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Original Research Article

An observational comparative study of intraocular pressure changes in post-operative cataract patients treated with dexamethasone, difluprednate and prednisolone in a tertiary care centre

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ABSTRACT

Background: Cataract is opacity of lens which is treated surgically. Topical corticosteroids are routinely used in the treatment of post-operative inflammation following cataract surgery. This study aims to compare the intraocular pressure changes caused by various topical steroids (prednisolone, dexamethasone and difluprednate) in post cataract patients. To compare compliance and to detect any significant adverse effects.
Methods: Patients admitted in ophthalmology department for cataract surgery operated by phacoemulsification were taken as subjects. Total number of patients enrolled in the study were 354. Subjects were separated into 3 groups depending on topical steroids which were prescribed after surgery: group 1 - difluprednate, group 2 -dexamethasone and group 3 - prednisolone. Changes in intraocular pressure (IOP) of patients were measured by ophthalmology department preoperatively and postoperatively after 1st, 2nd, 3rd, 4th week of surgery. These data were collected and analysed. Adverse effects, Compliance of patients and number of bottles of drug used after surgery were also noted.
Results: On comparing IOP, there was significant variation ($p<0.027$) between 3 drugs after one week of drug administration. When group 1 was compared with group 2 or group 3 there was no significant difference Average cost of difluprednate is about 3 times higher than the cost of dexamethasone or prednisolone.
Conclusions: All the three topical steroids cause a rise in intraocular pressure in post cataract patients. But in group 1 (difluprednate) there was a rise in IOP up to three weeks after surgery but after 3rd week IOP remained stable. Adverse effects were seen more in group 2 and group 3.

Keywords: Difluprednate, Prednisolone, Intraocular pressure

INTRODUCTION

An observational comparative study of intraocular pressure changes in post-operative cataract patients treated with dexamethasone, difluprednate and prednisolone in a tertiary care centre.

Cataract is opacity of lens which is treated surgically. Post-operative ocular inflammation after cataract surgery is usually self-limiting but can be associated with corneal oedema, spikes in intraocular pressure (IOP) and posterior capsule opacification.[1]

Topical corticosteroids are routinely used in the treatment of post-operative inflammation following cataract surgery, as well as after most other ocular surgical procedures.[2-9] Although topical ocular corticosteroids are a vital component of the treatment of post-operative inflammation, their prolonged use can produce side effects, such as increased IOP and lowered resistance to infection.[1]

Randomized, controlled studies to date, and clinical studies in known steroid responders, indicate that there are significant differences among the common topical ophthalmic corticosteroids used in the treatment of post-operative inflammation. One of these differences that has important clinical implications is their varying effects on intraocular pressure.

In the tertiary care hospital where this study was done all 3 drugs viz-dexamethasone, prednisolone, and difluprednate are routinely being used in the management of postoperative cataract surgery patients.

Aims and objectives of this study were: to compare the intraocular pressure changes caused by various topical steroids (prednisolone, dexamethasone and difluprednate) in post cataract patients; to compare compliance of prednisolone, dexamethasone and difluprednate in post cataract patients; and to detect any significant adverse effects with these three drugs.

METHODS

It was a randomized observational study done in the institute (SMIMER, Surat) after the institutional ethics committee (IEC) permission during the period April 2016 to March 2017. Total number of patients enrolled in the study were 354. Written informed consent was obtained from all patients. Confidentiality of information was maintained.

Patients above 18 years of age and willing to participate were included in our study. Patients admitted in ophthalmology department for cataract surgery operated by only phacoemulsification were included. Patients of age less than 18, children and patients of cataract with diabetes, glaucoma, and hypertension were excluded. Patients were selected randomly.

Sample size was calculated by doing pilot study of one month in department of ophthalmology. The proportion of patients without diabetes/hypertension/glaucoma by one-month pilot survey from department of ophthalmology were:

$$105/157 = 66\%$$

Number of patients without diabetes/hypertension/ glaucoma by one-month pilot survey were 105. The total number of patients operated for cataract in one-month pilot survey were 157.

Patients were selected randomly. Data of 374 patients was collected for this study. Twenty patients were not included in final calculation as they did not report for follow up.

The protocol for 3 groups was pre-decided by ophthalmology department as follows: topical steroids were given 12 hours after surgery in each group; subjects were separated into 3 groups depending on topical steroids which were prescribed after surgery.

Group 1

Patients operated on Mondays were prescribed difluprednate 0.05% eye drop.

Dosage

Drug was given four times a day for 1 week. Followed by three times a day for 1 week and then twice a day for 2 weeks

Group 2

Patients operated on Tuesdays were prescribed dexamethasone 0.3% eye drop.

Dosage

Drug was given 1 hourly for 1 week.

