

Comparative analysis of 0.4% vs 0.5% ketorolac tromethamine ophthalmic solution in post operative small incision cataract surgery patients

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Abstract

Purpose: The study was to compare the effectiveness and patient tolerability of two strengths of ketorolac tromethamine ophthalmic solution i.e. 0.4% vs 0.5% in post-operative small incision cataract surgery patients.

The study was conducted in Sri Guru Ram Dass institute of medical Sciences and research Amritsar.

Materials and Method: This is a randomized single blind investigator masked study. Total fifty patients (25 in each group) screened for cataract surgery were enrolled. The patients were randomized and either of study medication was used. Study medications were ketorolac 0.4% and ketorolac 0.5% eye drops. One drop of each drug was instilled in operative patient in each group thrice day. Thereafter, Slit-lamp examination was done for aqueous cell and flare. Intraocular pressure was checked. The patients were evaluated for subjective tolerance postoperatively at days 1, 3, 5, 7, 15 and 30. The results were compared between the groups, also with baseline.

Results: Only difference between two strength ketorolac is less stinging, discomfort and better ocular tolerability of ketorolac 0.4%. The patient operative outcome is same in the both strength. Ketorolac 0.4% has proven to better tolerated on the visual analogue scale. Ocular comfort was also much better. Although this difference is not statistically significant.

In other parameters, difference were not observed between the two groups for best-corrected visual acuity, IOP & slit-lamp assessment of cells and flare measured.

Conclusions: 0.4% ketorolac tromethamine ophthalmic solution is equally effective as 0.5% ketorolac tromethamine ophthalmic solution in reducing post cataract inflammation. But Patients with 0.4% ketorolac reported less discomfort.

Keywords: Ocular inflammation, Ketorolac, Ocular discomfort, Intraocular Pressure, Ocular pain, Visual analogue scale

Introduction

Post operative inflammation is common after surgery. After cataract surgery prescribing NSAID, little bit of steroid and antibiotic cover if required is a routine for any Ophthalmologist.

Cataract surgery being an invasive procedure, it requires surgical manipulation leading to the disruption of the blood aqueous barrier. Ocular pain, discomfort, photophobia, corneal edema, posterior synechiae, elevation in IOP and cystoid macular edema are the common outcomes of any ocular surgery.⁽¹⁾ Topical corticosteroids are effective for post operative inflammation as it helps in inhibiting the release of arachidonid from the cell membrane phospholipids. Further the formation of both leukotrienes and prostaglandins is inhibited and inflammatory cascade is disrupted.^(2,3) Corticosteroids although very effective still it carries carry a risk of increasing the intraocular pressure. Which can lead to glaucoma, if left untreated.⁽⁴⁾ The ocular inflammation can be assessed by slit lamp examination monitoring anterior chamber signs.

About ketorolac- Ketorolac is a NSAID used topically to treat ocular inflammatory pain after the surgery. It is found to be much more efficacious in treating post inflammatory sign & symptoms as compared to other drugs of NSAID group. It is a NSAID which is commonly prescribed but there are two different strengths available i.e. Ketlar 0.5%,

Ketlar- 0.4%. This study is planned to compare the efficacy of these strengths.

Two types of parameters were evaluated;

Subjective: Ocular pain and tolerance.

Objective: Number of aqueous cells, aqueous flare & conjunctival hyperemia.

Materials and Method

It was a randomized, parallel group 4-week trial. The study was conducted from June 2016 to August 2016 in Sri Guru Ram Dass Institute of Medical Sciences, Amritsar. Fifty patients enrolled for small incision cataract surgery were up taken in the study.

The ethics committee permission from the institution was taken. The written informed consent from the patients or the attendant was taken.

Patients older than 40 years & having non-complicated cataract as cortical /nuclear /posterior sub capsular cataract were included.

Exclusion criteria patient with any ocular inflammation like intraocular inflammation or uveitis, trauma & myopia, significant posterior chamber disease involving macular region, previous macular surgery, previous history of raised intraocular pressure, prolonged steroid therapy, ocular surface epithelial defect, h/o any type of steroid intake, any type of immunocompromised patients. The patients

hypersensitive to ketorolac, any ingredients of the study medication were excluded.

Surgical Technique: Preoperatively (Day-1) patients were examined with slit lamp to rule out any ocular surface defect. Briefly, mydriasis was achieved by instillation of Tropicamide 0.8% with phenylephrine 5%) eye drops. Surgery was performed under peribulbar anesthesia with lignocaine 2% with adrenaline 1:20000. For Surgery a temporal sclera tunnel based incision was used. In the capsular bag, a foldable posterior chamber intraocular lens was implanted. The same irrigating solution (solution Zysure; zydus) ophthalmic viscoelastic device were used in all cases. At the end of surgery, difluprednate emulsion along with ketorolac eye drops (depending upon the study group) was applied in the post operative dressing.

Study Medications and Study Protocol.

The patients were assigned in a 1:1 ratio to 1 of 2 treatment groups using a computer-generated randomization list. The study medications were ketorolac 0.4% eye drops and ketorolac 0.5% eye drops. On first post operative day, the study medication was instilled 3 times a day in each group. Except for the coordinator distributing the study medications, all other involved in the study remain blind throughout the entire study. For Anti-inflammatory efficacy, measurements were performed preceding the surgery (preoperative) and (day 1, 3, 5, 7, 15, 30).

