Comparison of Efficacy of Difluprednate Emulsion vs Topical Prednisolone Acetate on Post Phacoemulsification Inflammation

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ABSTRACT

Introduction: Phacosmulsification with IOL implantation is currently the procedure of choice for cataract surgery as it offers the best visual results. Two main groups of drugs used to control postoperative inflammation following cataract surgery are NSAIDS, which directly inhibit the cox enzymes and topical corticosteroids, which act at the level of phospholipase A2. Study objective was to compare the efficacy of 0.05% difluprednate emulsion and 1% prednisolone acetate suspension on post phaco inflammation.

Material and methods: 80 patients undergoing phacoemulsification in tertiary health care centre were randomly divided into 2 groups. Postoperatively, patients in group A were put on 0.05% difluprednate eye drops while group B were put on 1%prednisolone acetate eye drops for 42 days each. At each visit evaluation was done for BCVA, IOP, ocular pain grading, slit lamp for aqueous cells/ flare score.

Results: At end of study, 97.5% patients in group A and 95% patients in group B had BCVA of 6/6. None of patients in any group showed significant rise in IOP >21mmHg. 95% patients in both groups showed ocular pain grade of 1 while 2% patients in group A and 1% in group B showed ocular pain grade of 2. 97.5%in group A and 95% in group B presented with 100% aqueous cell clearing while 97.5% patients in both groups and showed flare score 0 at last follow up.

Conclusion: Topical 0.05%difluprednate ophthalmic emulsion is as effective as 1% prednisolone acetate in treating post phacoemulsification inflammation with the advantage of uniform drug dosage and no preservative.

Keywords: Phacoemulsification, Difluprednate, Prednisolone Acetate

INTRODUCTION

The principal cause of blindness today, in India, is cataract, responsible for about 62.6% of all cases.[1] Phacoemulsification with intraocular lens implantation is currently the procedure of choice for cataract surgery as it offers the best visual results.[2] Surgical manipulation of anterior segment structures alters the blood aqueous barriers triggering the release of arachidonic acid from cell membrane leading to ocular inflammation and production of prostaglandins and leukotrienes. Untreated inflammation can lead to complications such as pain, photophobia, corneal oedema, synechiae, glaucoma and cystoid macular oedema.[3,4]

Two main groups of drugs that are used to control post operative inflammation following cataract surgery are non steroidal anti inflammatory drugs(NSAIDS),which directly inhibit the cox enzymes and topical corticosteroids, which act at the level of phospholipase A2 with the resultant inhibition of prostaglandin release.[5,6]

Difluprednate 0.05% ophthalmic emulsion is a synthetic diflourinated prednisolone derivative for ophthalmic use.[7] Being a potent topical steroid exhibiting enhanced penetration, better bioavailability, rapid local metabolism, and strong efficacy with low incidence of adverse effects, it is effective in treating both postoperative inflammation and anterior uveitis.[8]

Prednisolone acetate contains benzalkonium chloride as preservative, which is known to break down cell wall by emulsifying membrane lipids, thus disrupting the tear film causing immune allergic reactions and creating direct toxicity to corneal and conjunctival epithelial cells. Difluprednate ophthalmic emulsion does not contain BAK and instead uses sorbic acid as preservative which causes little damage and irritation to ocular surface and is recommended for use in sensitive eyes. Study objective was to compare the efficacy of 0.05% difluprednate emulsion and 1% prednisolone acetate suspension on post phaco inflammation.

MATERIAL AND METHODS

A prospective single masked study was carried out on 80 patients of cataract admitted to undergo phacoemulsification in a tertiary health care centre in North India. After taking ethical clearance from the ethical committee of the institute, the study was initiated. Informed and written consent was taken from all the patients. The patients were randomly divided into two groups (A and B) comprising of 40 patients each. All the patients underwent phacoemulsification with IOL implantation performed by a single surgeon. Detailed pre operative work up was done for every patient who underwent phacoemulsification.

