Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Ophthalmology

Study of Intraocular Pressure Changes After Cataract Surgery with Topical Prednisolone Acetate 1% versus Topical Difluprednate 0.05%

Chandra Shekhar Majumder[1*], Mousumi Chowdhury[2], Sheikh Mohammad Rashedul Haque[3], Md. Shafiqul Alam[4], Robiul Islam[5]

[1]Professor & Head, Department of Ophthalmology, Dhaka Medical College, Dhaka, Bangladesh
[2]Senior Assistant Surgeon, Chittagong Eye Infirmary & Training Centre, Chittagong, Bangladesh
[3]Fellow, Department of Ophthalmology, Ispahani Islamia Eye Institute & Hospital, Dhaka, Bangladesh
[4]Consultant, Grameen GC Eye Hospital, Rupatali, Barisal, Bangladesh
[5]Assistant Professor, Department of Ophthalmology, Sir Salimullah Medical College, Dhaka, Bangladesh

DOI: 10.36347/sjams.2023.v11i02.007 | **Received:** 21.12.2023 | **Accepted:** 04.02.2023 | **Published:** 09.02.2023

***Corresponding author:** Chandra Shekhar Majumder
[1]Professor & Head, Department of Ophthalmology, Dhaka Medical College, Dhaka, Bangladesh

Abstract **Original Research Article**

Introduction: Topical corticosteroids are used to control postoperative intraocular inflammation. Prednisolone acetate 1% and difluprednate 0.05% are commonly used but difluprednate has a risk of increasing intraocular pressure. The aim of the present study was to compare the changes in intraocular pressure using prednisolone acetate 1% and difluprednate butyrate acetate 0.05% after cataract surgery with frequent dosing. ***Materials and Methods:*** The nonrandomized clinical trial study was performed in the Department of Ophthalmology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, from June 2019 to June 2020. A total of 84 patients were selected and were divided into two cohorts, group A and group B. In each group, there were 42 patients. ***Result:*** Intraocular pressure was elevated in 2.4% of group A and 4.7% of group B on the 7th postoperative day. Increased IOP >6 mm Hg from baseline was seen in 2.4% of group A and 7.2% of group B. Statistically significant difference in intraocular pressure from baseline was seen in the first and second follow-up. No significant elevation was seen on the 45th day and the difference returned to normal. ***Conclusion:*** Intraocular pressure was significantly different from baseline on the 7th and 21st postoperative day. It returned to normal after 45 days. Both drugs can be used with frequent monitoring of intraocular pressure in the first week.

Keywords: Cataract Surgery**,** Intraocular Pressure, Prednisolone acetate 1%, Difluprednate 0.05%.

INTRODUCTION

Topical corticosteroids are commonly used after cataract surgery to reduce ocular inflammation by suppressing cellular infiltration, capillary dilatation, fibroblast proliferation, and collagen deposition, thus reducing scar formation [1]. Prednisolone acetate (PA) 1% suspension has been used for a long time as a standard drug in treating postoperative inflammation [2]. Being a suspension, it contains large particles and has properties of sedimentation, aggregation, and recrystallization, which decreases its bioavailability [3]. Difluprednate Butyrate Acetate (DFBA) ophthalmic emulsion 0.05% was approved by the USA Food and Drug Administration (FDA) in 2008 to treat postoperative inflammation and pain [4]. It is a prednisolone derivative fluorinated at C6 and C9 positions, enhancing its potency, with a butyrate group added at C17 that increases its receptor binding affinity by 56 times. Additionally, it is acetylated at the C21 position, providing better ocular penetration [5]. As an emulsion, it dissolves in the oil phase and has better bioavailability and dose uniformity, and has been found to be more effective in controlling ocular inflammation after cataract surgery [6]. Though these drugs speed up recovery, prolonged use can result in raised intraocular pressure (IOP). The raised IOP, if left untreated for a long time, can lead to optic nerve damage and glaucoma [7]. Patients with a tendency to experience corticosteroid-induced raised IOP are called steroid responders and may experience worsening of postoperative side effects. It has been estimated that about 8% of the average population tends to develop corticosteroid-induced intraocular pressure elevation [8]. Patients with a family history of glaucoma and those classified as glaucoma suspect are at a higher risk [9]. Due to its high anti-inflammatory potency, difluprednate may result in significantly raised

