Comparison of Safety and Efficacy of Prednisolone Acetate Vs Difluprednate Vs Loteprednol Eye drops Post Cataract Surgery

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ABSTRACT

This study is done to compare safety and efficacy of antiinflammatory activity of 1% prednisolone acetate eye drops vs 0.05% difluprednate eye drops vs 0.5% loteprednol etobanate eye drops following uncomplicated cataract surgery. The patients distributed across the three groups were comparable in terms of age, sex and grade of nuclear sclerosis. The difference in the proportion of ocular pain and anterior chamber inflammatory markers (aqueous cells and aqueous flare) on day 1 and day 7 across post-operative drugs used was statistically not significant. The mean difference in IOP, mean macular thickness and mean Log Mar visual acuity on Day 1,7,14 and 28 across post-operative drugs used was not statistically significant. All three drugs were comparable in terms of the ocular pain, Corneal clarity, IOP, anterior chamber activity, macular thickness & visual acuity. In view of less frequent dosing, better patient compliance, reduced total steroid exposure combined with similar anti-inflammatory effect clinically when compared with prednisolone, it is concluded that soft steroids (loteprednol and difluprednate) can be used safely in the post-operative regimen of uncomplicated cataract surgery.

Key words: Cyclo-oxygenase; Intra-ocular lens; Intra-ocular pressure; Non-steroidal anti-inflammatory drug (NSAID); Polymerase chain reaction


BACKGROUND AND INTRODUCTION

Brian G, Taylor H. (2001) revealed that Cataract is the leading cause of blindness worldwide and the main cause of reversible decreased vision in the elderly in the world. Frick KD, Foster A.(2003) experimented that Patients with cataracts have a gradual loss in visual acuity that may be accompanied by reduced physical ability and loss of self-esteem, creating a considerable social and economic burden. Gollogly HE et.al (2013) diagnosed that Cataract surgery is, with more than 20 to 25 million procedures estimated annually, the most performed surgical intervention worldwide. Due to the invasive nature of modern cataract surgery 2 outcomes are common: infection and intraocular inflammation. Infection following cataract surgery remains a great concern and its prevention revolves around intracameral and postoperative care. On the other hand, Inflammation after cataract surgery, which can be persistent, remains an undesirable consequence despite many advances in surgical techniques (Braga-Mele R 2014).

Intraocular inflammation occurs due to the breakdown of cell membranes as a result of tissue injury. In effect, an inflammatory cascade occurs that involves the step-by-step enzymatic conversion of cell membrane phospholipids to bio active prostaglandin molecules. First, surgical trauma activates phospholipase A2, which releases arachidonic acid from the membrane phospholipids (fats that form the lipid bi layer). Arachidonic acid is then metabolized by cyclooxygenases (COX-1 and COX-2) into unstable endoperoxide intermediates (prostaglandin G2 and prostaglandin H2). This ultimately leads to the formation of prostaglandins. Prostaglandin H2 is then isomerized into different prostanoids (Chen L et.al, 2013). All of this leads to local vasodilation and increased vascular permeability. This results in a number of symptoms including hyperemia, miosis, pain, photophobia, diminished visual acuity, and cystoid macular edema. Inflammation is classically treated with steroids as well as with nonsteroidal anti-inflammatory drugs (NSAIDs). Nonsteroidal anti-inflammatory drugs, in particular, reduce inflammation and pain by blocking prostaglandin synthesis by inhibiting COX activity (Ahuja M et.al 2008).

The following figure depicts the inflammatory cascade and site of action of anti-inflammatory medications.

![Fig 1: Inflammatory cascade and site of action of anti-inflammatory agents](http://doi.org/10.36295/ASRO.2020.231511)
The management goals after cataract surgery are to address ocular inflammation, prevent CME, and treat or prevent postoperative pain. Ideally, postoperative anti-inflammatory treatment will prevent the flare and anterior chamber cell reaction that is common for up to 2 weeks after surgery; however, the optimum pharmacologic regimens and duration and dosing of treatment have been debated. When the cornea is inflamed, the patient’s vision remains poor until the inflammation resolves, which may take as long as a few weeks. The patient’s quality of life may consequently be reduced during this time, particularly if the patient is experiencing pain or is uncomfortable. Most ophthalmic surgeons use a standard prophylactic regimen to prevent infections and reduce postoperative inflammation and pain. Regimens to reduce inflammation and pain typically consist of a 4

Introduction corticosteroid and/or an NSAID. Treatment is usually initiated preoperatively because suppressing the inflammatory cascade before surgery can improve postoperative outcomes. Postsurgical anti-inflammatory therapy for uncomplicated surgery generally requires 2 –6 weeks of treatment, and insufficient treatment may contribute to prolonged post-surgical inflammation.