Patients with prior steroids usage within 14 days of surgery, pre operative presence of cells/flare on slit lamp examination, prior glaucoma, corneal or posterior segment surgery, history of diabetes, inflammatory or any other debilitating systemic disease were excluded from the study. Post operative examination was done on 7,21 and 42 days and included: snellen's visual acuity (unaided and pinhole),

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intraocular pressure measured with applanation tonometry, slit lamp evaluation of the anterior segment for aqueous cells and aqueous flare[9] and ocular pain was assessed by using the visual analogue scale[10]

Patients were called for follow up and above parameters were assessed at each visit.

Post operatively, group A was administered 0.05% topical difluprednate ophthalmic emulsion QID for two weeks, then tapered to BD dose.

Group B was administered 1% prednisolone acetate ophthalmic suspension QID for two weeks, then tapered to BD dose.

Patients in both the groups were additionally administered 0.5% moxifloxacin eye drops TDS and 0.03% flurbiprofen eye drops TDS.

The patients were called for follow up at day 7,21 and 42 postoperatively. Treatment failure was defined as patient presenting at any post operative visit with more than 15 cells, very dense flare or investigator assessed ocular pain score of grade 4.

Patients were considered cured if the sum of their aqueous cells score was 0 and flare was 0/+1 at all visits and at the end of the study.

STATISTICAL ANALYSIS

At the end of study all the data of patients in each group who completed the study protocol was collected and analysed by using Student's t- test and Chi-square analysis.

RESULTS

The mean age of patients in group A was 58.97+/-10.56 and in group B was 60.47+/-10.53. There was no statistically significant difference in overall mean age of patients in the 2 study groups (P>0.05).

Preoperative best corrected visual acuity

BCVA by snellen's distant type chart in all patients was recorded. Out of total 40 eyes examined, 6/36 BCVA was recorded in 4 (10%) in group A and 5 (12.5%) eyes in group B.BCVA of 6/60 was recorded in 30 (75%) eyes in group A and 29 (72.5%) eyes in group B. BCVA of 1/60 to 5/60 was recorded in 6 (15%) eyes in both group A and B.

Postoperative best corrected visual acuity (BCVA):

In group A, on the first postoperative, 1 (2.5%) patient had BCVA of 6/9, 8 (20%) cases had best corrected visual acuity

BCVA	Day 1	Day 7	Day 21	Day 42
6/6	0	16(40%)	36(90%)	39(97.5%)
6/9	1(2.5%)	17(42.5%)	4(10%)	1(2.5%)
6/12	8(20%)	7(17.5%)	0	
6/18	3(7.5%)	0	0	
6/24	15(37.5%)	0	0	
6/36	13(32.5%)	0	0	

Table-1: Post op best corrected visual acuity group A

BCVA	Day 1	Day 7	Day 21	Day 42
6/6	0	24(60%)	37(92.5%)	38(95%)
6/9	3(7.5%)	14(35%)	3(7.5%)	2(5%)
6/12	7(17.5%)	2(5%)	0	
6/18	1(2.5%)	0	0	
6/24	20(50%)	0	0	
6/36	9(22.5%)	0	0	

Table-2: Post op best corrected visual acuity group B

IOP mmHg	Day 1	Day 7	Day 21	Day 42
<14	0	0	0	0
14-15	10(25%)	8(20%)	9(22.5%)	9(22.5%)
16-17	24(60%)	28(70%)	28(70%)	26(65%)
18-19	6(15%)	4(10%)	3(7.5%)	5(12.5%)
19-20	0	0	0	0
>20	0	0	0	0

Table-3: Post operative IOP in Group A

IOP mmHg	Day 1	Day 7	Day 21	Day 42
<14	0	0	0	0
14-15	10(25%)	8(20%)	9(22.5%)	9(22.5%)
16-17	24(60%)	28(70%)	28(70%)	26(65%)
18-19	6(15%)	4(10%)	3(7.5%)	5(12.5%)
19-20	0	0	0	0
>20	0	0	0	0

Table-4: Post operative IOP in Group B

Grade	Day 1	Day 7	Day21	Day42
1	20(50%)	35(87.5%)	36(90%)	38(95%)
2	20(50%)	5(12.5%)	4(10%)	2(5%)
3	0	0	0	0
4	0	0	0	0