intraocular pressure [10, 11]. A randomized placebo-controlled trial of 438 patients concluded that 3% of patients using difluprednate had a clinically significant IOP versus 1% of the placebo group after intraocular surgery [12]. High-dose corticosteroids immediately after surgery have been proven to preserve and protect neural tissue, as the corneal endothelium and retina, like the brain and spinal cord, are of the same neuroectodermal origin and may also benefit from high-dose steroids. Based on this concept, Donnenfeld *et al*., conducted a randomized control trial comparing the efficacy of a pulsed dose of difluprednate [13]. In our hospital, we frequently use prednisolone acetate 1% or difluprednate 0.05% for a longer period and have observed better control of postoperative ocular inflammation. However, both drugs carry a potential risk of a significant rise in IOP, with difluprednate carrying a higher risk due to its greater potency than prednisolone acetate. A review of the literature showed that a few retrospective and prospective studies have been conducted on this issue [4, 14, 15, 16]. Therefore, we performed a non-randomized clinical trial to provide more clinical information on the subject. The aim of this study was to compare the changes in intraocular pressure after cataract surgery using topical prednisolone acetate 1% versus difluprednate ophthalmic emulsion 0.05% with an equivalent frequent dose schedule over an extended period. The goal was to provide suggestions for safe use of these drugs after cataract surgery.

MATERIALS AND METHODS

This prospective nonrandomized clinical trial was initially conducted with a total of 130 patients who underwent phacoemulsification and small incision cataract surgery at the department of Ophthalmology, Sir Salimullah Medical College and Mitford Hospital, Dhaka. The sample size was initially determined to be 65 patients in each group, A and B, but due to the COVID-19 pandemic, 23 patients from each group had to be excluded, leading to a final sample size of 84 patients (42 in each group). The study was approved by the Ethical Review Committee of Sir Salimullah Medical College and all participants provided signed informed consent. Inclusion criteria for the study were patients 40 years or older who underwent unilateral phacoemulsification or SICS, while exclusion criteria included age below 40 years, history of glaucoma or ocular hypertension, treatment with systemic or periocular corticosteroids, and presence of active viral, bacterial or fungal keratoconjunctival disease. Participants underwent visual acuity assessment and examination of the anterior segment and cataract morphology to rule out diseases. The baseline preoperative intraocular pressure (IOP) was measured in both groups, and patients in group A were treated with topical prednisolone acetate 1% at a dosing schedule of two hourly for the first seven days, then four hourly for seven days, six-hourly for seven days, eight hourly for seven days, twelve hourly for seven days and then once daily for a week. Patients in group B were treated with topical difluprednate ophthalmic emulsion 0.05% with a similar dosing schedule. IOP was measured on the 7th, 21st and 45th postoperative days using Goldmann applanation tonometer, and the changes from the baseline IOP were compared between the two groups. The main outcome was the measurement of significant elevation of IOP, defined as a rise of more than 6 mm Hg from the baseline or a rise of IOP greater than 21 mm Hg on each follow-up.

RESULTS

Data were collected by semi-structured research questionnaire and checklist. Data were analyzed by SPSS version 24. Test of significance, such as Student's t-test and ANOVA test for quantitative variables and Chi-square test for qualitative variables, were done. P-value at 95% confidence level less than 0.05 was regarded as statistical significance.

In our study, an equal number of patients was taken in both groups in each age range. Here, 6 patients were >70 years, 23 patients were between 60-69 years, 9 patients were in 50-59 years, and 4 patients were in 40-49 years age group. The mean age of the patients in each group was 61± 8.9 (Table-I). In each group, among 42 patients, 42.85% (18) were male, and 57.15% (24) were female.

Table 1: Distribution of patients according to age (N=84)

Age in years	Group A (n = 42)		Group B (n_1 = 42)		P value
	No	%	No	%	
40 – 49	4	9	4	9	
50 – 59	9	21	9	21	
60- 69	23	54	23	5	
≥ 70	6	14	6	14	
Mean ± SD	61± 8.9		61±8.69		0.97

Notes: The age difference was analyzed using Student's 'to test. Group A: using prednisolone. Group B: using difluprednate.

Both groups had similar age distributions, with the majority of patients falling between 60-69 years old (54% in group A and 55% in group B). The mean age of the participants in both groups was 61 years, with no statistically significant difference between the two groups (p value = 0.97). The age ranges from 40-49 years to over 70 years and the proportion of participants in each age group was similar in both groups.

