The effect of fluticasone furoate nasal spray on the intraocular pressure in patients of allergic rhinitis: A cross sectional study from eastern India

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Abstract

Background: Rhinoconjunctivitis is a common health problem that plagues the lives of children and adolescents alike with a significant impairment of the quality of life.

Purpose: Aim of this study was to investigate the effect of intranasal corticosteroid, fluticasone furoate, on the change of IOP in allergic rhinitis patients.

Materials and Methods: This was a prospective observational study carried at the Ophthalmology outpatient department of a Government Medical College in West Bengal involving all consecutive patients attending ENT OPD for allergic rhinitis of age group 12 years and above and prescribed fluticasone furoate nasal spray. The IOP of patients were measured before and after start of steroid nasal spray and follow up was done at regular interval. One and half year and follow up was done on 1st, 2nd, 4th, 8th and 12th week respectively.

Results: A total of 108 patients were selected for the study, out of which 100 remained till the end of all follow ups. The IOP for each eye was compared with baseline IOP values (RE: 16.02±2.29, LE: 16.04±2.20) and at the end of the study the P value for each follow up was calculated. The t test revealed that there was no significant change (increase/decrease) in IOP in any eye over the course of time. r values shows that there was a strong positive linear correlation of IOP between and within the eyes at different levels of assessment after the starting of the treatment. Even after age group adjustment, there was no statistical difference in IOP between the eyes among the various age groups.

Conclusion: The study demonstrates no statistically significant increase in IOP after the administration of fluticasone furoate nasal spray. We believe, therefore, that fluticasone furoate administered for a short time for the treatment of nasal allergy, is safe in terms of its effect on IOP in the Indian population.

Keywords: Allergic rhinoconjunctivitis, Fluticasone furoate, Intranasal steroids, Steroid induced glaucoma.

Introduction

Rhinoconjunctivitis, allergic or nonallergic, is a common condition that plagues approximately 30% of adults and 40% of children in the United States on a yearly basis.[1] The prevalence of allergic rhinitis ranges from 10% to 15% in the Indian context.[2] Allergic rhinitis can frequently lead to significant impairment of quality of life. The fatigue, drowsiness and malaise arising out of this disease has many ramifications. They can lead to impaired work and school performance, missed school or work days, and traffic accidents. It is important for the treating clinician to recognize, however, that more serious medical sequelae, such as sleep disruption, asthma exacerbations, otitis media, and rhinosinusitis, can be associated with rhinitis.[3]

Antihistamines and decongestants are the primary weapons in the armamentarium in the fight aimed at relieving the signs and symptoms of allergic rhinitis patients. Over the past several decades, nasal corticosteroids have gained favor as a way of avoiding the common and undesirable side effects of drowsiness and cardiovascular complications that can be associated with nonsteroidal medications. Intranasal corticosteroid sprays are the most effective treatment for allergic rhinitis.[4] The favorable response to nasal corticosteroids is largely due to their prolonged local action and few side effects. Fluticasone is a synthetic steroid of the glucocorticoid family of drugs that is used for treating allergic conditions involving the nose. Fluticasone mimic the naturally-ocurring hormone produced by the adrenal glands, cortisol or hydrocortisone. Fluticasone has potent anti-inflammatory actions. It is believed that fluticasone exerts its beneficial effect by inhibiting several types of cells and chemicals involved in allergic, immune and inflammatory responses. It is well known that steroids can cause an elevation of intraocular pressure (IOP), whether they are administered topically as skin cream[5] or ophthalmic drops, or when they are administered systemically for a long time.[6] The FDA approved fluticasone in October 1994. There have been reports of secondary cataract formation and rise in IOP after prolonged use of intanasal corticosteroids.[7] Very little literature exists from India as far as the study of IOP changes in response to Fluticasone intra nasal spray is concerned. This study was undertaken to address this gap in knowledge.

Aims and Objectives

The main objective of this study was to investigate the effect of intranasal corticosteroid, fluticasone furoate, on the change of IOP in allergic rhinitis

patients, who were receiving this nasal steroid for their treatment.

