

A Retrospective Study To Compare Moxifloxacin-Dexamethasone And Moxifloxacin-Difluprednate Eye Drops In Post Cataract Surgery.



Medical Science

KEYWORDS :

DR. ANKU H RAJA

Raja provision store, rajnagar-3, sarusection road, jamnagar.

DR. ASHISH C BHAROLIYA

B-601, earth heights, utran road, surat.

ABSTRACT

A retrospective randomized comparative study was carried out in 100 patients to compare efficacy between moxifloxacin difluprednate (group A-50 patients) vs. moxifloxacin dexamethasone (group B-50 patients) eye drops to reduce post cataract inflammation in terms of reduction in anterior chamber cells and flares and pain relief and were followed up on day 1, 3, 5, 7, 45 and 90.

On 5th postoperative day, cell count decreased from baseline by 96.75% in group B vs. 99.24% in group A. As well 100% reduction from baseline in anterior chamber flare found in group A as compared to 85.7% in group B.

Our study showed that speed of recovery from inflammation is more with moxifloxacin difluprednate than moxifloxacin dexamethasone. Study also showed that moxifloxacin difluprednate is more efficacious than moxifloxacin dexamethasone although costlier.

INTRODUCTION:

A Cataract is any opacity of lens, whether a small opacity or diffuse general loss of transparency causing significant reduction in visual acuity or functional impairment. It is one of the leading causes of blindness in the world, accounting for 50% of blindness worldwide.^[1]

In cataract surgery there occurs manipulation of anterior segment structures, which in turn trigger the release of arachidonic acid from cell membranes, leading to production of prostaglandins and leukotrienes. These inflammatory mediators, in turn, lead to cellular reaction and protein leakage. Although often self-limited, untreated inflammation can lead to complications such as pain/discomfort, photophobia, corneal edema, synechiae, glaucoma and cystoid macular edema endophthalmitis.^[2,3] The Mean Annual Incidence of post-operative endophthalmitis among cataract patients ranges from 0.05 to 0.14%.^[4-6]

In the immediate postoperative period, topical corticosteroids and antibiotic combined eye drops are effective in preventing infection and controlling inflammation after surgery of cataract extraction and IOL implantation.^[7] A fixed combination eye preparation not only helps in cutting costs but improves compliance of patients in dosing and application.^[8] Moxifloxacin, fourth generation fluoroquinolone, advantages of broad spectrum, excellent penetration & delivers a concentration thousand times minimal inhibitory concentration.^[9,10]

Dexamethasone or difluprednate are steroids which act by inhibiting the release of arachidonic acid from cell membrane phospholipids, corticosteroids prevent the formation of both leukotrienes and prostaglandins, disrupting the inflammatory cascade.^[11] These agents are continued until the anterior chamber (AC) reaction has resolved and the blood-aqueous barrier has been re-established.^[12]

AIMS AND OBJECTIVES:

To evaluate the efficacy of moxifloxacin-dexamethasone and moxifloxacin difluprednate eye drops in reducing ocular inflammation and pain in patients who had undergone cataract extraction.

PHARMACOLOGY:

At the molecular level, corticosteroids freely penetrate cell membranes and bind to a specific steroid-binding protein receptor in the cytoplasm, forming a steroid-receptor complex.^[12-15] This complex then moves into the nucleus and binds to chromatin,

signaling the production of messenger RNA and coding for enzymes and proteins that determine the responses of that particular cell to hormones.^[11]

These molecular and cellular changes result in steroid-induced inhibition of all the cardinal signs of inflammation, such as pain, heat, redness and edema.^[16,17]

Corticosteroids have dual properties of both being anti-inflammatory and immunosuppressant.^[18]

Difluprednate, a novel steroid, is classified as a very strong steroid. In June 2008, Difluprednate ophthalmic emulsion 0.05% was approved by the US Food and Drug Administration for treatment of inflammation and pain associated with ocular surgery.^[19]