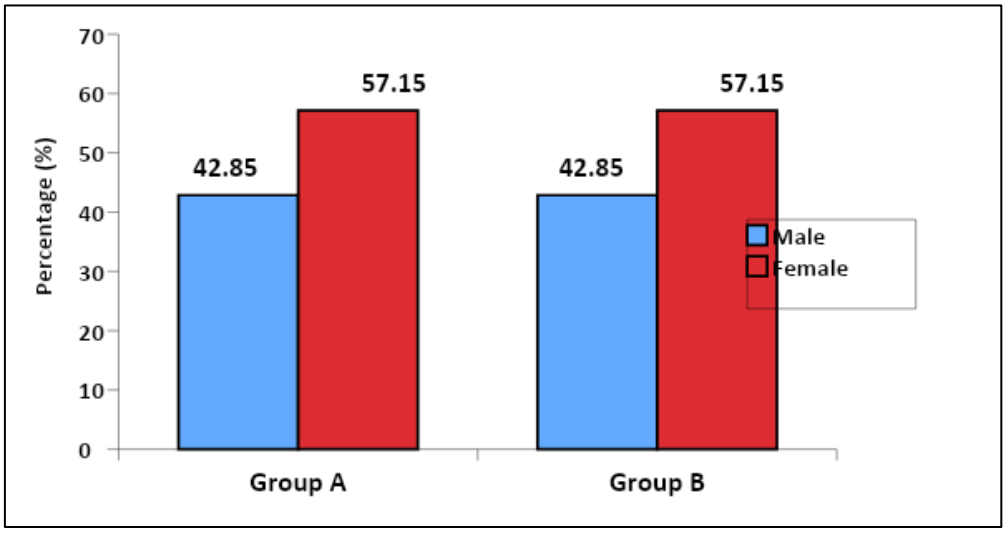

Fig 1: It demonstrates the distribution of study subjects according to gender (N=84)
Group A: using prednisolone, Group B: using difluprednate

Gender distribution of the study participants revealed that female prevalence was higher in both groups, with 57.15% female incidence among Group A and Group-B participants.

Table 2: Intraocular pressure (IOP) of preoperative (basal) and postoperative period (N=84)

Variables	**Group A (n = 42)**		**Group B (n = 42)**	
	No	%	No	%
Preoperative (Basal)				
>21	0	0	0	0
11-21	42	100	42	100
< 11	0	0	0	0
1st PO Follow Up (7th POD)				
>21	1	2.4	2	4.7
11-21	41	97.6	40	95.3
< 11	0	0	0	0
2nd PO Follow Up (21st POD)				
>21	0	0	0	0
11-21	42	100	42	100
< 11	0	0	0	
3rd PO Follow Up (45th POD)				
>21	0	0	0	0
11-21	41	97.6	40	95.2
< 11	1	2.4	2	4.8

Table 2 shows that intraocular pressure measurement was done preoperatively on the day before surgery. Preoperative intraocular pressure was within 11-21 mmHg in all the patients of both groups. At 7th POD, 1 patient in group A and 2 patients in group B showed IOP of more than 21 mm Hg. At 21st POD, all patients in both groups showed IOP between 11-21 mm Hg. At the 3rd follow up no patient showed IOP >21 mm of Hg.

Table 3: Difference between IOP of different follow-Up periods and Basal (preoperative) IOP (N=84)

IOP (mm of Hg)	Group A (n = 42)		Group B (n_1 = 42)	
	No	%	No	%
1st PO Follow Up (7th POD)				
>6	1	2.4	3	7.2
1-6	41	97.6	36	85.6
< 1	0	0	3	7.2
2nd PO Follow Up (21st POD)				
>6	0	0	0	0
1-6	22	52.4	35	83.3
< 1	20	47.6	7	16.7
3rd PO Follow Up (45th POD)				
>6	0	0	0	0
1-6	9	21.4	15	35.7
< 1	33	78.6	27	64.3

Table 3 shows the difference in IOP at 7th POD from baseline was >6 in 1 patient in group A and in 3 patients in group B, which was statistically significant. In the rest of the patients, the difference of IOP was within <6 in group A and in group B at 7th POD. In 21st and 45th POD, no patient showed a difference of IOP >6 from baseline.

