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Original Research Article

Comparison of safety of loteprednol 0.5%/difluprednate 0.05%/prednisolone 1% eye drops in the post cataract surgery patients

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ABSTRACT

Background: Post surgical ocular inflammation is a common happening after the cataract surgery. Topical steroids are the main stay of the treatment. Although it is quite effective in controlling it but it produces severe adverse drug reactions i.e. rise in intraocular pressure and dryness in the eyes. In present study we have compared the two newer topical steroids i.e. loteprednol and difluprednate with prednisolone for the safety issue.
Methods: Total n=150 patients of cataract were enrolled in the study. Institutional ethics committee approval was taken. After randomization, patients were allocated into three groups of 50 each. Baseline reading of intraocular pressure and tear film breakup time was recorded. Post operatively examination was done on day 7, 15 and 30 day. The results were compared as prednisolone versus loteprednol, prednisolone versus difluprednate.
Results: A. On intraocular pressure 1.prednisolone versus difluprednate statistically significant effect at day 7 (p=0.043), day15 (p=0.010) and at day 30(p=0.036) were there. 2. Prednisolone versus loteprednol- The difference was statistically highly significant at day 7 (0.00), day 15 (p=0.009) and at day 30th (p=0.00). B. On tear film breakup time-No significant effect on tear film breakup time is observed.
Conclusions: Both the newer drugs are much safer as compared to prednisolone for intraocular pressure. As they are equiefficacious to prednisolone their use in post cataract surgery inflammation is recommended.

Keywords: Cortico steroid, Difluprednate, Intraocluar pressure, Loteprednol, Ocular inflammation, Tear film break up time

INTRODUCTION

Post-surgical ocular inflammation is a common happening after the Cataract surgery. Surgical trauma to the eye initiates an inflammatory reaction. This reaction includes the release of prostaglandins and the recruitment of neutrophils and macrophages to the site of trauma. Although usually self-limited, post-operative ocular inflammation after cataract surgery can be associated with complications, including corneal edema, spikes in intraocular pressure (IOP), cystoid macular edema (CME), and posterior capsule opacification. As most patients expect 20/20 vision after cataract surgery without any complications, the use of anti-inflammatory agents is a standard practice.

Topical corticosteroids are routinely used in the treatment of post-operative inflammation following cataract surgery as well as after most other ocular surgical procedures.[1] So single eye drop not only decrease the financial load but also increase the chances of complications.[2]

Loteprednol/difluprednate/prednisolone eye drops are the topical steroids used to treat post-surgical inflammation. Steroid has inherent tendency to produce side effects like raising the intraocular pressure, dryness of eyes even in otherwise healthy subjects.

Prednisolone is considered as gold standard treatment for post-surgical ocular inflammation.[2] It is highly efficacious but produces severe adverse drug reaction i.e. increase in intraocular pressure.

The newer steroids i.e. loteprednol and difluprednate are claimed to be safe but convincing studies are lacking in the literature.

Difluprednate, a derivative of prednisolone that is difluorinated at the C6 and C9 positions is approved for treating post-operative inflammation. Originally developed for dermatologic applications, it was also found to rapidly penetrate the corneal epithelium.[3]

Loteprednoletabonate differs from other ophthalmic corticosteroids in that it has an ester rather than a ketone at the C-20 position of the core corticosteroid structure. Loteprednoletabonate was designed through retro-metabolic drug design; a process by which an inactive, non-toxic metabolite of a reference compound, in this case prednisolone, is chemically modified to a therapeutically active compound. Clinically, following ocular penetration and saturation of the glucocorticoid receptor in ocular tissues, unbound loteprednoletabonate undergoes rapid de-esterification to its inactive metabolite, cortienic acid etabonate, or PJ-91, resulting in a decreased impact on IOP.[4]

This study was planned to compare the effect of various topical steroids on the intraocular pressure on the otherwise healthy eyes.

METHODS

This study was conducted in Sri Guru Ram Dass Institute of Medical Sciences, Amritsar. After taking institutional ethics committee approval, total n=150 patients of either sex (50 in each group) of cataract desirous for surgery were enrolled. Patients were randomized by using computer generated technique. Informed written consent was obtained either from the patient or the attendant.

The patients were examined a day prior to the surgery for any eye pathology other than cataract. The special emphasis was on intraocular pressure and any symptom of dry eyes. Intraocular pressure was measured by using Nideknon-contacttonometer. For assessing the tear volume tear film break up time (TBUT) is checked. Tear film less than 6 sec was considered invalid.

