



Original article

Safety of Fixed drug Combination in Post –Operative Cataract Patients, at Tertiary Care Centre – In South India

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Abstract

Introduction: Cataract is any opacification in lens or its capsule, which accounts for about 50% of treatable blindness worldwide. The prevalence of cataract in India is about 62.6%. The incidence of post operative endophthalmitis ranges from 0.05% -0.14% and so the use of post-operative antibiotics and steroids is necessary to control infection and prevent inflammation. Fixed drug combinations not only cut the cost but also the dosage & improve the compliance of patients in the immediate post operative period. In this regard, the present study was conducted with the aim of studying the efficacy of using fixed drug combination (Difluprednate and Moxifloxacin) in reducing ocular inflammation & pain in post-operative patients undergoing cataract surgery. **Methodology:** Study design: Prospective interventional study, in which 749 eyes underwent SICS with IOL. All of them were treated with Difluprednate and Moxifloxacin, combination eye drops postoperatively 4 times a day, and reviewed on day 1, 5 and once in two weeks up to 6 weeks. **Results:** Out of 749 eyes, 730 were normal, 10 eyes had minimal raise in IOP in the range of 21 mmHg-31mmHg (considering 21mmHg as baseline) which decreased without any intervention within 3 weeks and only 9 eyes had raise in IOP of more than 31mmHg, which did not decrease in spite of discontinuing the drops and needed anti-glaucoma treatment. **Conclusion:** Our study clearly shows that fixed drug combination of antibiotic and steroid does not cause raised IOP in about 97% of cases of SICS in the post-operative period and also improves the compliance of the patients.

Key Words: Fixed Drug Combination, Difluprednate, Moxifloxacin, Steroid Induced Glaucoma

Introduction

Cataract surgery has an impact on both physical and mental health of any individual. Studies

have shown that elderly patients subjected to cataract surgery will have improved vision-related quality of life and their mental health will have a positive impact. They also will be benefitted by improvements in cognitive function (Chandrasekaran S et al, 2008; Ishii K et al, 2008)

Cataract is any opacification in lens or its capsule, which accounts for about 50% of

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treatable blindness worldwide. The prevalence of cataract in India is about 62.6%.(Govt. of India, 2006-07) with a mean incidence of post-operative endophthalmitis ranging from 0.05% -0.14% (Anku RH et al, 2016 ; Kamalrajah S, et al, 2004) and so the use of post-operative antibiotics and steroids, to control infection and prevent inflammation is necessary. Fixed drug combinations not only cut the cost but also the dosage and improve the compliance of patients in the immediate post operative period. (Anku RH et al, 2016; Bratin M et al, 2016; Sowbhagya HN et al, 2015; Michael S et al, 2009)

Efficacy of steroids as having anti-inflammatory action is well documented, which prevent common post-operative complications such as corneal oedema and cystoid macular oedema. They have few known complications such as ocular hypertension and steroid induced glaucoma. So careful monitoring of such patients is mandatory. Lack of consistent reporting criteria in various previous clinical studies, limits a meaningful comparison of steroids efficacy across the globe.

Our study also aims to review previous available publications about safety of the drugs used in post-operative patients, ease of administration and intra ocular pressure (IOP) fluctuations induced by them over a period of 6 weeks. Steroid induced ocular hypertension occurs usually secondary to use of steroids for short duration. When Armaly and Becker in 1960, studied steroid response in patients after 6 weeks of dexamethasone treatment, around 18-36% of population (Becker B, 1965; Armaly MF, 1965) were steroid responders. IOP in such patients usually returns to pre-treatment levels within 1-3 weeks.

Surgical trauma to eye induces inflammatory reaction through inflammatory mediators, with release of prostaglandins. Steroids mediate anti-inflammatory activity through glucocorticoid

receptors by direct and indirect effect at the genomic and non genomic levels by decreasing capillary non-permeability, vasodilation and leucocytic migration. Although they are efficacious in post-operative inflammation, they have a disadvantage of causing raised IOP and optic nerve damage resulting in steroid induced glaucoma and cataract formation in non-operated eyes (Uwe P et al, 2013).

Pharmacology

Difluprednate 0.05%

A novel steroid, classified as a very strong steroid ,it is a derivative of a prednisolone, differs in structural modification with addition of fluorine atoms at C6 and C9 positions which enhances specificity for glucocorticoid receptor by replacing 17-hydroxyl group with butyrate ester. It augments anti-inflammatory activity which in turn increases potency (Anku RH et al, 2016). By substituting 21-hydroxyl group with acetate group its lipophilic property and corneal penetration is enhanced. Glucocorticoids with 17, 21–double ester like difluprednate penetrate tissues better than monoester derivatives (Anku RH et al, 2016; Sowbhagya HN et al, 2015; Uwe P et al, 2013). Most steroid molecules are lipophilic in nature, hence unable to dissolve in solution. But majority of formulations are suspensions which sediment, hence bottle must be shaken prior to instillation of drops for homogenous distribution of active drug within the aqueous phase of distribution of the drug. Difluprednate ophthalmic emulsion is formulated as stable oil-in-water preparation to achieve optimum dosage consistency compared to suspensions, suggesting predictable efficacy and safety (Donnafield ED, 2011; Donnafield ED et al, 2011; Stringer W et al, 2010)

Moxifloxacin 0.05%

Is a synthetic fourth generation broad spectrum bactericidal fluoroquinolone, inhibits enzyme bacterial DNA gyrase and prevents replication of DNA during bacterial growth

and reproduction. It has enhanced action against gram positive cocci, mycobacterium tuberculosis, mycoplasma pneumonia, mycobacterium avium complex and anaerobes. It has better minimum inhibition concentration, good ocular penetration with less resistance (Moshirfar M et al, 2007).