Table 4: Mean distribution of IOP between group A and group B (N=84)

IOP (mm of Hg)	Group A (n =42)	Group B (n_1 = 42)	Statistics
	Mean ± SD	Mean ± SD	
Preoperative	14.57± 2.23	14.42 ± 2.04	t = 0.30 , P=0.763
1st PO Follow Up (7th POD)	16.85± 2.22	17.73±2.73	t = -1.60 , P=0.113
2nd PO Follow Up (21st POD)	15.35±2.15	16.14±2.35	t = -1.57 , P=0.119
3rd PO Follow Up (45th POD)	14.21±2.36	14.45±2.34	t = -0.46 , P=0.648
Significance of Increase	F=11.01 P< 0.05	F= 17.81 P < 0.05	

In Group-A, mean IOP increased from baseline in 7th and 21st POD. It was statistically significant. Mean IOP came near to baseline on 3rd follow up. In Group-B, Baseline IOP was 14.42 ± 2.04 mm Hg. Mean IOP increased on 7th and 21st POD, which was statistically significant. On the 45th day, mean IOP came near to baseline. Mean IOP at a different postoperative period in between two groups were statistically not significant.

Table 5: Mean distribution of difference of IOP from Basal in different follow-up periods between group A and group B (N=84)

IOP (mm of Hg)	Group A (n=42)	Group B (n= 42)	Statistics
	Mean ± SD	Mean ± SD	
1st PO Follow Up (7th POD)	2.28±1.53	3.28±1.76	t = -2.74 , P=0.007
2nd PO Follow Up (21st POD)	0.78±1.52	1.83±1.52	t = -3.11 , P=0.002
3rd PO Follow Up (45th POD)	-0.24±1.28	0.14±1.52	t = 1.22 , P=0.224

Table 5 compares the mean difference of IOP from basal in different follow-up periods between group A and group B (N=84). On 7th POD, a difference of IOP from basal in prednisolone and difluprednate group was 2.28±1.53 and 3.28±1.76 respectively. This difference was statistically significant (p= 0.007). On 21st POD, the IOP difference from baseline in between two groups was also statistically significant (p=0.002). However, after the 45th day of surgery, there was no significant difference between the two groups.

Table 6: Frequency of raised IOP in different follow-Up periods between group A and group B (N=84)

Frequency of raised IOP	Group A (n = 42)		Group B (n_1 = 42)		Statistics
	No	%	No	%	
Preoperative	0	0	0	0	-
1st PO Follow Up (7th POD)	1	2.4	2	4.7	$\chi 2$= 0.345, P=0.556
2nd PO Follow Up (21st POD)	0	0	0	0	-
3rd PO Follow Up (45th POD)	0	0	0	0	--

Table 6 shows the frequency of raised IOP on 7th POD was 2.4% in the prednisolone group and 4.7% in the difluprednate group. It was not statistically significant.

Table 7: Frequency of significant IOP difference from Basal in different follow-up periods between group A and group B (N=84)

Frequency of significant IOP difference	Group A (n = 42)		Group B (n_1= 42)		Statistics
	No	%	No	%	
1st PO Follow Up (7th POD)	1	2.4	3	7.2	$\chi 2$=1.05, P=0.305
2nd PO Follow Up (21st POD)	0	0	0	0	-
3rd PO Follow Up (45th POD)	0	0	0	0	-

Data were analyzed using the Chi-square test.

Table 7 shows; on 7th POD frequency of difference of IOP from basal is not statistically significant between the two groups.

