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TO COMPARE THE SAFETY AND EFFICACY OF LOTEPREDNOL ETABONATE 1% & PREDNISOLONE ACETATE 1% EYE DROPS IN CONTROLLING POSTOPERATIVE INFLAMMATION FOLLOWING AN UNEVENTFUL PHACOEMULSIFICATION WITH INTRAOCULAR LENS IMPLANTATION

Ophthalomology

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ABSTRACT

This study is done to compare the mean rise in intraocular pressure and postoperative inflammation between Loteprednol Etabonate 1% eyedrop & Prednisolone Acetate 1% eyedrop. Study was done at Out patient department of ophthalmology, Smt. Kashibai Navale medical college, Pune. It is a Prospective observational study. Patients aged 40 and older undergoing uneventful phacoemulsification surgery with intraocular lens implantation were divided into two groups, Group A (n=30) was prescribed 1% Loteprednol Etabonate eyedrop two times a day without tapering, Group B (n=30) was prescribed 1% Prednisolone Acetate eyedrop four times a day with tapering dose weekly for one month. Loteprednol Etabonate 1% eyedrop and Prednisolone Acetate 1% eyedrop were not equally efficacious in decreasing postoperative inflammation but the intraocular pressure control in patients treated with Loteprednol Etabonate eyedrop 1% and Prednisolone Acetate 1% eyedrop is equivalent in both the groups.

KEYWORDS

Prednisolone Acetate, Loteprednol Etabonate, Postoperative Inflammation , Intraocular Pressure

INTRODUCTION

Cataract surgery has made remarkable advancements over the past few decades, resulting in better visual outcomes and reduced tissue trauma. Nevertheless, some level of postoperative inflammation remains an inevitable aspect in the healing process following surgery.

Corticosteroids remain the mainstay for treatment of postoperative inflammation in cataract surgery.(1,2) However, most topical steroids are associated with increased intraocular pressure, increased risk of infection, decreased wound healing and suppression of hypothalamic-pituitary axis after long term use.(3-6) Loteprednol Etabonate, a unique ester based steroid, works on the principle 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 Acetate 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)

A variety of ophthalmic formulations of Loteprednol Etabonate have been available for clinical use for more than a decade. While Loteprednol Etabonate has demonstrated effectiveness in managing inflammation associated with cataract surgery, clinicians often report anecdotally that it may not provide the same level of inflammatory control as conventional topical corticosteroids like Prednisolone Acetate. This study was performed to evaluate Loteprednol Etabonate 1% eyedrop versus Prednisolone Acetate 1% eyedrop for the treatment of postoperative inflammation in patients having routine cataract surgery.

MATERIAL AND METHOD

A Prospective observational study was conducted at Outpatient Department of Ophthalmology, Smt Kashibai Navale Medical College Pune from September 2024 to February 2025.

The present study was designed to compare the safety and efficacy of Loteprednol Etabonate 1% eyedrop and Prednisolone Acetate 1% eyedrop in controlling the postoperative inflammation following an uneventful phacoemulsification surgery with intraocular lens implantation for one month postoperative period. The study was approved by institutional ethical committee.

The patients with age more than 40, who are diagnosed with senile cataract, were planned for cataract extraction with intraocular lens implantation are included in this study. Exclusion criteria: patients age less than 40, patients with uveitis, congenital anomalies, patients undergone any intraocular surgery in past, patients with secondary cataract (post trauma, steroid induced). The written informed consent was taken prior to enrollment.

Following uneventful phaecoemulsification surgery with intraocular lens implantation, patients were randomly divided into Group A and B. Group A received Loteprednol Etabonate 1% eye drop two times a day without tapering for 1 month and Group B received Prednisolone Acetate 1% eye drop four times a day with tapering dose weekly for a month. Patients were followed on 1st, 7th and 30th day postoperative day for measurement of intraocular pressure using non contact tonometer and postoperative inflammation using slit-lamp examination. Postoperative inflammation was assessed by Chemosis, conjunctival and ciliary congestion, membrane and anterior chamber reaction [with a slit-lamp keeping the beam measuring (2X1) mm] at maximum intensity with maximum magnification.

RESULTS

1. Visual Acuity (VA) Comparison Over Time Between Groups (Mann-Whitney U Test)

Tables: "Ranks" + "Test Statistics" (VA_D1, VA_D7, VA_D30)

Time Point	Mann-Whitney U	Z value	p-value	Interpretation
Day 1 (VA_D1)	420.000	-0.465	0.642	No significant difference in VA between groups.
Day 7 (VA_D7)	399.000	-0.796	0.426	No significant difference.
Day 30 (VA_D30)	396.000	-0.887	0.375	No significant difference.