Cataract surgery is one of the most frequently performed elective surgical procedures in developed countries. The surgical methods have improved significantly over the years, thus lowering the risk of complications and raising patient’s and surgeon’s expectations of a successful visual outcome. Like other types of surgery, cataract surgery induces a surgical inflammatory response.

Chen L et.al (2013) in their study on ocular tissue revealed that arachidonic acid is metabolized by cyclooxygenase (COX) to prostaglandins which are the most important lipid-derived mediators of inflammation. Ocular inflammation is characterized by redness, swelling, and/or pain associated with irritation or trauma to the eye. Surgical trauma causes a trigger of the arachidonic acid cascade which in turn generates prostaglandins (PG) by activation of COX-1 and COX-2. Phospholipids in the cell membrane are the substrate for phospholipase A to gene rate arachidonic acid from which a family of chemically distinct prostaglandins and leukotrienes are produced. Clinical symptoms of prostaglandin production include hyperemia, miosis, impaired vision, pain, and diminished visual acuity secondary to cystoid macular edema (CME).

Ahuja M et.al (2008) and Pfuefelder S et.al (2004) through their diagnosis opined that Prostaglandin synthesis can be reduced by inhibiting phospholipase A2, which inhibits the release of arachidonic acid from cell membrane phospholipids, or by inhibiting the conversion of arachidonic acid to prostaglandins via the COX pathway. Different classes of anti-inflammatory medications may block different portions of this pathway. Corticosteroids interfere with the activity of phospholipase A2, thereby inhibiting the release of arachidonic acid and the production of all arachidonic acid metabolites, including prostaglandins. In contrast, nonsteroidal anti-inflammatory drugs (NSAIDs) nonspecifically and irreversibly inhibit the synthesis of prostaglandins by interfering with the activity of COX-1 and COX-2.

Pathogenesis of postoperative inflammation following cataract surgery

Clark W et.al (1999) disclosed that normal post cataract surgical inflammation is thought to be due to the breakdown of the blood aqueous barrier (BAB). This inflammation reaches a peak within the first few postoperative days and then decreases over 2–3 weeks after surgery. Studies of the natural history of untreated cataract surgery show a mean anterior chamber cell grade of 2+ on postoperative day 1 and of 1+ on postoperative day 15.

Aldave A et.al (1999) on the other hand stated that in routine phacoemulsification cataract extraction and intraocular lens implantation with use of topical corticosteroids, most eyes have little inflammation after 4 weeks. However, in ex trabascular cataract extraction with a large wound and manual expression of the nucleus, there may be visible inflammation for up to 8 weeks. Diabetic patients may show more prolonged postoperative inflammation due to increased compromise of the BAB. Complicated cataract surgery may also have more postoperative inflammation than routine phacoemulsification. Surgical factors such as longer operative times, prior surgery, extensive procedures, intraoperative complications, and younger patient age may be associated with increased postoperative inflammation (Clark W et.al 1999) and ( Aldave A et.al 1999).

Acute postoperative inflammation

In the series by Al-Mezaine et.al (2009), culture results showed that 35% of cases were positive for Staphylococcus species (Staphylococcus epidermidis and Staphylococcus aureus), 35% were positive for Streptococcus species (Streptococcus pneumonia, Streptococcus viridans, Streptococcus oralis, and Streptococcus salivarius), 15% of cases were positive for polymicrobial or mixed infections, and 5% were positive for Propionibacterium acnes. Evidence based management of postoperative endophthalmitis as suggested by the study 1, which demonstrated equivalent outcomes for intravitreal antibiotics or pars plana vitrectomy with antibiotics for patients with hand -motions or better presenting vision, but superior outcomes with vitrectomy for patients who were light perception or worse. Even in this latter group, 56% of patients achieved 20/100 or better vision with vitrectomy treatment.