DISCUSSION

Corticosteroids are used as first-line anti-inflammatory agents after cataract surgery due to their ability to reduce inflammation. However, they can also produce adverse effects. In a few studies, it was found that difluprednate 0.05% raised the IOP more than prednisolone acetate 1% [2, 14]. The present study aimed to compare and record the IOP changes from the baseline at different postoperative follow-ups using both drugs to see if there is a significant rise in IOP with difluprednate compared to prednisolone acetate. The patients in the respective groups were given prednisolone acetate 1% and difluprednate 0.05% at two-hourly intervals for 7 days from the first postoperative day, then four-hourly for 7 days, followed by six-hourly, eight-hourly, and finally, once daily for 7 days. Steroid-induced intraocular pressure elevation usually occurs 2-4 weeks after the commencement of treatment [18]. The steroids were applied 24 hours after surgery and IOP changes were measured in both groups at the 7th, 21st, and 45th postoperative day (POD). A significant number of studies have been carried out with different dose schedules. Donnenfeld *et al*., applied a pulsed dose of DFBA and PA in respective groups at two-hourly intervals beginning on the day of surgery, then four times daily for the first week and twice daily for the second week. They compared the efficacy and IOP changes between DFBA and PA [13]. Tijunelis et al. applied DFBA twice daily and PA four times daily for a month and measured IOP after one month between the two groups [4]. Garg *et al*., applied both DFBA and PA six times a day for one month [14]. Kusne *et al*., applied prednisolone 1 drop four times daily and difluprednate twice daily starting on the day of surgery [14]. They continued both drugs for 14 days and measured the IOP changes between the 5th-10th POD and then again 3-6 weeks postoperatively. Saman *et al*., applied PA 5 times a day and DFBA 4 times a day for 15 days, then tapered the doses for the last 2 weeks [16]. These dose schedules differ from the dose schedule studied in the present study. In our study, we measured the change in postoperative IOP from the baseline and compared the postoperative IOP in different follow-up periods between the groups. A significant rise in the IOP was considered if the difference was >6 mm of Hg or if the postoperative IOP was >21 mm of Hg [4, 16]. The criteria for a significant rise in IOP aligned with the studies conducted by Tijunelis *et al*., and Saman *et al*., The IOP was measured using Goldmann applanation tonometry, which is a standard gold method for measuring IOP [17]. There was no significant difference in the mean baseline (preoperative) IOP between the two groups. At 7th postoperative day (POD), a significant increased IOP that was >21 mm of Hg was found in 4.7% of patients in the difluprednate group and 2.4% in the prednisolone group. The rise of IOP >6 mmHg from baseline was 2.4% in prednisolone and 7.2% in the difluprednate group. The mean difference of IOP from baseline on 7th and 21st POD was statistically significant between the two groups. However, on the follow-up at 45th POD, there was no statistically significant difference between the two groups. For the patients who had raised IOP after 7 days, we tapered the

dose, and the IOP came down to normal range without applying IOP-lowering agents. Our study differs from the study conducted by Jeng *et al*., In a retrospective chart review of 100 patients treated with prednisolone acetate or difluprednate after vitreoretinal surgery, they applied both drugs 4 times daily for 1 month in respective groups. They found that difluprednate caused a significant rise of intraocular pressure (>10 mmHg from baseline or >21 mmHg) after 1 month [2]. Kusne *et al*., [15] found a significant rise of IOP in both prednisolone and difluprednate groups after 5-10 POD, which returned to baseline at 6 weeks. In a study by Tijunelis *et al*., [4], they showed no statistically significant difference in change of IOP from baseline after one month; however, their study used a twice-daily dose of both drugs that was much lower than our dose schedule. Saman *et al*., [16] found a statistically significant rise of IOP from baseline at the 1st and 2nd week of treatment. But, their study showed no significant increase of IOP after 1 month, although with a much lower dose than what was used in our study. Our study found that patients aged 60 years and above were more susceptible to a significant rise of IOP in both groups. In group B, among 3 patients who showed IOP >21 mm Hg and a rise of IOP >6 mm Hg from baseline, one was 42 years, and two were 60 and 65 years [2]. In group A, a patient of 60 years showed a significant rise of IOP >21 mm Hg, and a patient of 60 years showed a rise of IOP >6 mm Hg from baseline [3]. In a study by Kusne et al., it was shown that patients over 70 years had a more significant IOP rise after 5-10 days, which returned to baseline after 1 month [15]. A frequent dose schedule was used in our study, starting 24 hours after surgery and given every 2 hours for 7 days. This was then reduced to a once-daily dose for 1 week, with a total duration of one and a half months. As difluprednate was more potent than prednisolone, we suspected that it might increase IOP more significantly. With the frequent dose schedule, a significant IOP rise was found in both groups after 7 days of surgery, with a significant difference between the two groups on 7th postoperative day (POD). Patients aged 60 years or above were found to be more susceptible to a significant IOP rise. However, after tapering both drugs, IOP returned close to baseline in both groups.

Limitations of the study

The study was done with a small sample size and in a single center, so it might not reflect the findings of the overall community. There might be bias related to mixing patients of SICS and Phacoemulsification.