Materials and Methods

This was a prospective observational study carried at the Ophthalmology outpatient department of a Government Medical College in West Bengal, India.

Study Population: Patients attending ENT OPD for allergic rhinitis of age group 12 years and above and prescribed fluticasone furoate nasal spray.

Study Pattern: The IOP of patients were measured before and after start of steroid nasal spray and follow up was done at regular interval. Study period was one and half year and follow up was done on 1st, 2nd, 4th, 8th and 12th week respectively.

Sample Size: A total of 100 patients of allergic rhinitis were recruited based on existing hospital attendance rates prevalent at the time of the study.

Sample Design: Patients having normal IOP, normal angle of anterior chamber & normal optic disc having allergic rhinitis using only fluticasone furoate nasal spray as once daily dose were included if they met the inclusion criteria. The parameters that were studied at each visit were intarocular pressure by Goldman's applanation tonometry (AT), gonioscopy by Zeiss 4 mirror gonilens and stereoscopic optic disc and retinal nerve fibre layer evaluation. The inclusion criteria were 1) Patients aged 12yrs and above having allergic rhinitis. 2) Patients presenting with any three of four symptoms of-sneezing, rhinorrhoea, nasal obstruction & nasal itching. 3) Patients with IOP < 20mmHg. 4) Patients having normal anterior chamber. 5) Patients having normal optic disc. The following exclusion criteria were applied: 1) Patients having ophthalmic disease other than allergic rhino conjunctivitis. 2) Patients having narrow anterior chamber or C:D > 0.3 or abnormal disc changes. 3) Receiving any drugs topically or systemically other than nasal steroids. 4) Patients having previous history of corticosteroid use within last 3 months. 5) If patient require any treatment for other systemic illness during study period. 6) In any follow up the IOP was > 25mmHg or rise of IOP> 8mmHg in two successive follow up from base line IOP.

Statistical Analysis: Data collected was entered in Microsoft Excel then into statistical database SPSS (statistical package for social sciences, version 20.0, windows compatible). Data was analyzed using standard statistical technique like tabulation, proportions, percentage, mean and standard deviation. Suitable statistical test was performed (Chi Square test, t-test, ANOVA etc.) A probability value ('p' value) of < 0.05 was considered as statistically significant.

Results

The patient of age group >12 years and of both sexes were considered in the present study. The age of the patient was between 14-71 years. The age and sex distribution of the total study group is mentioned in Table 1. A total of 108 patients were selected for the study, but some patients were lost to follow up at different stages of the study and few of them showed irregular medication. Thus, the data obtained from 100 patients were considered for final analysis with a dropout rate of 7.4%.

Table 1: **Distribution of patients by age and sex (N=100)**

Age group (years)	No. of cases (%)	Female (%)	Male (%)
10<20	18 (18)	7(19.44)	11(17.18)
20<30	34(34)	12(33.33)	22(34.37)
30<40	24(24)	11(30.56)	13(20.31)
40<50	14(14)	5(13.89)	9(14.06)
50<60	7(07)	1(2.77)	6(9.37)
60<70	2(02)	----	2(3.12)
≥70	1(01)	-----	1(1.56)
Total	100(100.0)	36(100.0)	64(100.0)

In the present study 36% (36/100) patients were female and 64% (64/100) were male. Male: Female ratio is 1.78:1. On the whole, the average age of the participants was 33.03±12.50 years with a median age of 30 years. The highest number of cases belonged to the 20 to < 30 age group (34%).

Before patients started therapy, their base line IOPs (Table 2) ranged from 11 to 20 mmHg.

