

## Efficacy of Topical Difluprednate in Control of Inflammation after Phacoemulsification

Md Abdur Rashid<sup>1</sup>, Farhana Rahman<sup>2</sup>, Mohosana Khanam<sup>3</sup>, Farjana Sharmeen Shimu<sup>4</sup>,  
KM Mizanur Rahman<sup>5</sup>, Farzana Hossain<sup>6</sup>

### Abstract

**Objective:** To study the efficacy of topical Difluprednate 0.05% ophthalmic emulsions in control of post-operative inflammation following phacoemulsification. **Methods:** This randomized control study included hundred diagnosed cases of age-related cataract who visited at the National institute of Ophthalmology and Hospital in Bangladesh over one year period. The patients were divided into two groups –Difluprednate group and Prednisolone group. The post-operative grades of inflammation following phacoemulsification were assessed by slit-lamp examination. **Results:** In the present study, majority of the patients were in age group of 55 to 65 years. Male: female ratio in Dfluprednate group was 29:21 and in Prednisolone group was 35:15. Anterior chamber flare and cells was seen in 52% of patients in Prednisolone group and in 56% of patients in the Difluprednate group by day 07, which regressed to mild (1-3) in both the groups by day 28. On day 42, the cells and flair were reduced to 4% in Difluprednate group and 8% at Prednisolon group. When the total scoring of all these parameters were compared, in Prednisolone group 34% of the patients persisted with mild (Grade1-3) inflammation on Day 28 as compared with 26% of the patients in Difluprednate group. **Conclusion:** Both Difluprednate Ophthalmic Emulsion 0.05% eye drops and Prednisolone Acetate 1% eye drops were equally effective in reducing the inflammation following uncomplicated phacoemulsification. With proven efficacy of Difluprednate, we now have a new standard for potency in a topical corticosteroid, with excellent anti-inflammatory properties and an ideal formulation for our patients.

**Keywords:** Difluprednate, Prednisolone Acetate, anti-inflammatory, phacoemulsification.

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<sup>1</sup> Junior consultant, National institute of Ophthalmology and Hospital (NIO&H), Dhaka.

<sup>2</sup> Medical officer, NIO&H, Dhaka.

<sup>3</sup> Junior consultant, Shaheed Suhrawardy Medical College and Hospital, Dhaka.

<sup>4</sup> Assistant surgeon, NIO&H, Dhaka.

<sup>5</sup> Long Term Fellow Glaucoma, NIO&H, Dhaka.

<sup>6</sup> Epidemiologist, NIO&H, Dhaka

### Address of correspondence:

Dr. Md Abdur Rashid  
Junior consultant,  
National institute of Ophthalmology and  
Hospital (NIO&H), Dhaka.

E-mail: rashidkmc11@gmail.com

Cell No: 01916610359

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### Introduction

Vision is the most concern in any ophthalmologist. Controlling and preventing inflammation after cataract surgery is important to achieve optimal results following surgery. The physician can proactively help to reduce the risk of inflammation that can occur after the operation take place. Although recent advances in cataract extraction (CE) surgery decreases the physical trauma associated with ocular surgery, disruption of the blood brain barrier during surgery can lead to post-operative ocular inflammation. This condition is often self-limiting, but untreated inflammation can interfere with the patient's visual rehabilitation, and in rare cases can result in complications such as cystoid macular edema, posterior capsule fibrosis, keratopathy, fibrin reaction, or chronic uveitis<sup>1-3</sup>. Because of their broad anti- inflammatory activity, corticosteroids are typically the cornerstone of these treatment regimes. In the immediate post-operative period, topical corticosteroids are employed to suppress

the production of inflammatory mediators, offering local treatment without the risk of systemic adverse effects. By inhibiting the release of arachidonic acid from cell membrane phospholipids, corticosteroids prevent the formation of both leukotrienes and prostaglandins, disrupting the inflammatory cascade<sup>4</sup>. These agents are continued until the anterior chamber reaction has resolved and the blood-aqueous barrier has been reestablished<sup>5</sup>. The most common method of controlling intraocular inflammation is with corticosteroids. Thus, the majority of treatment of ophthalmic inflammation today is by topical drops or local injections. Local injections can profoundly decrease ocular inflammation, and are particularly useful in cases of patient noncompliance. Topical corticosteroids are a very effective treatment for post-operative ocular inflammation since they effectively block the initial release of inflammatory mediators. In June 2008, the US Food and Drug Administration approved difluprednate ophthalmic emulsion 0.05% a strong topical steroid, for the treatment of post-operative ocular inflammation and pain-the first steroid to be indicated for pain associated with ocular surgery. The approved dosing for difluprednate is 1 drop in the affected eye(s) 4 times daily beginning 24 hours after surgery and continuing for 2 weeks followed by twice daily for a week and then tapering based on patient's response. Difluprednate is a pro-drug. It rapidly penetrates the corneal epithelium where it quickly deacetylates to difluprednisolonebutyrate (DFPB) the active metabolites. Currently the most widely prescribed strong topical steroid in our country is prednisolone acetate 1% which it controls inflammation effectively; it has not been shown to consistently address post-operative pain and discomfort in a large clinical trial. A study was done to assess the efficacy of difluprednate 0.05% ophthalmic emulsion to placebo in the treatment of inflammation associated with ocular surgery. Difluprednate 0.05% ophthalmic emulsion safely clears post-operative inflammation with no serious adverse effects. Thus, difluprednate is the first ophthalmic steroids developed in the past 35 years with high potency favorable safety profile and have got the ability to reduce post-operative pain.