http://doi.org/10.36295/ASRO.2020.231511
Cutler Peck C et.al (2010) explained on TASS is a sterile inflammatory reaction that generally occurs within 12–48 h after surgery. TASS can be difficult to distinguish from acute bacterial endophthalmitis; however, TASS usually has an earlier onset, often within 24 h after cataract surgery, whereas endophthalmitis usually occurs approximately 4–7 days after surgery. TASS also is usually limited to the anterior chamber without substantial vitritis. Patients with TASS usually present with blurred vision without pain, but patients with endophthalmitis often have pain associated with decreased vision. Common clinical features of TASS include diffuse corneal edema from toxic injury to the corneal endothelium, a marked anterior chamber inflammatory response, often resulting in hypopyon and fibrin formation in the anterior chamber, irregularity or dilation of the pupil, iris transillumination defects, and glaucoma due to trabecular meshwork damage. Many possible causes of TASS have been identified and include endotoxin, denatured ophthalmic viscoelastic devices, preservatives, heavy-metal residue, fine-matter particulates, free radicals in intracameral preparations, and residue from cleaning and sterilization of ophthalmic instruments.

The case series by Sengupta S et.al (2010) on recent retrospective case series of TASS cases at Aravind Eye Hospital from 2008 to 2009 showed that TASS is often associated with a good visual outcome. Of the patients with at least 6 months of follow-up following TASS, 25% of eyes had patchy iris atrophic changes with pupil distortion, 4% had cystoid macular edema (CME), 12.5% developed anterior capsular phimosis, 16.6% developed posterior capsular opacification (PCO), 16.6% had a combination of these complications, and 41.6% did not have any complications attributable to TASS. None developed corneal endothelial decompensation or secondary glaucoma. TASS cases will often occur in clusters. Once a TASS diagnosis is made, surgery at the affected center should be suspended and a thorough investigation should be undertaken to identify the cause for the cases.

Chronic postoperative inflammation

Lohmann C et.al (2000) The causes of chronic postoperative inflammation are broadly similar to those for acute disease, including g infection and lens-related inflammation. Additionally, mechanical iritis may result in chronic inflammation following surgery. Chronic endophthalmitis is defined as intraocular infection occurring greater than 6–12 weeks postoperatively. Infectious chronic endophthalmitis must always be considered, particularly in cases presenting with significant vitritis or visible capsular plaque. The incidence of this rare complication is about 0.02% after cataract surgery. Common causes are: P. acnes, S. epidermidis, aerobic streptococci, Actinomyces, and fungi such as Candida parapsilosis. Infection by P. acnes was the most common cause of delayed-onset pseudophakic endophthalmitis and had the most favorable visual outcome, whereas fungal endophthalmitis (17.6% of cases) had worse visual prognosis. Chronic pseudophakic endophthalmitis is often diagnosed by aqueous and/or vitreous cultures; however, there can be culture-negative cases which are responsive to antibiotic therapy, and these are also presumed to be infectious in etiology. PCR diagnostics have higher sensitivity for detection of P. acnes than does traditional culture, but are not widely available. Laser flare photometry may be helpful in determining when chronic postoperative inflammation is infectious in cause. Notably, eyes that were treated with systemic antibiotics showed a significant decrease in mean flare values after 2 weeks of treatment, whereas topical treatment of the inflammation was ineffective in reducing the flare values.

Assessment of Inflammation following cataract surgery

Eye is a unique organ, which can be visualized through direct examination for real time pathological or inflammatory changes apart from clinical history and its assessment. Moreover, non-invasive imaging modalities like ultrasound and other modalities can assist in accessing the areas that cannot be visualized directly. The changes can be quantified in different ocular inflammations and these conditions are categorized based on layers involved such as uveitis (uveal tract), scleritis (sclera), retinitis (re tina), and vitritis (vitreous humor).

In the present research article the authors elected various clinical indicators to assess the ocular inflammation, of which the only subjective clinical parameter was ocular pain. Many different types of scales have been developed to measure pain, including visual analogue scales a and various categorical scales using faces, numbers, or verbal categorical descriptors. However, no pain scale specific to ophthalmic pain has been developed and validated. The majority of previous investigators have used general pain scales to measure pain after ophthalmic procedures or the impact of treatments for ophthalmic pain. We followed the Eye sensation scale 2.0. It is a five-point grading scale, were the patient is requested to only assess the sensation that bothered them the most, if they had experienced multiple sensations, and asks them to rate its severity using one of five categories on the severity scale (“none,” “mild,” “moderate,” “severe,” and “extreme”).