Difluprednate potency:

Difluprednate is a derivative of prednisone but differs substantially due to structural modifications. The first is the addition of fluorine atoms at C6 and C9 positions. It is well known that fluorination of steroids greatly enhances specificity for the glucocorticoid receptors.^[20] Its anti-inflammatory activity is further augmented by replacing the 17-hydroxyl group with a butyrate ester. This has been shown to further increase the potency of difluprednate.^[21] While its lipophilicity and hence corneal penetration is enhanced by substituting the 21-hydroxyl group with an acetate group.^[22] In fact, glucocorticoids with 17,21-double esters, such as difluprednate, generally penetrate tissue better than monoesters derivatives.^[23]

Difluprednate dose uniformity:

Due to the lipophilic nature of the steroid molecules, and so their inability to dissolve in a solution, the majority of steroid preparations are formulated as suspensions.

Ophthalmic suspensions tend to settle over time, and as a result, must be shaken by the patient prior to instillation to ensure a homogeneous distribution of active drug within the aqueous phase of suspension.

Unfortunately, as most clinicians know, patients are not very compliant when it comes to shaking their medications. This was borne out of a study of steroid preparations, in which only 37% of patients followed the prescribed shaking instructions.^[24]

Difluprednate ophthalmic emulsion was formulated as stable oil-in-water to achieve optimum dosage consistencies. Difluprednate ophthalmic emulsion demonstrated excellent and consistent dose uniformity compared with suspensions, suggesting that clinical use of difluprednate may produce more predictable efficacy and safety.

FIXED DRUG COMBINATION:

In the immediate postoperative period, topical corticosteroids and antibiotic combined eye drops are effective in preventing infection and controlling inflammation after surgery of cataract extraction and IOL implantation.^[7]

A fixed combination eye preparation not only help in cutting costs but improve compliance of patient in dosing and application.^[8]

METHOD & MATERIOLOGY

The study design is retrospective, comparative study .In study we are going to collect data of 100 patients, coming to ophthalmology department GGH, Jamnagar had diagnosed as a case of cataract and need cataract extraction and IOL implantation.

INCLUSION CRITERIA: - Adult (>18 year) with diagnosis of cataract.

EXCLUSION CRITERIA: - Uncontrolled glaucoma, Steroid responder, diabetes mellitus, History of corticosteroid allergy, Ocular inflammatory condition like iritis, uveitis, dacrocystitis, fungal or viral infection.

Data will be collected after 60 days of discharge of patient. Pre-operative assessment of patient was done which include torch light examination, slit lamp examination, fundus examination, A-scan, keratometry, intra ocular pressure measurement. Systemic examination was done to rule out disease like hypertension, diabetes.

Patients had been undergone cataract extraction either by SICS-small incision cataract surgery or phacoemulcification and IOL implantation.

Patient had advised either moxifloxacin-dexamethasone or moxifloxacin-difluprednate eye drop post operative period. Patients had been examined post operatively on day 1,3,5,7,45,60. At each visit, patients were examined for sign of infection, inflammation and ocular pain. Best corrected visual acuity and intraocular pressure measured & recorded.

Grading scheme was achieved for standardization of grading anterior chamber cells and flare. The first international Workshop on the Standardization of Uveitis Nomenclature(SUN) was held in 2004 to standardize some aspects of uveitis, including classification criteria, inflammation grading scheme, and evaluation of outcomes.^[25]

AC (anterior chamber) inflammation, major criterion of effectiveness, were evaluated based on number of cells per high power field measure using narrowest (0.5 at height of 8 mm) slit beam of lamp and recorded as SUN CLASSIFICATION:

Anterior Chamber Cell Grading by SUN :

Grade	Cells in Field
0	< 5
1+	6-15
2+	16-25
3+	26-50
4+	> 50

Anterior Chamber Flare Grading by SUN:

Grade	Descriptors
0	None
1+	Faint
2+	Moderate (iris & lens detail clear)
3+	Marked (Iris & lens detail hazy)
4+	Intense (fibrin or plastic aqueous)

OBSERVATIONS AND ANALYSIS:

In this comparative retrospective study,100 patients were underwent cataract surgery with implantation of PCIOL in eye department of our institute which were divided into two groups of 50 patients having instilled either moxifloxacin-dexamethasone(group A) or moxifloxacin-difluprednate(group B). The data was evaluated on day 1,3,5,7,45 and 60.