Table-5: Post operative pain assessment (Group A)

Grade	Day 1	Day 7	Day 21	Day42
1	23(57.5%)	36(90%)	37(92.5%)	38(95%)
2	15(37.5%)	3(7.5%)	2(5%)	1(2.5%)
3	2(5%)	1(2.5%)	1(2.5%)	1(2.5%)
4	0	0	0	0

Table-6: Post operative pain assessment (Group B)

Aqueous cell score	Day 1	Day 7	Day 21	Day 42
0	0	28(70%)	34(85%)	39(97.5%)
0.5+	1(2.5%)	15(37.5%)	6(15%)	1(2.5%)
1+	19(47.5%)	7(17.5%)	0	0
2+	19(47.5%)		0	0
3+	1(2.5%)		0	0
4+	0		0	0

Table-7: Post operative aqueous cell score (group A)

Aqueous cell score	Day 1	Day 7	Day 21	Day 42
0	0	32(80%)	36(90%)	38(95%)
0.5+	1(2.5%)	4(10%)	4(10%)	2(5%)
1+	27(67.5%)	4(10%)	0	0
2+	12(30%)	0	0	0
3+	1	0	0	0
4+	0	0	0	0

Table-8: Post operative aqueous cell score (group B)

of 6/12, 3 (7.5%) cases had BCVA of 6/18, 15 (37.5%) had BCVA of 6/24 and 13 (32.5%) patients had BCVA of 6/36.
On the last follow up visit on day 42, the BCVA of 6/6 was seen in 39(97.5%) patients and BCVA of 6/6 in 1(2.5%) [Table 1].
In group B, on the first post operative day, 3 (7.5%) patients had BCVA of 6/9, 7 (17.5%) patients had visual acuity of 6/12, 1(2.5%) patients had BCVA of 6/18, 20(50%) patients had BCVA of 6/24 and 9(22.5%)patients had BCVA of 6/36.
At each follow up visit, the BCVA difference in the two groups was found to be insignificant (p>0.05).At the end of study on day 42, the BCVA was found to be statistically not significant *(P*>0.05) [Table 2]

Postoperative IOP by applanation tonometer: In Group A on postoperative day 1, 10(25%) patients had IOP in range of 14-15mmHg, 24(60%) had IOP in range of 16-17mmHg and 6(15%) had in range of 18-19 mmHg. On subsequent follow ups IOP settled. On last follow up 9(22.5%) had in range of 14-15mm Hg, 26(65%) had in range of 16-17mmHg and 5(12.5%) had IOP in range of 18-19 mmHg. [Table 3]
In Group B on postoperative day 1, 17(42.5%) patients had IOP in range of 14-15mmHg, 21(52.5%) had IOP in range of 16-17mmHg and 2(5%) had in range of 18-19 mmHg. On subsequent follow ups IOP settled. On last follow up 14(35%) had in range of 14-15mm Hg, 23(57.5%) had in range of 16-17mmHg and 3(7.5%) had IOP in range of 18-19 mm Hg. [Table 4] So at the end none of the patients had any acute rise of IOP at any time needing additional therapy for control of IOP. IOP risewas found to be statistically not significant.

Ocular pain assessment-In group A, on first postoperative day, 20 (50%) patients presented with ocular pain of 1 and 20(50%) patients presented with ocular pain of grade 2. There was marked improvement in pain score in subsequent visits. On last follow up, 38(95%) patients presented with ocular pain of grade 1and 2(5%) presented with grade 2. [Table 5]
In group B, on first postoperative day 23(57.5%) patients had ocular pain of grade 1, 15(37.5%) had grade 2 and 2(5%) presented with pain grade 3. There was improvement on subsequent visits. On last follow up, 38(95%)presented with grade 1 and 1(2.5%) each of grade 2 and 3.Thus ocular pain grading was found to be statistically not significant (*P*>0.05). [Table 6]