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Corneal clarity is another marker of inflammation studied in our study, the light transmissibility of human cornea has been accredited to the lattice arrangement of collagen fibrils, with consequent minimization of light scattering and destructive interference at the stromal level in combination with corneal crystallins; and the relative state of dehydration maintained at the endothelial level by an array of molecular pumps, chemical modulators, and cell junctional properties. Among the several myriad complications that might ensue a cataract surgery, corneal edema is frequently encountered on. Post cataract surgical corneal edema may occur due to endothelial pump failure, which may be due to mechanical injury, chemical injury, subsequent infection/inflammation, or concurrent/preexisting endothelial compromise.

**Management options of Intraocular inflammation following cataract surgery**

The management goals after cataract surgery are to address ocular inflammation, prevent PCME, and treat or prevent postoperative pain. Ideally, postoperative anti-inflammatory treatment will prevent the flare and anterior chamber cell reaction that is common for up to 2 weeks after surgery; however, the optimum pharmacologic regimens and duration and dosing of treatment have been debated. When the cornea is inflamed, the patient’s vision remains poor until the inflammation resolves, which may take as long as a few weeks. The patient’s quality of life may consequently be reduced during this time, particularly if the patient is experiencing pain or is uncomfortable. Most ophthalmic surgeons use a standard prophylactic regimen to prevent infections and reduce postoperative inflammation and pain. Regimens to reduce inflammation and pain typically consist of a corticosteroid and/or an NSAID. Treatment is usually initiated preoperatively because suppressing the inflammatory cascade before surgery can improve postoperative outcomes. Post-surgical anti-inflammatory therapy for uncomplicated surgery generally requires 2 –6 weeks of treatment, and insufficient treatment may contribute to prolonged post-surgical inflammation. Broadly the options available are either glucocorticoids or NSAIDS. This study will discuss in detail the use of corticosteroids, in management of ocular inflammation following cataract surgery.

**OBJECTIVES**

To compare safety and efficacy of anti-inflammatory activity of 1% prednisolone acetate eye drops vs 0.05% difluprednate eye drops vs 0.5% loteprednol etobanate eye drops following uncomplicated cataract surgery.

**MATERIALS & METHODS**

Inclusion criteria:
1. Patients willing to participate in this study.
2. Patients with immature senile cataract, up to grade 3 sclerosis
3. Age > 40 years

**Exclusion criteria:**

1. Signs of uveitis, intraocular inflammation, macular edema due to previous intraocular surgery in any one of the eyes.
2. Patients with diabetes, complicated cataract, nuclear sclerosis more than grade 3.
3. Patients with intraoperative complications.
4. One eyed patients

This is an interventional randomized double blinded study comparing ocular pain, intraocular pressure, anterior chamber inflammation (aqueous flare and cells) and macular thickness after uncomplicated cataract surgery by phacoemulsification with foldable IOL. The observations are made on Day 1, Day 7, Day 14 and Day 28 postoperatively. The patients are divided into three groups – 100 in each group. Group A to be started on 1% prednisolone acetate six times a day and gradually tapered over 4 weeks. Group B to be started on 0.05% difluprednate four times a day and gradually tapered over 4 weeks. Group C to be started on 0.5% loteprednol etabanate four times a day and gradually tapered over 4 weeks. The results of anterior and posterior segment inflammation and adverse effects of the drugs in each group were strategically analyzed.

**Sample size calculation:**

\[ N = \left( Z_\alpha + Z_\beta \right)^2 \times p \times q \times 2 \times d^2 \]

\[ N = \text{Sample size per group} \]

\[ Z_\alpha = Z \text{ value for alpha error (at 5% level)} \]

\[ Z_\beta = Z \text{ value for beta error (90% power)} \]

\[ p = \text{Average percentage between two groups} \]

\[ q = 100-p \]

\[ d = \text{clinically meaningful difference between two groups} \]

- Alpha error is 5%
- Power of the study is 90%
- The expected difference between the groups was 10% (from literature analysis)
- Average percentage between two groups was 4%
- Z is the cumulative distribution function of a standardized normal deviate \( N = 39.81; 40 \text{ per group} \)