Table 2: Showing distributions of base line IOP

Base line intraocular pressure in mmHg	Eye		Total No. (%)
	Right No. (%)	Left No. (%)	
11	0(00.0)	1(01.0)	1(00.5)
12	8(08.0)	4(04.0)	12(06.0)

13	8(08.0)	8(08.0)	16(08.0)
14	16(16.0)	18(18.0)	34(17.0)
15	8(08.0)	9(09.0)	17(08.5)
16	16(16.0)	16(16.0)	32(16.0)
17	7(07.0)	13(13.0)	20(10.0)
18	23(23.0)	15(15.0)	38(19.0)
19	11(11.0)	13(13.0)	24(12.0)
20	3(03.0)	3(03.0)	06(03.0)
Total	100(100.0)	100(100.0)	200(100.0)

After first week: For RE, 83% patients showed no change in IOP, 14% showed 1mm increase and 3% showed 2mm increase. For LE of study patients, 78% showed no change, 16% showed 1mm increase, 5% showed 2mm increase and 1% showed 3mm increase in IOP. After 2nd week: For RE, 74% showed no change in IOP, 19% showed 1mm increase, 5% showed 2mm increase and 2% showed 3mm increase. And for LE 69% showed no change, 21% showed 1mm increase, 7% showed 2mm increase, 2% showed 3mm increase and 1% showed 4mm increase. After 4th week: For RE, 67% showed no change, 17% showed 1mm increase, 11% showed 2mm increase, 4% showed 3mm increase and 1% showed 5mm increase. For LE, 71% showed no change in IOP, 15% showed 1mm increase, 12% showed 2mm increase, 1% showed 3mm increase and 1% showed 4mm increase. After 8th week: For RE, 64% showed no change in IOP, 18% showed 1mm increase, 11% showed 2mm increase, 5% showed 3mm increase, 1% showed 4mm increase, and 1% showed 5mm increase. For LE, 67% showed no change, 16% showed 1mm increase, 8% showed 2mm increase, 6% showed 3mm increase, 2% showed 4mm increase and 1% showed 5mm increase in IOP. After 12th week: For RE, 63% showed no change in IOP, 15% showed 1mm increase, 11% showed 2 mm increase, 3% showed 3mm increase, 5% showed 4mm increase, and 3% showed 5mm increase. For LE, 60% showed no change in IOP, 17% showed 1mm increase, 12% showed 2mm increase, 5% showed 3mm increase, 5% showed 4mm increase and 1% showed 5mm increase in IOP.

Table 3: **Change in IOP within and between eyes at different time of assessment (N=100)**

Time of assessment	**Right eye**			**Left eye**			**r_2, p**
	Mean±sd	**Paired t, df, p**	**r_1, p**	**Mean±sd**	**Paired t,df,p**	**r_1, p**	
Base line	2.76±0.15	*	*	2.77±0.14	*	*	0.889,0.000
1st Week after the start of therapy	2.77±0.15	1.263,99,0.209	0.871,0.000	2.77±0.14	1.107,99,0.271	0.839,0.000	0.887,0.000
2nd Week after the start of therapy	2.77±0.14	1.009,99,0.315	0.863,0.000	2.77±0.15	0.023,99,0.982	0.860,0.000	0.915,0.000
4th Week after the start of therapy	2.77±0.15	1.024,99,0.308	0.832,0.000	2.77±0.14	1.188,99,0.238	0.851,0.000	0.922,0.000
8th Week after the start of therapy	2.77±0.15	1.097,99,0.225	0.846,0.000	2.78±0.14	1.235,99,0.220	0.824,0.000	0.896,0.000
12th Week after the start of therapy	2.78±0.15	1.236,99,0.219	0.795,0.000	2.78±0.14	1.156,99,0.250	0.786,0.000	0.889,0.000

As most of the data sets pertaining to the IOP of both the eyes at different times of evaluation showed skewed distribution, all of them were transformed into their logarithmic values and then parametric tests were done and these were the 'paired t test' and 'Pearson correlation coefficient'(r).

The t test revealed that there was no significant change (increase/decrease) in IOP in any eye over the course of time. r values shows that there was a strong positive linear correlation of IOP between and within the eyes at different levels of assessment after the starting of the treatment.

The patients were categorized as per their age into three groups viz- <20 years, 20-40 years and >40 years. The change in IOP among different groups was compared to find out that whether there was any role of age in IOP change over the period of time with the same steroid medication. At the start that there was no statistical difference in IOP between the eyes among the age groups. [For <20 years age group t_{34}=0.075, p=0.941; for 20-40 years age group t_{110}=-0.239, p=0.811 and for >40 years age groups t_{50}=0.207, p=0.837].