Followed by 2 hourly for 1 week and then four times a day for 2 weeks.

Group 3

Patients operated on Thursdays were prescribed prednisolone 1% eye drop.

Dosage

Drug was given 1 hourly for 1 week. Followed by every 2 hourly for 1 week and then four times a day for 2 weeks.

Changes in IOP of patients were measured and documented by the ophthalmology department preoperatively and postoperatively after 1st, 2nd, 3rd, and 4th week of surgery. These data were collected and analysed to assess if any of the drugs had caused significant change in intra-ocular pressure and whether there was any difference among the test drugs in this regard. Other parameters recorded were: adverse effects if any, compliance of patients and number of bottles of drug used after surgery. All data were analysed by using statistical software statistical package for the social sciences (SPSS) 16 version and Microsoft 2010. Data were analysed by applying paired t test, analysis of variance (ANOVA) test followed by Turkey's post hoc test for all multiple comparisons. P value less than 0.05 was considered as significant in this study.

RESULTS

Comparison of IOP changes amongst different steroids

After application of ANOVA test for multiple variable comparisons, there was significant variation ($p<0.027$)

between 3 drugs after one week of drug administration (Table 1).

During 1st week when mean IOP between 3 drugs was compared it showed that mean IOP of prednisolone group was higher than dexamethasone and difluprednate group.

However on comparison of mean IOP of 3 drugs at the end of 2nd, 3rd, and 4th week there was no significant difference ($p>0.05$). Mean IOP of prednisolone was higher than dexamethasone and difluprednate group (Figure 1).

After applying post hoc test after 1st week for multiple variable comparisons when difluprednate (group 1) was compared with dexamethasone (group 2) or prednisolone (group 3) there was no significant difference ($p>0.05$) (Table 2).

When dexamethasone (group 2) was compared with difluprednate (group 1) there was no significant difference ($p>0.05$). When dexamethasone (group 2) was compared with prednisolone (group 3) there was significant difference ($p<0.05$). But when prednisolone (group 3) is compared with difluprednate (group 1) there is no significant difference ($p>0.05$). When prednisolone (group 3) was compared with dexamethasone (group 2) there was statistically significant difference ($p<0.05$).

Cost analysis of topical steroids

Group 1

Average number of difluprednate eye drop bottles (5 ml) used were 2-3.

Average cost of difluprednate 5 ml is 100-110 rupees.

Group 2

Average number of dexamethasone eye drop bottles (10 ml) used were 2-3.

Average cost of dexamethasone 10 ml is 25-30 rupees.

Group 3

Average number of prednisolone eye drop bottles (10 ml) used were 2-3.

Average cost of prednisolone 10 ml is 25-30 rupees.

Comparison of the three shows that the average cost of difluprednate is about 3 times higher than the cost of dexamethasone or prednisolone.

Analysis of adverse effects of different steroids

In group 1, redness of eyes and watering of eyes were reported.

In group 2 and 3, pain, itching of eyes and watering of eyes were reported.

Blurring of vision was reported only in group 2.

Analysis of compliance of patients

Compliance of patient was good in group 1. None of the patients missed any dose. In group 2, number of patients who missed one or more doses during 1st week and 2nd week were 19 and 12 respectively. In group 3, number of patients who missed the dose during 1st week and 2nd week were 16 and 6 respectively (Table 3).

Compliance of patient was 100% in group 1 throughout the four weeks' duration of treatment (Table 4).

In group 2, compliance of patient was 86% in 1st week, 91.1% in 2nd week, and 100% in 3rd and 4th week.

In group 3, compliance of patient was 85.1% in 1st week, 94.4% in 2nd week, and 100% in 3rd and 4th week.