Aims

1. Study the safety of using fixed drug combination of Difluprednate and Moxifloxacin in reducing ocular inflammation & pain in post-operative patients who underwent cataract surgery.
2. Assess the compliance of patients in dosing and application.

A written informed consent was obtained from all patients who underwent surgery and were prescribed the above drug combination.

Methodology

A prospective study, conducted from January 2013 to May 2016 at Minto Eye Hospital & Regional Institute of ophthalmology. All eyes, diagnosed as having cataract and fulfilling the following criteria were included in the study group.

Inclusion criteria:

1. Senile Cataract
2. Pre-senile cataract
3. Congenital cataract above 2years of age
4. Secondary IOL implantation

Exclusion criteria:

1. Cataract with glaucoma
2. Complicated cataract

Manual Small incision cataract surgery with or without IOL implantation was performed on all the 749 eyes at Minto Eye Hospital and Regional Institute of Ophthalmology, Bangalore. Patients who were left aphakic underwent surgical peripheral iridectomy as described in standard protocols.

Procedure

Demographic profile of each patient was noted. Clinical profile including distant visual acuity by Snellen's chart and near visual acuity by Jaeger's chart was performed. Detailed anterior segment examination including angle evaluation by Van Herrick method and gonioscopy by zeiss four mirror lens, followed by IOP recording using Goldmann applanation tonometer, slit lamp biomicroscopy using +78D or +90D lens and indirect ophthalmoscopy using +20D lens wherever required were performed and documented. In this study we have used Difluprednate ophthalmic emulsion 0.05% which was approved in 2008 by FDA, European and Asian countries for post-operative inflammation (Michael S et al, 2008; Uwe P et al, 2013). Moxifloxacin a fourth generation fluoroquinolone, advantages being broad spectrum with excellent penetration & drug delivery having thousand times MIC (Anku RH et al, 2016; Donnafield ED, 2011) .

Small Incision Cataract Surgery was performed on all the eyes with or without IOL implantation. Surgical peripheral iridectomy was performed in aphakic eyes according to standard protocol. All patients were treated postoperatively with fixed drug combination of Moxifloxacin 0.05% and Difluprednate 0.05% (Ishii K et al, 2008; Kamalrajah S et al, 2004), 4 times a day for 6 weeks. Patients were reviewed on day 1, 5 and every 2 weeks up to 6 weeks. During follow up of these patients, visual acuity, detailed anterior segment examination to grade flare and cells, fundus examination in cases of low visual acuity to rule out cystoid macular edema were performed along with IOP recording. It was considered significant if raise in IOP was ≥ 10 mmHg from baseline and were managed accordingly (Becker B, 1965; Armaly MF, 1965).

Results

Among 749 eyes or patients who underwent cataract procedure, there were 290 males and

459 females. 746 eyes underwent SICS with IOL 3 eyes had secondary PCIOL.

8 patients had vitreous loss, 6 patients were left Aphakic and 2 Patients had an ACIOL. Surgical iridectomy was done in all 8 patients.

All patients (749 eyes) were put on the fixed combination of Moxifloxacin 0.05% and difluprednate 0.05% eye drops post-operatively and followed on day 1, 5 and every 2 weeks for upto 6 weeks, unlike the routine protocol of post-operative cataract management in India (Vision 2020, India).

97.46% (730) patients showed a good response to eye drops without significant rise in IOP at 6 weeks.

Discussion

Table 1

Group	Our study	Sahasrabudhe et al, study	Donnefeld et al, study	Sowbhagya et al, study
No of Eyes	749	56	56	50
Increase of IOP ≤ 10 mmHg from baseline of 21 mmHg	10	-	06	-
Increase of IOP $\geq 10-30$ mmHg from base line	09	02	-	05

Our study is comparable to studies of Donnafield et al, where they used only difluprednate 0.05% for their post cataract patients, where a raised IOP was noted in only 6 out of 56 eyes, which was not significant.

In the study done by Sowbhagya et al where they used fixed drug combination, 5 out of 50 patients showed raised IOP who were treated by withdrawing the drug and administering anti-glaucoma medication.

In study done by Sahasrabudhe, et al with fixed drug combination on 56 patients, 2 showed raised IOP and were treated with anti-glaucoma drugs.

In our study, 19 had raised IOP, among them 10 reached the baseline IOP by the end of 3 weeks. Remaining 9 patients showed a significant raise

0.013% (10) patients had an initial increase in IOP ≤ 10 mm Hg from baseline (≤ 21 mm Hg) which normalized by 6 weeks without intervention.