Table 4: IOP change in right eye as per age categories

		Sum of Squares	df	Mean Square	F	Sig.
Right 0	Between Groups	7.138	2	3.569	.678	.510
	Within Groups	510.822	97	5.266		
	Total	517.960	99			
right 1	Between Groups	5.837	2	2.919	.544	.582
	Within Groups	520.273	97	5.364		
	Total	526.110	99			
right 2	Between Groups	7.910	2	3.955	.701	.499
	Within Groups	547.400	97	5.643		
	Total	555.310	99			
right 3	Between Groups	9.295	2	4.647	.794	.455
	Within Groups	567.465	97	5.850		
	Total	576.760	99			
right 4	Between Groups	17.489	2	8.745	1.544	.219
	Within Groups	549.271	97	5.663		
	Total	566.760	99			
right 5	Between Groups	26.942	2	13.471	2.544	.084
	Within Groups	513.648	97	5.295		
	Total	540.590	99			

Table 5: ANOVA scores summated

		Sum of Squares	df	Mean Square	F	Sig.
left 0	Between Groups	3.098	2	1.549	.315	.730
	Within Groups	476.742	97	4.915		
	Total	479.840	99			
left 1	Between Groups	6.724	2	3.362	.746	.477
	Within Groups	437.386	97	4.509		
	Total	444.110	99			
left 2	Between Groups	5.287	2	2.643	.501	.607
	Within Groups	511.463	97	5.273		
	Total	516.750	99			
left 3	Between Groups	3.398	2	1.699	.339	.713
	Within Groups	485.992	97	5.010		
	Total	489.390	99			
left 4	Between Groups	5.204	2	2.602	.518	.597
	Within Groups	487.386	97	5.025		
	Total	492.590	99			
left 5	Between Groups	7.915	2	3.958	.772	.465
	Within Groups	497.245	97	5.126		
	Total	505.160	99			

From the table it is evident that the change of IOP in neither eye whatsoever explored at different level of assessment was not age dependent.

Table 6: **Magnitude of change in IOP of both eyes in the final assessment in respect to the base line value**

EYE	Increase in Intraocular pressure Mean±sd (range)	*U(Mann-Whitney U test), Z, p
Right(n=100)	0.5±1.59 (-3.0 to 5.0)	4754.500, 0.621, 0.535
Left(n=100)	0.55± 1.55 (-4.0 to 5.0)	
Total(N=200)	0.525±1.57 (-4.0 to 5.0)	---------

*The values have skewed distribution and that's why Non-parametric test between the means (unpaired) was adopted.

The table 5 shows that the change of IOP in both eyes at different levels of assessment was revealed to be statistically insignificant across the gender. Analysis also revealed that at the beginning, there was no significant difference in IOP between the eyes among the genders [in male group t_{128}=-0.117, p=0.907 (mean ± sd of IOP=16.05±2.29 in right eye and 16.09±2.19 in left eye) and in female group it was t_{68}=0.053, p=0.958 (mean ± sd of IOP =15.97±2.31in right eye vs 15.94±2.24 in left eye)].