**Statistical analysis:**

Visual acuity (log Mar), Ocular pain, IOP, Macular thickness and corneal clarity were considered as primary outcome variables. (Study group) Post-operative drugs used (Prednisolone acetate Vs Difluprednate Vs Loteprednol) was considered as primary explanatory variable. age, gender, Eye etc., were considered as other explanatory variables.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram. All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro - wilk test was also conducted to assess normal distribution. Shapiro wilk test \( p \text{ value of }>0.05 \) was considered as normal distribution. For normally distributed Quantitative parameters the mean values were compared between study groups using One -way Anova (3 groups). Categorical outcomes were compared between study groups (Post-Operative Drug Used) using Chi square test \( p \text{ value < 0.05} \) was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.)
RESULTS
A total of 120 subjects were included in the final analysis.

Table 1: Comparison of mean Age (in years) across the study groups (N=120)

<table>
<thead>
<tr>
<th>Post-operative drug used</th>
<th>Age (in years)</th>
<th>Mean ± SD</th>
<th>Mean difference</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Prednisolone acetate</td>
<td>59.93 ± 9.63</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone acetate</td>
<td>56.9 ± 7.34</td>
<td>3.03</td>
<td>-0.81</td>
<td>6.86</td>
<td>0.121</td>
</tr>
<tr>
<td>Loteprednol</td>
<td>58.65 ± 8.84</td>
<td>1.28</td>
<td>-2.56</td>
<td>5.11</td>
<td>0.511</td>
</tr>
</tbody>
</table>

The mean age with in Prednisolone acetate was 59.93 ± 9.63, it was 56.9 ± 7.34 in Difluprednate and it was 58.65 ± 8.84 in Loteprednol. Taking Prednisolone acetate as base line, the mean difference of AGE (3.03) in Difluprednate was statistically not significant (P value >0.05) and in Loteprednol (1.28) was also statistically not significant (P value >0.05).

Table 2: Comparison of gender across post-operative drug used (N=120)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Post-Operative Drug Used</th>
<th>Chi square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prednisolone Acetate (N=40)</td>
<td>Difluprednate (N=40)</td>
<td>Loteprednol (N=40)</td>
</tr>
<tr>
<td>Male</td>
<td>16 (40%)</td>
<td>15 (37.5%)</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>Female</td>
<td>24 (60%)</td>
<td>25 (62.5%)</td>
<td>24 (60%)</td>
</tr>
</tbody>
</table>

In Prednisolone Acetate group, 16 (40%) participants were male and 24 (60%) participants were female. In Difluprednate group, 15 (37.5%) participants were male and 25 (62.5%) participants were female. In Loteprednol group, 16 (40%) participants were male and 24 (60%) participants were female. The difference in the proportion of gender across post-operative drug used was statistically not significant (P value 0.966).

Table 3: Comparison of eye across post-operative drug used (N=120)

<table>
<thead>
<tr>
<th>Eye</th>
<th>Post-Operative Drug Used</th>
<th>Chi square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prednisolone Acetate (N=40)</td>
<td>Difluprednate (N=40)</td>
<td>Loteprednol (N=40)</td>
</tr>
<tr>
<td>Right Eye</td>
<td>22 (55%)</td>
<td>17 (42.5%)</td>
<td>25 (62.5%)</td>
</tr>
<tr>
<td>Left Eye</td>
<td>18 (45%)</td>
<td>23 (57.5%)</td>
<td>15 (37.5%)</td>
</tr>
</tbody>
</table>

In Prednisolone Acetate group, 22 (55%) participants were Right Eye and 18 (45%) participants were Left Eye. In Difluprednate group, 17 (42.5%) participants were Right Eye and 23 (57.5%) participants were Left Eye. In Loteprednol group, 25 (62.5%) participants were Right Eye and 15 (37.5%) participants were Left Eye. The difference in the proportion of Eye across post-operative drug used was statistically not significant (P value 0.194).
### Table 4: Comparison of pre-operative diagnosis across postoperative drug used