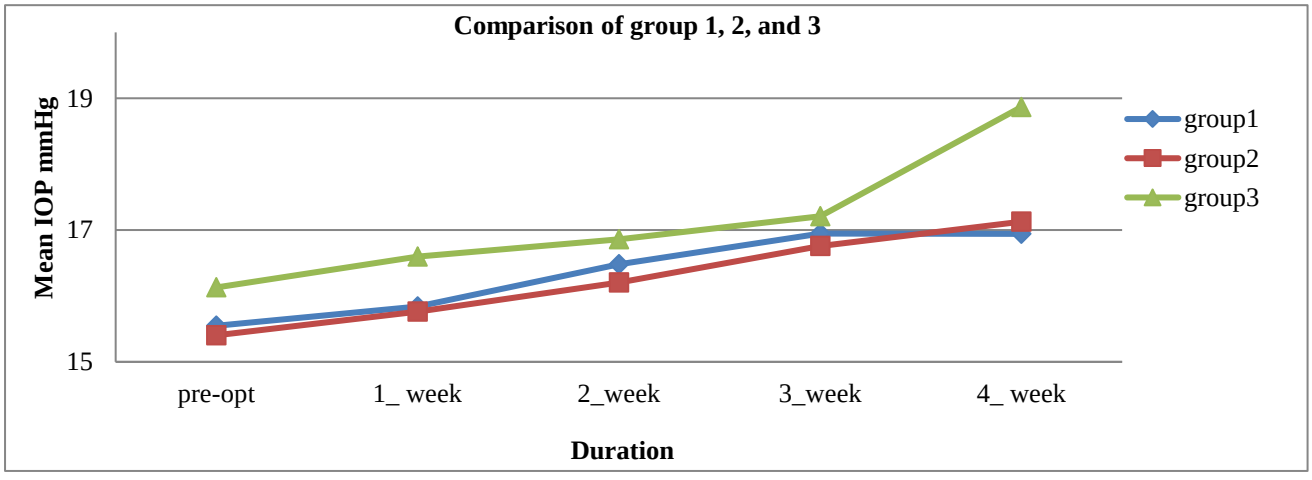

Figure 1: Comparison of mean IOP changes amongst different steroids.
Graphical presentation of IOP changes between 3 groups by taking duration of drug treatment on X-axis and IOP on Y-axis

Table 1: Comparison of variation in mean IOP amongst different steroids.

Duration	Drugs	N	Mean	Standard deviation	Minimum	Maximum	P value
Pre-opt	1	110	15.5473	2.48543	9.00	21.00	0.048
	2	136	15.4029	2.26611	10.00	20.00	
	3	108	16.1287	2.34485	10.00	21.00	
	Total	354	15.6692	2.37372	9.00	21.00	
1st week	1	110	15.8409	2.60220	8.00	22.00	0.027
	2	136	15.7610	2.41683	11.00	22.00	
	3	108	16.5991	2.77709	7.70	22.50	
	Total	354	16.0415	2.60776	7.70	22.50	
2nd week	1	110	16.4818	2.66170	11.90	25.70	0.191
	2	136	16.2044	2.41948	11.00	23.00	
	3	107	16.8598	3.29023	9.00	34.30	
	Total	353	16.4895	2.78783	9.00	34.30	
3rd week	1	110	16.9464	2.88621	12.00	26.00	0.441
	2	136	16.7551	2.38718	12.00	22.00	
	3	107	17.2093	3.00555	9.00	23.90	
	Total	353	16.9524	2.74234	9.00	26.00	
4th week	1	110	16.9409	2.77500	11.00	25.00	0.137
	2	136	17.1272	2.40855	11.00	23.00	
	3	107	18.8682	13.84316	9.20	157.00	
	Total	353	17.5969	7.93902	9.20	157.00	

Table 2: Application of post hoc tests for comparing IOP changes of 3 groups.

Dependent variable	(I) F1	(J) F1	Mean difference (I-J)	P value	95% confidence interval	
					Lower bound	Upper bound
Pre-opt	1	2	0.14433	0.882	-0.5680	0.8566
		3	-0.58143	0.165	-1.3339	0.1710
	2	1	-0.14433	0.882	-0.8566	0.5680
		3	-0.72576*	0.046	-1.4417	-0.0098
	3	1	0.58143	0.165	-0.1710	1.3339
		2	0.72576*	0.046	0.0098	1.4417
1st week	1	2	0.07988	0.969	-0.7014	0.8612
		3	-0.75816	0.079	-1.5835	0.0672
	2	1	-0.07988	0.969	-0.8612	0.7014
		3	-0.83804*	0.033	-1.6233	-0.0528
	3	1	0.75816	0.079	-0.0672	1.5835
		2	0.83804*	0.033	0.0528	1.6233

Turkey HSD

Table 3: Compliance of patients of different groups.

Drug	Number of patients missed the dose during subsequent intervals			
	1st week	2nd week	3rd week	4th week
Group 1	0	0	0	0
Group 2	19	12	0	0
Group 3	16	6	0	0

Table 4: Comparison of compliance of patients of different groups.

Drug	1st week (%)	2nd week (%)	3rd week (%)	4th week (%)
Group 1	100	100	100	100
Group 2	86	91.1	100	100
Group 3	85.1	94.4	100	100