The aim of this study was to study the efficacy of topical difluprednate 0.05% ophthalmic emulsion versus topical prednisolone acetate 1% ophthalmic suspension in the treatment of post-operative ocular inflammation after phacoemulsification.

## Methodology

This was a Randomized control study conducted in the National institute of ophthalmology and hospital, Dhaka, from June 2016 to July 2018. A total of hundred patients diagnosed with age related cataracts without any other ocular diseases were enrolled in the study. The patients were divided into two groups (Difluprednate and Prednisolone). The post-operative grades of inflammation following phacoemulsification were assessed by slit-lamp examination.

The patients were examined postoperatively on days 1, 7, 28 and 42. At each visit, symptoms like pain, watering and any other experienced by the patient were noted. Visual Acuity was assessed by Snellen's chart and a slit lamp examination was done for evaluation of inflammation. All Slit lamp examinations were conducted under standard conditions: dim room illumination, highest lamp voltage, 3x1 millimeter aperture for Anterior chamber Flare and Cells, illumination angle of 30 degrees and magnification of 16x. Lid oedema, conjunctival congestion, ciliary congestion, corneal oedema, anterior chamber cells and anterior chamber flare were checked in each follow up. The AC cells grading were assessed as follows-

Grade	Cells in field
None	<1
Mild	1-5
Moderate	6-25
Severe	26 and above

Data were analyzed with the help of SPSS (Statistical Package for Social Science) 26.0 Version. To find out association between qualitative data, Fisher Exact test was used. A probability value (p) of <0.05 was considered statistically significant.

**Results****Table 1** – Baseline characteristics of the patients

Criteria	Difluprednate	Prednisolone
<b>Age group (in years)</b>		
50-54	15 (30.0%)	16 (32.0%)
55-59	31 (62.0%)	25 (50.0%)
60-65	4 (8.0%)	8 (16.0%)
Above 65	0 (0.0%)	1 (2.0%)
<b>Gender</b>		
Male	29 (58.0%)	35 (70.0%)
Female	21 (42.0%)	15 (30.0%)
<b>Type of cataract</b>		
Immature	34 (68.0%)	31 (62.0%)
Mature	11 (22.0%)	14 (28.0%)
Hypermature	5 (10.0%)	5 (10.0%)

In the present study, majority of the patients were in age group of 55 to 65 years. Male: female ratio in Difluprednate group was 29:21 and in Prednisolone group was 35:15 (Table 1).

**Table 2** – Grading of inflammatory parameters of the patients

Grading	Difluprednate	Prednisolone	p value
<b>Day 1</b>			
None	0 (0.0%)	0 (0.0%)	0.119
Mild	0 (0.0%)	0 (0.0%)	
Moderate	40 (80.0%)	32 (64.0%)	
Severe	10 (20.0%)	18 (36.0%)	
<b>Day 7</b>			
None	12 (24.0%)	16 (32.0%)	0.648
Mild	28 (56.0%)	26 (52.0%)	
Moderate	10 (20.0%)	8 (16.0%)	
Severe	0 (0.0%)	0 (0.0%)	
<b>Day 28</b>			
None	37 (74.0%)	29 (58.0%)	0.064
Mild	13 (26.0%)	17 (34.0%)	
Moderate	0 (0.0%)	4 (8.0%)	
Severe	0 (0.0%)	0 (0.0%)	

**Day 42**

None	48 (96.0%)	46 (92.0%)	0.678
Mild	2 (4.0%)	4 (8.0%)	
Moderate	0 (0.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	

The number of patients with moderate inflammation on day 1 was 40 patients (80%) in Difluprednate group and 32 patients (64%) in Prednisolone group. The other 10 patients (20%) in Difluprednate group and 18 patients (36%) in Prednisolone group had severe inflammation. By Day 7, 28 patients (56%) in Difluprednate group and 26 patients (52%) in Prednisolone group had mild inflammation. Ten patients (20%) in Difluprednate group had moderate inflammation as compared with 8 patients (16%) in Prednisolone group. Thirteen patients (26 %) in Difluprednate group and 17 patients (34%) in Prednisolone group had mild inflammation on day 28. Only 4 patients (8%) in Prednisolone group had moderate inflammation. By Day 42, two patients (4%) in Difluprednate group and 4 patients (8%) in Prednisolone group had mild inflammation (Table 2).