<table>
<thead>
<tr>
<th>Preoperative Diagnosis</th>
<th>Post-Operative Drug Used</th>
<th>Chi square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prednisolone Acetate (N=39)</td>
<td>Difluprednate (N=40)</td>
<td>Loprednol (N=40)</td>
</tr>
<tr>
<td>NS 1</td>
<td>3 (7.5%)</td>
<td>4 (10%)</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>NS 2</td>
<td>27 (67.5%)</td>
<td>26 (65%)</td>
<td>18 (45%)</td>
</tr>
<tr>
<td>NS 3</td>
<td>10 (25%)</td>
<td>10 (25%)</td>
<td>18 (45%)</td>
</tr>
</tbody>
</table>

In Prednisolone Acetate group, 3 (7.5%) participants were NS 1, 27 (67.5%) participants were NS 2 and 10 (25%) participants were NS 3. In Difluprednate group, 4 (10%) participants were NS 1, 26 (65%) participants were NS 2 and 10 (25%) participants were NS 3. In Loprednol group, 4 (10%) participants were NS 1, 18 (45%) participants were NS 2 and 18 (45%) participants were NS 3. The difference in the proportion of Pre-operative Diagnosis across postoperative drug used was statistically not significant (P value 0.231).

### Table 5: Comparison of mean Frequency of drug used across the study groups (N=120)

<table>
<thead>
<tr>
<th>Post-operative drug used</th>
<th>Frequency of drug used Mean ± SD</th>
<th>Mean difference</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Prednisolone acetate</td>
<td>6 ± 0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone acetate</td>
<td>4.05 ± 0.32</td>
<td>1.950*</td>
<td>1.84</td>
<td>2.06</td>
</tr>
<tr>
<td>Loprednol</td>
<td>4.05 ± 0.32</td>
<td>1.950*</td>
<td>1.84</td>
<td>2.06</td>
</tr>
</tbody>
</table>

The Mean Frequency of drug used in Prednisolone acetate was 6 ± 0, it was 4.05 ± 0.32 in Difluprednate and it was 4.05 ± 0.32 in Loprednol. Taking Prednisolone acetate as base line, the mean difference of Frequency of drug used (1.950) in Difluprednate was statistically significant (P value <0.05) and in Loprednol (1.950) was also statistically significant (P value <0.05)

### Table 6: Comparison of ocular pain day 1 & 7 across post-operative drug used (N=120)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Post-Operative Drug Used</th>
<th>Chi square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prednisolone Acetate (N=40)</td>
<td>Difluprednate (N=40)</td>
<td>Loprednol (N=40)</td>
</tr>
<tr>
<td>Ocular Pain Day 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>23 (57.5%)</td>
<td>21 (52.5%)</td>
<td>25 (62.5%)</td>
</tr>
<tr>
<td>Nil</td>
<td>17 (42.5%)</td>
<td>19 (47.5%)</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>Ocular Pain Day 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>38 (95%)</td>
<td>37 (92.5%)</td>
<td>37 (92.5%)</td>
</tr>
<tr>
<td>Nil</td>
<td>2 (5%)</td>
<td>3 (7.5%)</td>
<td>3 (7.5%)</td>
</tr>
</tbody>
</table>

In Prednisolone Acetate group, 23 (57.5%) participants had mild ocular pain day 1. In Difluprednate group, 21 (52.5%) participants had mild ocular pain day 1. In Loteprednol group, 25 (62.5%) participants had mild ocular pain day 1. The difference in the proportion of ocular Pain Day 1 across post-operative drug used was statistically not significant (P value 0.664).

In Prednisolone Acetate group, 38 (95%) participants had mild ocular pain day 7. In Difluprednate group, 37 (92.5%) participants had mild ocular pain day 7. In Loteprednol group, 37 (92.5%) participants had mild ocular pain day 7. The difference in the proportion of ocular Pain Day 1 across post-operative drug used was statistically not significant (P value 0.875).