Post operative aqueous cell score: In group A on first post operative day, 1(2.5%) patient presented with aqueous score of 0.5+,19(47.5%) presented with cell score of 1+,19(47.5%) with cell score of 2+ and only 1(2.5%) with score of 3+.On subsequent visit it reduced. On last follow up day, 39(97.5%) presented with aqueous cell score of 0 and one with score of 0.5+. [Table 7]
In group B on first post operative day, 1(2.5%) patient presented with aqueous score of 0.5+,27(67.5%) presented with cell score of 1+,12(30%) with cell score of 2+. On subsequent visit it reduced. On last follow up day, 38(95%) presented with aqueous cell score of 0 and 2(5%) with score of 0.5+. At the end of study aqueous cell scoring was statistically not significant between the two groups. [Table 8]

DISCUSSION

In our study, best corrected visual acuity (BCVA) on last follow up day was recorded and compared in both study groups at day 42 post operatively. BCVA of 6/6 was found in 97.5% patients of group A and 95% patients of group B. BCVA of 6/9 was found in 2.5% patients in group A and 5% patients in group B. Similar observations were made by Richard L[11] in his study when he compared visual acuity parameter. But a study conducted by Stephen Smith[12] showed same BCVA of 6/6 in all patients.
At the end of our study, intraocular pressure was measured in the two groups and was analysed statistically using Chi-square test. Maximum number of patients had IOP in the range of 16-17 mmHg which included 65% patients in group A while 57.5% in group B. It was found to be statistically not significant (p>0.05). None of the patients showed clinically significant rise > 21 mmHg. This was in accordance with a study conducted by Jamal KN[13] which showed similar observations regarding intraocular pressure while using both drops. Results of another study conducted by Foster CS et al[14] showed 11% patients having clinically significant IOP elevation.
In the present study, ocular pain assessment was done using the visual analogue scale and compared in both the groups. Both the groups showed 95% patients having ocular pain grade of 1 at end of the study and the data was found statistically nonsignificant (*P*>0.05). In study by Foster CS et al[14] the results regarding pain resolution were found to be slightly faster with difluprednate emulsion as compared to prednisolone acetate suspension.
At the end of our study the slit lamp evaluation of aqueous cells score between group A and B showed comparable results.100% AC cell clearance was more in group A (97.5%) as compared to group B (95%). The cell score was 0 in 97.5% in group A and the score was 0 in 95%in group B. This evaluation was also statistically not significant. The results of our study was in accordance with the study conducted by Foster CS et al[14] that showed higher percentage of patients in difluprednate showing AC cell clearing than prednisolone acetate. Another study conducted by William et al[15] showed equal percentage of patients in both groups showing AC cell clearing.
The post operative slit lamp evaluation for aqueous flare score at the end of our study was done and compared. The results were found to be comparable as both the study groups had 97.5% patients each with flare score of 0. The data was compared statistically and found to be non significant. Similar results were shown by Foster CS et al[14] who concluded that difluprednate was non inferior to prednisolone acetate in showing improvement in aqueous flare clearing and cells.
In our study, difluprednate was found to be at least equivalent to prednisolone acetate in all follow up visits with a comparable safety profile. Extended use of strong steroids

like prednisolone acetate is known to be associated with the development of glaucoma, visual field defects, loss of visual fields and posterior sub capsular cataract formation. These may be avoided by newer drugs like difluprednate. In different studies conducted by Foster CS et al[14] and William S et all[15] and, it was found that drop concentration of difluprednate emulsion was uniform in all simulated patient usage condition whereas drop concentration of prednisolone acetate suspension was highly variable. The difluprednate emulsion formation, which does not require shaking, delivers a constant concentration of the active ingredient in each drop. Prednisolone acetate ophthalmic suspension requires vigorous shaking prior to each instillation, a requirement that might be overlooked.

Another study conducted by Stringer[16] demonstrated that the amount of drug delivered with prednisolone acetate suspension is inconsistent, sometimes resulting in significantly less drug delivery to the eye than what is indicated in drug label.

CONCLUSION

Topical 0.05%difluprednate ophthalmic emulsion is as effective as 1% prednisolone acetate in treating post cataract surgery inflammation with the advantage of uniform drug dosage and an absence of harmful preservative.

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