Table 1: Percentage Reduction In Anterior Chamber Cell Count from Baseline.

Group	Day 1	Day 3	Day 5	Day 7
Group A	0%	53.66%	96.75%	100%
Group B	0%	61.36%	99.24%	100%

Above data indicates that speed of recovery from inflammation is greater with moxifloxacin-difluprednate than moxifloxacin-dexamethasone eye drops

Table 2: Change in anterior chamber cell grade from baseline.

Group	Day 1	Day 3	Day 5	Day 7
Group A	2.46	1.14	0.08	0
Group B	2.64	1.02	0.02	0

The above data indicates that, although both moxifloxacin-difluprednate and moxifloxacin-dexamethasone eye drops are capable of reducing inflammation, moxifloxacin-difluprednate is more efficacious in reducing postoperative inflammation than moxifloxacin-dexamethasone eye drops.

Table 3 : Pharmaco-economic analysis.

Drug	Dosage	Size	No of bottle used per patient	Price per bottle
Moxifloxacin-dexametason	2 hourly for first 3 day, 6 times a day for 7 day, 4 times a day for 14 days	5 ml	1	9-15 Rs/-
Moxifloxacin-difluprednate	4 times a day for first 14 days, 2 times a day for next 14 days	5 ml	1	136-140 Rs/-

The above data indicate moxifloxacin difluprednate is costlier than moxifloxacin dexamethasone.

Conclusion:

Moxifloxacin-difluprednate and moxifloxacin- dexamethasone eye drops both are effective in reducing post cataract inflammation.

Speed of recovery from inflammation is more with Moxifloxacin-difluprednate and pain relief is also more with Moxifloxacin- difluprednate eye drops.

Good patient compliance was determined from patient accounts during follow up consultations. This can be attributed to the tolerability profile of the drug and ease of administrations of Moxifloxacin- difluprednate eye drops although Moxifloxacin -difluprednate is costlier than moxifloxacin- dexamethasone.

References:

1. Javitt JC, Wang F: Blindness due to cataract: epidemiology and prevention. Annu Rev Public Health 1996; 17:159-177.

2. Apple DJ, Solmon KD, Tetz MR, et al. posterior capsule opacification. *Surv Ophthalmol.* 1992; 37: 73-116.
3. Miyake K, Maekubo K, Miyake Y, et el. Pupillary fibrin membrane; a frequent early complication after posterior chamber lens implantation in japan. *Ophthalmol.*1989;96: 1228-1233.
4. S. Kamalarajah, G. Silvestri, N.Sharma et al., " Surveillance of endophthalmitis following cataract surgery in the UK," *Eye* volume 18,pp. 580-587,2004.
5. PLalitha , J.Rajagopalan, K.Prakash, K.Ramasamay, N.V.Prajna, and M.Srinivasan, "Post cataract endophthalmitis in south India Incidence & Outcome." *Ophthalmology* vol. 112,no. 11, pp.1884-1889,2005.
6. T.Y. Wong and S.P.Chee," The epidemiology of acute endophthalmitis after cataract surgery in Asian population", *Ophthalmology* vol. 111 no. 4, pp. 699-705,2004
7. F.I. Camesasca, C.Bianchi, G. Beltrame e al., "Control of inflammation and prophylaxis of endophthalmitis after cataract surgery: a multicenter study," *European Journal of Ophthalmology*, vol.17, pp 733-742, 2007.
8. L. L. Freitas, E. Soriano, C. Muccioli, A.L. Hofling-Lima, and R. Belfort,"Efficacy and tolerability of a combined moxifloxacin/ dexamethasone formulation for topical prophylaxis and reduction of inflammation in phacoemulsification : A comparative double masked clinical trial." *Current Medical Research and opinion*, col.23,no.12,pp.3123-3130.
9. D.W. Stroman, J. J. Dajcs, G. A. Cupp and B. A. Schlech. "In vitro and in vivo potency of moxifloxacin and moxifloxacin ophthalmic solution 0.5%, a new topical fluoroquinolol," *Survey of ophthalmology* , vol.50, p.16-31, 2005.
10. Daryl K. Granner, MD. *The Diversity of the endocrine system.* Harper's illustrated biochemistry. 26th edition. 2003; 42: 438-439.
11. Mark B Abelson, Salim Butrus. *Corticosteroids in ophthalmic practice.* Albert and Jakobiec's; *Principles and Practice of ophthalmology.* 3rd edition. 2008;23: 249-50.
12. Ballard PL, Baxter JD, Higgins SJ, et al: General presence of glucocorticoid receptors in mammalian tissues. *Endocrinology* 1974; 94:998-1002.
13. Baxter JD, Rousseau GG, eds. *Glucocorticoid hormone action.* Berlin: Springer; 1979.
14. Cake MH, Litwack G: The glucocorticoid receptors in biochemical action of hormones. In: Litwack G, ed. *Biochemical actions of hormones.* New York: Academic press;1975.
15. 27. Thompson EB, Lippman ME: Mechanism of action of glucocorticoids. *Metabolism* 1974; 23:159-202.
16. Fahey JV, Guyre PM, Munck A: Mechanisms of anti-inflammatory action of glucocorticoids. In: Weissmann G. *Advances in inflammation research.* New York: Raven; 1981.
17. Jasami MK: Anti-inflammatory steroids: Mode of action in rheumatoid arthritis and homograft rejection. In: Vane JR, Ferriera SH, eds. *Antiinflammatory drugs.* Berlin: Springer; 1979
18. Melby JC: Systemic corticosteroid therapy: pharmacology and endocrinologic considerations. *Ann Intern Med* 1974; 8: 505-512.
19. Richard Lindstorm, MD. Clinical pearls and the latest evidence for Corticosteroid use in Cataract and Anterior segment Surgery. Corticosteroid use in Cataract and Anterior segment inflammation. Difluprednate 0.05% emulsion: An overview. *Advanced ocular care.* September 2010:3-4.
20. Bush IE, Mahesh VB. Metabolism of 11-oxygenated steroids. 3. Some 1-dehydro and 9 alpha-fluoro steroids. *Biochem J.* 1964; 93(2): 236-255.
21. Wang RH. Sytkowski A, Shetty KR. Relating corticosteroid structure and function. *Drug Ther.* 1975; 143-148.
22. Bartlett JD, Bennet ES, Fiscella RG, Jannus SD, Zimmerman TJ. *Ophthalmic Drug facts.* 19 ed. St. Louis, MO:Wolters Kluwer; 2008
23. Hammer S, Spika I, Sippl W, et al. Glucocorticoid receptor interactions with glucocorticoids. Evaluation by molecular modeling and sdfsd functional analysis Of mutants. *Steroids.* 2003; 68(4): 329-339.
24. Apt I, Hendrick A, Silverman L. Patient compliance with use of topical ophthalmic corticosteroid suspensions. *Am J Ophthalmol.* 1979; 87(2): 210-214.
25. Jabs DA, Nussenblatt RB, Rosenbaum JT, Standardization of Uveitis Nomenclature (SUN) working group: Standardization of Uveitis Nomenclature (SUN) for reporting clinical data. Results of the first international workshop, *Am J Ophthalmol* 2005; 140:509-516.