Inclusion criteria

Inclusion criteria were non complicated cataract as cortical/ nuclear/ posterior sub capsular cataract. Exclusion criteria were complicated cataract associated with uveitis, trauma and myopia, previous history of raised intraocular pressure, prolonged steroid therapy. Surgical technique- preoperatively (day-1) patients were examined with slit lamp to rule out any ocular surface defect. All operations were performed in a standard way and by the same experienced surgeon. Briefly, mydriasis was achieved by instillation of Tropac-p (tropicamide 0.8%with phenylepherine 5%) eye drops. Surgery was performed under peribulbar anesthesia with lignocaine 2%with adrenaline 1:20000. Small incision cataract surgery was carried out via a temporal sclera tunnel based incision, and a foldable posterior chamber intraocular lens was implanted into the capsular bag. The same irrigating solution (solution Zyonate; Zydus) ophthalmic viscoelastic device were used in all cases.

At the end of surgery, Moxicip ointment was applied in the post operative dressing.

A day after the surgery the intraocular pressure was measured. All the patients were prescribed one study drug depending upon the randomization key groups.

Table 1: Different study groups and their medicines.

Groups	Tradename/strength
Group 1	Predacetate, Alcon labs (Prednisolone acetate 1%)
Group 2	Lotepred, Sun Pharma (Loteprednol 0.5%)
Group 3	Diflucor, Ajanta Pharma (Difluprednate 0.05%)

Table 2: Schedule of various drugs.

	1st week	2nd week	3rdweek	4th week
Group 1	6	5	4	3
Group 2	6	5	4	3
Group 3	4	4	2	2

After the surgery, at the time of dressing removal (day 1) intraocular pressure was measured by Nideknon-contact tonometer. All the Patients were put on the one study drug along with (moxifloxacin 0.05%) eye drops qid for 7days.

On subsequent visits (days 7, 15, 30) intra ocular pressure of the operated was checked and reading was recorded on patient performa. The tear film breakup time was also recorded.

Tear break up time test (TBUT test)

In this, Fluorescein dye was instilled in lower fornix of the study eye. Then Patient was asked to blink several times and then stop. A filter paper was inserted to examine the appearance of dry area is the end point.

The BUT is the interval in last blink and the appearance of first randomly distributed dry spots.

Reading less than 10 seconds was taken as abnormal. This was a safety analysis and all the drugs from the literature were found equiefficaceous.

Emergency measure

As no antibiotic or additional painkiller was given to the patients. Patients were educated about any untoward

event like any disproportionate pain or swelling in the operated eye. If the intraocular pressure has raised above 30mm of Hg with any drug. Patient had to be taken out of the study and taken care accordingly.

Statistical analysis

By using instant statistical analysis software the data was analysed. Two-way ANOVA test was applied to see the relation of the variables between in the groups. For the data analysis TUKEY's test was applied.

RESULTS

1. Effect on Intraocular pressure-In comparison of prednisolone with Difluprednate at day 7 statistical significant (p= 0.043) difference in IOP is found. This difference is still more significant at days 15 (p=0.010) and 30day (p= 0.036). Indifluprednate group maximum rise in intraocular pressure was upto 18mmhg (base line was 10-12mm hg) only in 2 patients out of 50.
   In comparison of prednisolone with loteprednol the difference in intraocular pressure raising potential is found statistically more significant at days 7 (p=0.000), at day 15 (p=0.009). At day 30th it is again highly significant (p=0.00). The IOP raising potential of the loteprednol is almost zero from preoperative (0 day) to post-operative 30 days.
2. Tear film break up time- no significant effect on the tear film breakup time is observed with any of the study drug.

DISCUSSION

Prednisolone being the most efficacious has produced maximum rise in intraocular pressure as compared to other newer drugs i.e. difluprednate and loteprednole. The result of the study comparable to Korenfeld et al in which the efficacy and safety of difluprednate ophthalmic emulsion 0.05% with that of placebo (vehicle) in 438 patients with inflammation after ocular surgery.[8] 3% of patients in both difluprednate groups exhibited an increase in IOP of ≥10 mmHg from baseline to an IOP of ≥21 mmHg as compared to 1% of patients in the placebo group.

Another study by Smith et al, also compared the efficacy and safety of difluprednate ophthalmic emulsion 0.05% with that of placebo (vehicle) in 121 patients undergoing cataract surgery.[9] Again, three patients (3.7%) in the difluprednate group had an increase in IOP of ≥10 mmHg from baseline to an IOP of ≥21 mmHg as compared with none of the patients in the placebo group.

In our present study the small sample size can be a drawback. Secondarily efficacy of the drug although is established yet it can also be simultaneously compared.

Dry eye is also an important side effect of steroids but in our study no drug has significantly altered the tear film break up time. It can be due to the shorter duration of the study period.

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