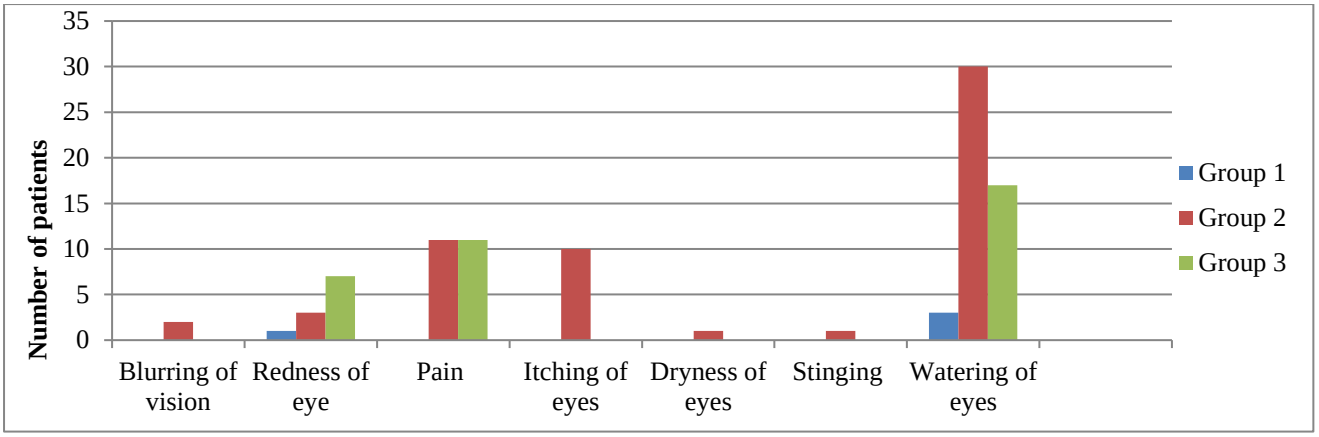

Figure 2: Comparison of adverse effects of different groups.

DISCUSSION

Steroids when used in post-cataract patients, inhibit the production of leukotrienes and prostaglandins, thereby reducing potentially hazardous ocular inflammation.[10] In most patients, postoperative increase in IOP following cataract surgery is transient.[11] Clinical data suggests that patients with healthy eyes can tolerate a transient postoperative rise in IOP with no detectable effect on visual function.[12]

A study done by with Patil et al in 90 patients to compare the anti-inflammatory efficacy of dexamethasone, difluprednate and prednisolone after phacoemulsification showed that there were no IOP spikes.[13] The result of this study also showed that all three steroids are equally efficacious in controlling inflammation but difluprednate was found to control inflammation more rapidly.[14]

A randomized, prospective study was conducted by Roth et al on 54 patients. Results of this study showed that eyes that received topical prednisolone 1% had a lower IOP 18 months following trabeculectomy than the eyes that received no prednisolone. These results were opposite to our study. In our study IOP was significantly raised in the group receiving prednisolone.[15]

Laurell and Zetterstrom et al (2002)[16] compared the effects of treatment with dexamethasone, diclofenac, or placebo in 180 patients after phacoemulsification. Results were similar to our study which proves dexamethasone increases IOP throughout the duration of four weeks.

Various studies have been documented on steroid responders which shows that even a small dose of corticosteroid result in disproportionate increases in IOP.[17] Effects on IOP in such patients are generally reversible and when treatment is discontinued IOP usually return to pre-treatment levels within 1–3 weeks.[18]

Results of Korenfeld et al study were also similar to our study, in which the efficacy and safety of difluprednate ophthalmic emulsion 0.05% was compared with that of placebo (vehicle) in 438 patients with inflammation after ocular surgery.[19]

Results of Sheppard et al were similar to our study which showed increase in IOP during 1st week. This was multicentric randomized study which proves that the mean IOP increased at day 3 that is 2.5 mm Hg for difluprednate-treated patients and 0.1 mm Hg for prednisolone acetate-treated patients. This study also proves that difluprednate is well tolerated and is not inferior to prednisolone.[20]

Result of one study conducted by Sood et al is similar to our study which shows that prednisolone being the most efficacious has also produced maximum rise in intraocular pressure as compared to other newer drugs i.e. difluprednate.[21]

However, limitation of our study was that follow up of patients was short, that was only up to 4 weeks. Further studies with longer follow up period may elucidate a better picture. In our study only 3 steroids were used. Further studies comparing the effects of other newer steroids in addition to those tested in our study, may help in identifying a more acceptable steroid.

CONCLUSION

All the three topical steroids cause a rise in intraocular pressure in post cataract patients.

In group 1 (difluprednate) there was a rise in IOP up to three weeks after surgery but after 3rd week IOP remained stable. In group 2 (dexamethasone) rise in IOP was seen throughout the 4 weeks of treatment. In group 3 (prednisolone) IOP was raised throughout the four weeks of treatment but during 4th week there was even more significant rise in IOP. This rise can possibly be attributed to steroid responders.

Adverse effects such as pain, redness and watering of eyes seen more in group 2 and group 3 in comparison to group

1. Compliance of patients was better in group 1 compared to group 2 and group 3. This may be possibly due to lower frequency of instillation of drug in group 1 compared to group 2 and 3 specially in 1st and 2nd week postoperatively.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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