Conclusion: Visual acuity improved over time in both groups, but there was no statistically significant difference between the 1% Loteprednol Etabonate and 1% Prednisolone Acetate eyedrops groups at any time point.

2. Intraocular Pressure (IOP) Comparison Between Groups (Mann-Whitney U Test)

Time Point	Mann-Whitney U	Z value	p-value	Interpretation
Day 1 (IOP_D1)	435.5	-0.218	0.827	No significant difference.
Day 7 (IOP_D7)	300.5	-2.245	0.025	No Significant difference.

Day 30 (IOP_D30)	238.0	-3.164	0.002	No significant difference.

Conclusion: IOP fluctuations during postoperative period is comparable in both the groups. 1% Loteprednol etabonate eyedrop and 1. prednisolone acetate eyedrop appears to be safer in terms of IOP elevation with mentioned doses.

3. Visual Acuity Over Time (Within-Groups Repeated Measures ANOVA)

Tests of Within-Subjects Effects

- **Time Effect ($p < 0.001$):** Significant change in VA over time.
- **Time × Group Interaction ($p = 0.924$):** No significant difference in trend between groups.

Pairwise Comparisons (TIME 1 → 3):

All pairwise comparisons are statistically significant ($p < 0.001$).

Conclusion: VA significantly improved over time within both groups, but the pattern of improvement did not differ between groups.

4. Intraocular Pressure (IOP) Over Time (Repeated Measures ANOVA)

Multivariate Tests & Tests of Within-Subjects Effects:

- **Time Effect:** $p = 0.002$ →No Significant changes in IOP across time points.
- **Time × Group Interaction:** $p = 0.001$ → Statistically no significant difference in IOP change patterns between groups.

Pairwise Comparisons (TIME 1 → 3):

- Day 1 vs Day 2: $p = 0.046$
- Day 1 vs Day 3: $p = 0.001$
- Day 2 vs Day 3: $p = 0.098$ (not significant)

Conclusion: The 1% loteprednol etabonate eyedrop group and 1% prednisolone acetate eyedrop had relatively stable IOP.

5. Anterior Chamber (AC) Reaction Over Time (Friedman Test)

Friedman Test (Entire Sample):

- Chi-square = 34.787, $p < 0.001$ → Significant change in AC reaction over time.

Post-hoc (Bonferroni-adjusted):

- **AC_D7 vs AC_D1:** Not significant after adjustment.

Conclusion: Increased AC reaction observed at day 7 in 1% Loteprednol Etabonate eyedrop group, 10 patients of loteprednol etabonate group were shifted to 1% Prednisolone acetate eyedrop. AC reaction reduced significantly over time, especially between Day 1 and Day 30.

6. Conjunctival Congestion on Day 7 (Chi-Square Test)

Group	Congestion Present	Nil
Group 1 (Loteprednol)	5	25
Group 2 (Prednisolone)	0	30

- Chi-square $p = 0.020$, Likelihood ratio $p = 0.007$, Fisher exact $p = 0.052$

Conclusion: Conjunctival congestion was significantly more frequent in the 1% Loteprednol Etabonate eyedrop group at Day 7. This could suggest a delayed anti-inflammatory effect or less efficacy in surface inflammation control.

Summary Table

Parameter	Statistical Test	Time Points	Group Difference	p-value	Interpretation
VA	Mann-Whitney U	D1, D7, D30	Not significant	> 0.05	There was no statistically significant difference in visual acuity between the 1% loteprednol etabonate eyedrop and 1% prednisolone acetate eyedrop groups at any time point. This indicates that both medications were equally effective in improving postoperative visual acuity.
IOP	Mann-Whitney U	D7, D30	Not Significant	0.025, 0.002	This suggests that 1% loteprednol etabonate eyedrop and 1% prednisolone acetate eyedrop are safer in terms of minimizing steroid-induced ocular hypertension.
IOP over time	RM-ANOVA	D1 to D30	Not Significant	0.001	IOP remained relatively stable in both the groups, reinforcing the safety profile of loteprednol and prednisolone acetate.
AC reaction	Friedman	D1, D7, D30	Time effect	< 0.001	There was a significant reduction in AC inflammation over time in the overall sample. This indicates a successful postoperative inflammatory response control with both drugs, particularly evident by Day 30.
Conjunctival congestion	Chi-square	D7	Significant	0.020	Conjunctival congestion was significantly more common in the loteprednol group on Day 7. This may suggest a comparatively delayed or less potent surface anti-inflammatory effect of loteprednol compared to prednisolone.