Table 7: Comparison of corneal clarity POD #1 across postoperative drug used (N=120)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Post-Operative Drug Used</th>
<th>Chi square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prednisolone Acetate (N=19)</td>
<td>Difluprednate (N=17)</td>
<td>Loteprednol (N=19)</td>
</tr>
<tr>
<td>Corneal Clarity Day 1</td>
<td>Clear</td>
<td>31 (77.5%)</td>
<td>35 (87.5%)</td>
</tr>
<tr>
<td></td>
<td>Edema</td>
<td>9 (22.5%)</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>Corneal Clarity Day 7</td>
<td>Clear</td>
<td>37 (92.5%)</td>
<td>40 (100%)</td>
</tr>
<tr>
<td></td>
<td>Edema</td>
<td>3 (7.5%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*No statistical test was applied due to 0 subjects in the cells.*

In Prednisolone Acetate group, 31 (77.5%) participants had Clear cornea and 9 (22.5%) participants had corneal Edema. In Difluprednate group, 35 (87.5%) participants had Clear cornea and 5 (12.5%) participants had corneal Edema. In Loteprednol group, 24 (60%) participants had Clear cornea and 16 (40%) participants had corneal Edema. The difference in the proportion of corneal Clarity Day 1 across post-operative drug used was statistically not significant (P value 0.241).

In Prednisolone Acetate group, 37 (92.5%) participants had Clear Cornea day 7 and 3 (7.5%) participants had corneal Edema day 7. In Difluprednate group, 40 (100%) participants had clear cornea day 7. In Loteprednol group, 33 (82.5%) participants had Clear cornea day 7 and 7 (17.5%) participants had corneal Edema day 7.

**DISCUSSION**

In managing postoperative ocular inflammation, the ophthalmic surgeon’s ultimate goal is to be able to choose from among several therapeutic options to best meet an individual patient’s needs. There is a strong need for consensus clinical guidelines, additional comparative research concerning existing therapeutic options and understanding of treatment intensity and duration. Deciding which anti-inflammatory agent to use as standard in patients undergoing cataract surgery is important to ensure a favorable outcome.

In the present study, the authors analyzed whether less potent newer steroids (difluprednate and loteprednol) could replace the conventional more potent steroid prednisolone, with similar clinical effect and no increased morbidity. The newer steroids were selected for their better clinical profile like less frequent dosing, better patient compliance, reduced total steroid exposure, Similar anti-inflammatory effect clinically with no adverse changes in IOP. The clinical markers of ocular inflammation such as ocular pain, corneal clarity, IOP, anterior chamber activity, macular thickness & visual acuity were studied at periodic intervals for 28 postoperative days.

The analysis revealed that majority of patients undergoing cataract surgery in this study belonged to nuclear sclerosis NS grade 2 (59.2%), followed by NS grade 3 (31.7%) and NS grade 1 (9.2%) respectively. Also, the patients distributed across the three groups were comparable in terms of age and sex, thereby making the results of this study applicable to all cases of uncomplicated cataract we encounter in the clinical practice. The patient with various nuclear sclerosis grades were distributed to the different drugs under study were also comparable as the P value was significant (P value 0.231).

Ultimately uncontrolled inflammation following cataract surgery leads to compromise of visual acuity, hence the importance of analyzing the visual acuity is core to the study. The analysis of data on visual acuity in our study, revealed that The Mean Log Mar Visual acuity (day 1) of Prednisolone acetatedrug used was 0.15 ± 0.14.
it was 0.18 ± 0.08 in Difluprednate and it was 0.18 ± 0.12 in Loteprednol and it was not statistically significant (P value >0.05). The Mean Log Mar Visual acuity (day 7) of Prednisolone acetate drug used was 0.09 ±0.11, it was 0.13 ± 0.1 in Difluprednate and it was 0.12 ± 0.1 in Loteprednol and it was not statistically significant (P value >0.05). The Mean Log Mar Visual acuity (day 14) of Prednisolone acetate drug used was 0.09 ± 0.1, it was 0.12 ± 0.1 in Difluprednate and it was 0.09 ± 0.1 in Loteprednol and it was not statistically significant (P value >0.05). The Mean Log Mar Visual acuity (day 28) of Prednisolone acetate drug used was 0.06 ± 0.09, it was 0.09 ± 0.1 in Difluprednate and it was 0.09 ± 0.1 in Loteprednol and was not found to be statistically significant (P value >0.05).

CONCLUSION

All three drugs were comparable in terms of the ocular pain, corneal clarity, IOP, anterior chamber activity, macular thickness & visual acuity. In view of less frequent dosing, better patient compliance, reduced total steroid exposure combined with similar anti-inflammatory effect clinically when compared with prednisolone, it is concluded that soft steroids (loteprednol and difluprednate) can be used safely in the post-operative regimen of uncomplicated cataract surgery in patients with no significant history of systemic illness.

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