0.012% (9) patients had a significant IOP rise in initial 3 weeks, among whom 3 patients were aphakic. In all 9 eyes, the drug was withdrawn and put on loteprednol eye drops (Sahasrabudhe Vivek M et al, 2016), 4 times a day along with systemic and topical anti-glaucoma medications (Pavesio CE et al, 2008). These patients subsequently showed a normal IOP at 6 weeks. None of them required glaucoma surgery.

which needed discontinuation of medication along with anti-glaucoma treatment and IOP normalized by the end of six weeks.

In the present study, among the 3 aphakic eyes, the raise in IOP could also be due to inflammation and/or Difluprednate.

Since there may be a raise in IOP, which can be effectively treated by withdrawing drug, it is mandatory for the surgeons to monitor all patients.

Conclusion

We therefore conclude that fixed drug combination of Difluprednate and Moxifloxacin eye drops is an effective post-operative medication, for patients undergoing Small incision cataract surgery to control inflammation and infection.

Post-operative topical steroids are given in decreasing dosage over 6 weeks. In our study difluprednate eye drops was given 4 times per day for a duration of 6 weeks with good response and no significant complications. This dosing is simpler yet effective, more potent and reduces the need for hourly topical steroids.

Conflicts of interest: Authors do not have any conflict of interest

References

Anku RH, BC Chandrasekaran S, Wang JJ, Rochtchina E, Mitchell P (2016). A Retrospective study to compare Moxifloxacin-Dexamethasone and Moxifloxacin-Difluprednate Eye Drops In post cataract surgery. *IJSR*; 5 (4):582-584

Armaly MF (1965). Statistical attributes of the steroid hypertensive response in the clinical normal eye.1: The demonstration of three levels of response. *Invest Ophthalmol Vis Sci*; 14:187

Becker B (1965). Intraocular pressure response to topical corticosteroids. *Invest Ophthalmol Vis Sci*; 4:198.

Bratin M, PS Bharoti (2016). Efficacy and safety of Difluoprednate Ophthalmic emulsion and Prednisolone acetate ophthalmic suspension in Post Cataract Surgery Inflammation-a Comparative study. *IOSR JDMS*; 15:51-58

Chandrasekaran S, Wang JJ, Rochtchina E, Mitchell P.(2008).Change in health related quality of life after cataract surgery in a population-based sample. *Eye*; 22:479-484.

Donnafield ED (2011).Difluprednate for the prevention of ocular inflammation postsurgery:an update. *Clinical Ophthalmol*; 5:811-816.

Donnafield ED,Holland EJ,Solomon KD,et al(2011).A multicenter randomized controlled fellow eye trial of pulse-dosed difluprednate 0.05% versus prednisolone

acetate 1% in cataract surgery. *Am J Ophthalmol*; 152(4):609-617.

Guidelines for management of cataract surgery in India , A vision 2020: Right to sight India publication.

Ishii K, Kabata T, Oshika T (2008). The impact of cataract surgery on cognitive impairment and depressive mental status in elderly patients. *Am J Ophthalmol*; 146:404-409.

Kamalrajah S, G Silvestri ,N Sharma et al(2004).Surveillance of endophthalmitis following cataract surgery in the UK. *Eye*; 18: 580-587.

Michael S, Korenfeld, Steven M, Silverstein,C David ,V Roger,C Robert(2009).Difluprednate Ophthalmic emulsion0.05%(Durezol) Study Group Difluprednate Ophthalmic emulsion0.05% for postoperative inflammation and pain. *Journal of Cataract & Refractive Surgery*; 35:(1):26-34

Moshirfar M, Feiz V, Vitale AT, Wegelin JA, Basavanthappa S, Wolsey DH (2007). Endophthalmitis after uncomplicated cataract surgery with the use of fourth-generation fluoroquinolones, a retrospective observational case series. *Ophthalmology*; 114:686-691.

National programme for control of blindness directed general of health services of health and family welfare, Government of India. 2006-07.

Pavesio CE, HH Decory (2008) .Treatment of ocular inflammatory conditions with loteprednol etabonate. *Br J Ophthalmol*; 92:455-9.

Sahasrabudhe Vivek M, Kamble Nikil R, Shankarrao Chavan (2016). Study of Effect of Topical 0.05% Difluprednate on Intra Ocular Pressure in Patients Operated By Small Incision Cataract Surgery, *Saudi J.Med.Pharm. Sci* 2:(3):56-58

Sowbhagya HN, N Manjunath, S Shetty, LK Kumar (2015). Intraocular Pressure Changes with the Use of Difluprednate :An Observational Study. *Int J Sci Stud*; 3:(5):54-57

Stringer W, Bryani R(2010).Dose uniformity of topical corticosteroid preparation:

difluprednate ophthalmic emulsion 0.05% versus branded and generic prednisolone acetate ophthalmic suspension 1%. *Clin. Ophthalmol*; 4:1119-1124

Uwe P, Paul G, Ursell , Paolo R(2013) . Intraocular pressure effects of common Topical steroids for post-cataract inflammation: Are they all the same?. *Ophthalmol Ther* 2 : 55-72

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