**Discussion**

In order to compare the effectiveness of topical difluprednate 0.05% ophthalmic emulsion versus topical prednisolone acetate 1% ophthalmic suspension in the treatment of post-operative ocular inflammation after phacoemulsification, a total of 100 patients with age-related cataract underwent phacoemulsification in NIO&H. They were divided into two groups. Group A - 50 cases (Difluprednate ophthalmic emulsion 0.05% group) Group B- 50 cases (Prednisolone Acetate Ophthalmic Suspension 1% group). Maximum of the total patients were in age group of 50 to 65 years & above. In a similar study done in USA mean age group of patients in Difluprednate group was 47 years and in Prednisolone group was 43 years.<sup>6,7</sup>

There was no statistical difference between the two groups at any time. In USA a similar study

was done, where Difluprednate was compared to a placebo found that clearing of inflammation on Day 14, defined as an AC cell grade of 0 (<5 cells) and a flare grade of 0 (complete absence), was achieved in a significantly greater percentage of subjects treated with Difluprednate, compared with placebo (74.7% v/s 42.5% p=0.0006). A significantly greater percentage of Difluprednate-treated subjects were free of ocular pain/discomfort on Day 14 than placebo-treated subjects (64.6% v/s 30.0%; (p=0.0004)<sup>8,9</sup>.

In the present study, 02 patients (4%) in Difluprednate group and 4 patients (8%) in Prednisolone group had Grade 1 cells in the anterior chamber on day 42. Sirion therapeutics conducted a similar study where in the primary endpoint was the difference from baseline in AC cell grades between the Difluprednate and Prednisolone groups. At Day 14, the Difluprednate group achieved a mean cell grade reduction of 2.1 compared to 1.9 in the Prednisolone group, confirming the noninferiority of Difluprednate to Prednisolone<sup>10</sup>. Another similar study was done by Sirion therapeutics, where comparison was done between Difluprednate and Betamethasone found that Difluprednate was effective in reducing AC cell, flare, and total signs and symptom scores. After 14 days of Difluprednate treatment, 72% of patients had less than 10 cells and 11% had no cells in the anterior chamber<sup>11</sup>. Another similar study was done in Arizona, USA, where comparison was done between Difluprednate and Betamethasone found that there were no statistically significant differences between the treatment groups in mean AC cell count, mean AC flare on days 3,7 or 14. This study showed that treatment with Difluprednate 0.05% was at least as effective as Betamethasone 0.1% in

reducing postoperative inflammation and its safety profile was acceptable<sup>7</sup>. A similar study was also done in Florida where Difluprednate was compared to a placebo found that clearing of inflammation on Day 14, defined as an AC cell Grade of 0 (<5 cells) and a flare Grade of 0 (complete absence), was achieved in a significantly greater percentage of subjects treated with Difluprednate, compared with placebo (74.7% v/s 42.5% p=0.0006). A significantly greater percentage of Difluprednate-treated subjects were free of ocular pain/discomfort on Day 14 than placebo-treated subjects (64.6% v/s 30.0%; p=0.0004)<sup>12</sup>.

A similar study was done in Texas, USA where comparison was done between Difluprednate and Betamethasone found that there were no statistically significant differences between the treatment groups in mean AC cell count, mean AC flare on days 3,7 or 14. This study showed

that treatment with Difluprednate 0.05% was at least as effective as Betamethasone 0.1% in reducing postoperative inflammation and that its safety profile was acceptable<sup>13</sup>.

## Conclusion

In conclusion, Difluprednate Ophthalmic Emulsion 0.05% was as effective as Prednisolone Acetate 1% Ophthalmic Suspension in treating postoperative inflammation following phacoemulsification. Thus, Difluprednate Emulsion 0.05% appears to be a promising addition to the surgical armamentarium for treating postoperative inflammatory conditions. With proven efficacy of Difluprednate, we now have a new standard for potency in a topical corticosteroid, with excellent anti-inflammatory properties and an ideal formulation for our patients.

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