CONCLUSION

Our study found that there was a significant rise in IOP one week after cataract surgery due to frequent use of both difluprednate and prednisolone acetate. The difluprednate group showed a more significant increase in IOP compared to the prednisolone acetate group after the first week. However, after one and a half months, there was no statistically significant difference in IOP between the two groups and the IOP returned to baseline after tapering the dose. In conclusion, both topical difluprednate 0.05% and prednisolone acetate 1% can be used with frequent and tapered doses after cataract surgery, with close monitoring of IOP, especially for difluprednate in the first week.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Pleyer, U., Paul, G., & Paolo, R. (2013). Intraocular pressure effects of common topical steroids for post-cataract inflammation. *Ophthalmology Therapy*, 2, 55-72.
2. Jeng, K. W., Fine, H. F., & Wheatley, H. M. (2013). Incidence of steroid-induced ocular hypertension after vitreoretinal surgery with difluprednate versus prednisolone acetate. *Retina*, 34, 1990-1996.
3. Roberts, C. W., & Nelson, P. L. (2006). Comparative analysis of prednisolone acetate suspensions. *Journal of Ocular Pharmacology and Therapeutics*, 23(2), 2007.
4. Tijunelis, E. P., Leslie, M. N., David, C. M., Paul, E., Madeline, M., & Shahzad, I. M. (2017). Comparison of prednisolone acetate 1% and difluprednate ophthalmic emulsion 0.05% after cataract surgery: Incidence of postoperative steroid-induced ocular hypertension. *Journal of Cataract and Refractive Surgery*, 43, 223-227.
5. Patel, M., & Singhal, D. (2017). Difluprednate in ophthalmic practice. *National Journal of Physiology, Pharmacy and Pharmacology*, 4(1), 92-94.
6. Foster, C. S., & Mulki, L. (2011). Difluprednate for inflammatory eye disorders. *Drugs of Today*, 47(5), 327-333.
7. Hussar, A. D. (2008). New drugs: clevidipine butyrate, difluprednate and tetrabenazine. *Journal of the American Pharmacists Association*, 6, 815-821.
8. Donnenfeld, E. D. (2011). Difluprednate for the prevention of ocular inflammation post-surgery: an update. *Clinical Ophthalmology*, 5, 811-816.
9. Reazeghinejad, M. R., & Katz, L. J. (2012). Steroid-induced iatrogenic glaucoma. *Ophthalmic Research*, 47(2), 66-80.
10. Birnbaum, A. D., Jiang, Y., Tessler, H. H., & Goldstein, D. A. (2001). Elevation of intraocular pressure in patients with uveitis treated with topical

difluprednate. *Archives of Ophthalmology*, 129(5), 668-668.
11. Meehan, K., Vollmar, L., & Sowka, J. (2010). Intraocular pressure elevation from topical difluprednate use. *Optometry*, 81(12), 658-662.
12. Korenfeld, M. S., Silverstein, S. M., Cooke, D. L., Vogel, R., & Crockett, R. S. (2009). Difluprednate ophthalmic emulsion 0.05% for postoperative inflammation and pain. *Journal of Cataract & Refractive Surgery*, *35*(1), 26-34.
13. Donnenfeld, E. D., Holland, E. J., Solomon, K. D., Fiore, J., Gobbo, A., Prince, J., ... & Perry, H. D. (2011). A multicenter randomized controlled fellow eye trial of pulse-dosed difluprednate 0.05% versus prednisolone acetate 1% in cataract surgery. *American journal of ophthalmology*, *152*(4), 609-617.
14. Garg, P., Tuteja, N., & Qayum, S. (2016). To study the efficacy of difluprednate ophthalmic emulsion versus prednisolone acetate ophthalmic suspension on postoperative inflammation in cataract surgery. *Journal of Clinical and Diagnostic Research*, 10(12), 1-8.
15. Kusne, Y., Kang, P., & Fintelmann, R. E. (2016). A retrospective analysis of intraocular pressure changes after cataract surgery with the use of prednisolone acetate 1% versus difluprednate 0.05%. *Clinical Ophthalmology*, 2329-2336.
16. Saman, I. S. E, Mostafa, E. M., Kamel, A. G., & Mohammed, O. A. (2019). Comparison of difluprednate 0.05% versus prednisolone acetate 1% eye drops following uneventful cataract surgery. *J Clin Ophthalmol*, 3(1), 104-107.
17. American Academy of Ophthalmology. 2016-2017. Intraocular pressure and aqueous humor dynamics, 10, 2-43.
18. Salmon, J. F. (2020). Glaucoma. In: Salmon JF (editor). Kanski's Clinical Ophthalmology, 9th ed. Edinburgh: Elsevier; p. 388.