Overall Conclusion

- IOP control was equivalent in both the groups with given dosage 1% Loteprednol Etabonate eye drops and 1% Prednisolone Acetate eye drops making both safer in patients at risk of steroid-induced IOP elevation.
- AC inflammation was more in 1% Loteprednol Etabonate eyedrop group at day 7 seen in 10 patients. Those 10 patients were shifted to 1% prednisolone acetate eyedrop with tapering dose and AC reaction reduced over time.
- Conjunctival congestion was slightly more in the 1% loteprednol etabonate group at Day 7.

Thus,1% Prednisolone Acetate eye drop offers better efficacy with comparable IOP safety in controlling postoperative inflammation.

DISCUSSION

In this study, we found that ocular adverse effects noted in 1% loteprednol etabonate eyedrop group were predominantly conjunctival congestion and AC cells. At day 7 increased AC reaction was observed which in turn suggest delayed anti-inflammatory effect or less efficacy in inflammation control. Add on treatment was given to 10 patients of group A (Loteprednol Etabonate) on day 7 and patients were shifted to more potent topical steroids (Prednisolone Acetate eyedrop). AC reaction observed more in 1% Loteprednol Etabonate eyedrop group.

The use of topical corticosteroids to control pain and inflammation after surgical procedures is a commonly accepted practice. Although prednisolone acetate is generally considered a high-potency steroid among the ketone based steroid class, evaluation of the relative potency between topical steroids in a clinical setting is challenging.

This study was designed to allow evaluation of the relative safety profile of loteprednol etabonate and prednisolone acetate in same 1% concentrations of eye drops.

Use of topical steroids in various ocular surgeries has been well established. They reduce the postoperative inflammation as well as the associated symptoms like pain, swelling and photophobia. Early generation corticosteroids like Prednisolone acetate have been used in postoperative inflammation after cataract surgery for many years. Smerdon et al conducted a study to compare the efficacy of Prednisolone acetate with vehicle in postoperative inflammation after cataract surgery and found Prednisolone acetate to be an effective drug for resolution of postoperative inflammation when compared to vehicle.(10) Lorenz et al also found the similar results. (11) 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 2011 conducted 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. (12)

The study done by Lane, Stephen S. MD, et al evaluated the efficacy of loteprednol etabonate 0.5% versus prednisolone acetate 1% for the control of postoperative inflammation in patients having routine cataract surgery. The results indicate that equivalent control of inflammation can be obtained through treatment with loteprednol etabonate or prednisolone acetate after cataract surgery. In addition, treatment with loteprednol etabonate may result in less IOP fluctuation.(13)

Other comparative study done by Vijaya Gupta, Dinesh Gupta on the

safety & efficacy of Loteprednol Etabonate 0.5% & Prednisolone Acetate 1% in the postoperative inflammation following cataract extraction with intraocular lens implantation has given a conclusion that both loteprednol etabonate 0.5% & Prednisolone acetate 1% were found to be highly effective agents for control of postoperative 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.(14)

In above mentioned two studies, 0.5% Loteprednol Etabonate showed equivalent efficacy with 1% Prednisolone Acetate. But in our study 1% Loteprednol Etabonate eye drop showed poor efficacy compared to 1% Prednisolone Acetate eye drop, this difference in efficacy might be due to less dosage (BD) of 1% Loteprednol Etabonate compared to QID dose of 0.5% of Loteprednol Etabonate eye drops. Observation about IOP fluctuations in our study are different from above mentioned studies this might be due to small sample size in our study compared to larger sample size in above mentioned studies.

WHAT WAS KNOWN : 0.5% Loteprednol Etabonate and 1% Prednisolone Acetate are effective for the treatment of postoperative inflammation after cataract surgery.

WHAT THIS PAPER ADDS : This study is conducted with minimal dose of 1% Loteprednol Etabonate eyedrop (BD) versus 1% Prednisolone Acetate eyedrop (QID). Whereas previous studies were based on 0.5% Loteprednol Etabonate versus 1% Prednisolone Acetate eyedrops.

The findings of this study indicate that control of postoperative inflammation in patients having routine uneventful phacoemulsification with intraocular lens implantation is better with 1% Prednisolone Acetate eye drop in QID dose Compared to 1% Loteprednol Etabonate eyedrop in BD dose but IOP fluctuations are equivalent in both groups which is normal.

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