vehicle over a period of 14 days and found that loteprednol etabonate was efficacious and well tolerated in the treatment of ocular inflammation and pain after cataract surgery.(13) Bartlett JD *et al* in 1993 studied the effect of topical loteprednol etabonate and prednisolone acetate on intraocular pressure in a known steroid responders and they found that loteprednol etabonate has less effect on intraocular pressure compared to prednisole acetate.14 Similar studies have been done to establish that loteprednol etabonate causes less intraocular pressure fluctuation as compared to prednisolone acetate.(15-18)

Table 1. Comparison of Intraocular Pressure (IOP) and Anterior Chamber Inflammation (Anterior Chamber (AC) Cells and Anterior Chamber Flare)

Time interval	GROUP A			GROUP B		
	AC cells	AC flare	IOP(in mmHg)	AC cells	AC flare	IOP(in mmHg)
Baseline			12.16±2.74			12.12±2.17
1st day	2.32±0.71	1.90±0.73	13.74±2.71	2.35±0.74	2.10±0.70	12.69±2.02
3rd day	2.24±0.67	1.80±0.65	13.56±2.85	2.10±0.66	1.82±0.56	12.69±2.16
8th day	1.74±0.44	1.33±0.51	14.14±2.99	1.72±0.55	1.34±0.51	13.70±2.33
15th day	1.15±0.62	0.74±0.52	14.83±3.16	1.04±0.62	0.77±0.51	14.91±2.47
30th day	0.55±0.56	0.29±0.45	15.68±3.25	0.44±0.56	0.43±1.16	16.82±2.25
42nd day	0.08±0.27	0.06±0.24	16.21±3.34	0.05±0.22	0.05±0.22	18.62±2.36

Player U *et al* in 2013 compared the effects of topical steroids on the intraocular pressure from the available published studies and found that early generation corticosteroids such as dexamethasone and prednisolone are more likely to result in raised intraocular pressure as compared to newer generations corticosteroids, such as rimexolone and loteprednol etabonate with similar anti-inflammatory effect.(19) Sheppard JD *et al* in 2016 also reviewed the available published data to study the effect of loteprednol etabonate on intraocular pressure with short term and long term use. In all studies, it was observed that loteprednol etabonate had low tendency to raise IOP, regardless of formulation, dosage regimen, or treatment duration, including in steroid responders. (20) Also two trials evaluated the safety and efficacy of LE ophthalmic suspension 0.5% given four times a day for 2 weeks for treatment of postoperative pain and inflammation after cataract surgery. In one trial, no clinically significant rise of intraocular pressure (less than 10mmHg) was reported in the loteprednol etabonate treatment group (21), while in other trial, a clinical significant, but transient rise of intraocular in 3% of loteprednol etabonate treated group was reported.3 Another study by Ilyas et al in 2004 among 397 patients in which long term use of 0.2% loteprednol etabonate was studied for seasonal and perennial allergic conjunctivitis. No adverse effecs of long term use of loteprednol etabonate 2% were reported. (22)

Fong et al and Rajpal *et al* evaluated the safety and efficacy of loteprednol gel 0.5%. In both studies loteprednol treated patients had complete resolution of anterior chamber cells on day 8 and grade 0 pain as compared to vehicle. In both studies mean intraocular pressure was lower than baseline at follow-up. (23,24) However, Karalezli A *et al*, in 2009 compared the effects of topical loteprednol etabonate 0.5% and prednisolone acetate 1% on postoperative inflammation after cataract surgery and it was found that there were no statistically significant differences in mean visual acuity or mean intraocular pressure measurements between the two groups at any postoperative visit.(25) Also another study has been done to compare the effects of prednisolone acetate and loteprednol etabonate in patients with acute anterior uveitis in which LE was found to be less effective than PA (26). Results of these studies were found to be different from our study

The limitation of this study was that post-operative pain has not been assessed. Randomised control trial would have been the better study design instead of comparative case series.

Conclusion

Both loteprednol etabonate 0.5% and prednisolone acetate 1% were found to be highly effective agents for control of post-operatoive inflammation following cataract surgery but loteprednol etabonate 0.5% was found to have lesser propensity to elevate intraocular pressure as compared to prednisolone acetate 1% which is one of the most significant side -effects of topical steroids.

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