First day (day 1) Postoperatively, the dressing was removed and patient examined under slit lamp for inflammatory signs i.e. aqueous flare, number of aqueous cells & Conjunctival hyperemia The readings were recorded on every subsequent visits (day 1, 3, 5, 7, 15, 30). The study medication was prescribed according to the randomization key. Moxifloxacin eye drops (QID) will also be given along with to all the patients for first 7 days.

Measurements of Ocular Tolerability

Subjective Tolerability/Pain: The patients tolerability was assessed at each visit. Depending upon pain severity, the patient was asked to mark on a visual analog scale (0 to 100 mm). A mark near to 0 is comfortable and close to 100 mm is painful. Each assessment was independent from the previous one. The patients was given new Performa on every visit.

Measurements of Anti-inflammatory Efficacy

All the three signs of inflammation i.e. anterior chamber cells, flare, Conjunctival hyperemia were examined with slit lamp. The slit lamp magnification and intensity being maximum. The number of cells and flare is counted in an oblique slit lamp beam size 3 mm × 1 mm & then graded accordingly. While for the pain assessment numeric type of Visual analog scale was used. To compare the safety i.e. dry eye we used the tear film breakup time (in minutes).

Scale for assessment

1. Pain was recorded by visual analogue scale⁽²⁾ in which investigator asked the patient to record it on the performa provided. Every time a new performa is given then it is entered in the patient performa by the investigator. Scale used is
Absent 0, mild 1, moderate 2, severe 3 and extreme 4.
2. Aqueous cells – it was counted by slit beam and according to the number of cells present data was entered at each visit in the patient performa by the principal investigator.
3. Aqueous flare was recorded as follows: Faint-just detectable +1, Moderate-iris detail clear +2, Marked-iris detail hazy+3 and for severe fibrinous exudates +4.
4. Conjunctival hyperemia (bulbar hyperemia): very slight+1, slight+2, moderate+3, Severe+4

Safety Parameters

1. Visual Acuity- No VA measurements were recorded on day 1 after surgery.

For the best corrected visual acuity, Snellen charts were used. The Jaeger reading charts for near Visual Analogue were used on later stage.

Tear break up time test (BUT test): In this, Fluorescein dye is instilled in lower fornix. Patient is asked to blink several times & then stop. A filter paper is inserted to examine; appearance of dry area is the end point.

The BUT is the interval in last blink & the appearance of first randomly distributed dry spots. Reading less than 10 seconds is not considered.

In addition, on every visit examination with slit-lamp and indirect funduscopy was done at every visit.

Patient counselling: The Patients were educated for any disproportionate swelling or pain in eye if experience, to report back immediately. Mobile telephone number of the PI (principal investigator) were also provided.

Rescue medicine- Prednisolone acetate 1% eye drop was kept as rescue drug. In case of excessive inflammation, it had to be used.

Statistical Analysis: Quantitative variables are described using mean ± standard deviation (SD) or median as well as minimum and maximum value where appropriate. For nominal and ordinal variables, absolute frequencies and percentages are given. To check the normality of the data Kolmogorov –Smirnov with lifeforms significance correction or Shapiro-Wilk were applied.

The Mann-whitney test was used to check quantitative variables for changes over time and influence of medication.

Wilcoxon signed ranks test were applied compare the effect on tear film break up time pre/post operatively. All tests used were 2-tailed, the level of significance was set at $\alpha = 0.05$.

Instat statistical pack (free) was used for calculation purposes.

Results

Table 1: Comparison of inflammatory marker

	Day	0.5% ketorolac	0.4% ketorolac	P value
Aqueous cells	7	1.40+0.10	1.35+0.05	0.035
Aqueous flare	15	0.52+0.10	0.56+0.10	0.040
Conjunctival hyperemia	5	0.60+0.10	0.62+0.10	0.052

Table 2: Tear film stability

Days	Ketorolac(0.5%)	Ketorolac(0.4%)	P value
3	12.68+0.11	12.56+0.10	0.01
5	12.40+0.13	12.35+0.10	0.011
7	11.72+0.18	11.42+0.10	0.016
15	11.24+0.21	11.02+0.25	0.015
30	10.24+0.26	10.24+0.26	0.012

Only difference between two strength ketorolac is less stinging, discomfort and better ocular tolerability of ketorolac 0.4%. The patient operative outcome is same in the both strength.

Ketorolac 0.4% was shown to be better tolerated both subjective rating on the visual analogue scale as well as in ocular discomfort. The effect was not statistically significant in the tolerability parameter. Although Visual analogue is a proven scale in measuring ocular discomfort and pain. As rating performed by the patient is more sensitive than an observer based assessment of clinical sign.

In the present study the anterior chamber flare and cells shown no statistically significant change but ocular discomfort found to be less as compared to 0.5% Ketorolac.

Discussion

The results were compared with the studies with 0.4%/0.5% and 0.45% strength, as the studies comparing the different strengths were not found even after thoroughly researching the Medscape, Cochrane library & Pubmed. In efficacy studies all strengths were found to be equi-efficacious.

The difference occurs only in ocular discomfort and ocular tolerance. In our study it was not statistically not much significant still with 0.4% of ketorolac (5%) of patients felt less pain as compared to 0.5% of ketorolac at day 5. As the results are based on the visual analogue scale so 0.4% ketorolac can be used for more comfort as it has better ocular tolerability.

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