Discussion

Steroids administered in the form of nasal sprays are indicated mainly for the treatment of seasonal and perennial allergic rhinitis. Before this study, only a few reports correlated the administration of nasal steroid sprays with change in intraocular pressure in abroad. In this present study intranasal administration of corticosteroid (fluticasone furoate) was carried out in a group of well selected 100 cases of allergic rhinitis. The results were analyzed to reestablish any effect of nasal spray of corticosteroid on intraocular pressure. After the start of nasal steroid IOP was recorded on each follow up done on 1st, 2nd, 4th, 8th and 12th week respectively. The IOP for each eye was compared with baseline IOP values (RE: 16.02±2.29, LE: 16.04±2.20) and at the end of the study the P value for each follow up was calculated. In this study we have found no clinically and statistically significant (P>0.05) increase in IOP from baseline values after using nasal steroid for a period of 12 weeks. Clearly, it appears that there is no consensus as to whether nasal steroids truly impact IOP. Several studies declare them safe for usage in patients, whereas there is also strong evidence supporting their effect in increasing IOP. The question also remains whether this impact, even if only a slight increase in IOP, is significant enough to warrant any change in treatment practices, especially in patients with no personal or family history of glaucoma. Patients with a history of glaucoma or with a first degree relative with glaucoma are much more likely to experience an increase in IOP associated with steroid use. Based on the current literature[7-9] in the general population of rhinoconjunctivitis patients, the risk of a steroid-induced IOP elevation is extremely low. The administration of intranasal steroids, certainly for the short-term and probably for the long-term, is safe for the treatment of rhinoconjunctivitis.[10] Garbe et al.[11] found no increased risk of developing glaucoma or ocular hypertension in the intranasal steroid users compared with the general population. Bui et al.[12] on the contrary, demonstrated a significant decrease in IOP following discontinuation of intranasal steroids in patients with glaucoma or ocular hypertension. Patients who have glaucoma or a family history of glaucoma must be approached with caution when considering treatment with intraocular nasal steroids. There appears to be a demonstrable link between nasal steroid use and increased IOP in these susceptible patients. In these susceptible patients, this rise could be great enough to result in glaucomatous damage to the optic nerve and resultant loss of vision.[12] Change in IOP can be more problematic than the absolute measured IOP. It is also important to consider the rare patient who has a normal pre-steroid treatment IOP. A small increase in IOP may be enough to result in damage to a susceptible optic nerve. For example, consider a patient with a normal IOP of 12 mm Hg, which should not be detrimental to his/her optic nerve prior to steroid use. After initiating intranasal steroids, the patient has a 6 mmHg–increase in IOP to 18 mm Hg. Although the IOP is still within the normal range, this represents a 50% increase in IOP. A patient with a pretreatment-compromised optic nerve may experience glaucomatous changes at a pressure in the upper teens that would not have been experienced in the lower teens. A single IOP screening after initiation of an intranasal steroid may not be enough, especially if pretreatment IOP was not known. Increased IOP due to steroid exposure can occur at any time during that exposure.[13] Closer attention should be given to patients with risk factors for the development of glaucoma and associated steroid responsiveness.

Conclusion

This study demonstrates no statistically significant increase in IOP after the administration of fluticasone furoate nasal spray. We believe, therefore, that fluticasone furoate administered for a short time for the treatment of nasal allergy, is safe in terms of its effect on IOP in the Indian population.

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References

1. Dykewicz MS, Fineman S. Executive summary of joint task force practice parameters on diagnosis and management of rhinitis. Ann Allergy Asthma Immunol 1998;81:463-8.
2. Rao S, Ramalingam R, Ramalingam KK, Sriraam L, Jha S, Joseph N. Impact of surgery and intranasal corticosteroid therapy on quality of life of patients with allergic rhinitis. *Indian Journal of Allergy, Asthma and Immunology*. 2016 Jan 1;30(1):22.
3. Willsie SK: Improved strategies and new treatment options for allergic rhinitis**.** *J Am Osteopath Assoc* 2002, 102(6 Suppl 2):S7–S14.
4. Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, et al. The diagnosis and management of rhinitis: an updated practice parameter. *J Allergy Clin Immunol*. 2008 Aug:122(2).
5. Aggarwal RK, Potamitis T, Chong NH, et al. Extensive visual loss with topical facial steroids. Eye 1993;7(Pt 5):664-6.
6. Rennie IG. Clinically important ocular reactions to systemic drug therapy. Drug Saf 1993;9(3):196-211.

7. Opatowsky I, Feldman RM, Gross R, Feldman ST. Intraocular pressure elevation associated with inhalation and nasal corticosteroids. Ophthalmology. 1995;102(2):177–179.
8. Dreyer EB. Inhaled steroid use and glaucoma. *New England Journal of Medicine*. 1993 Dec 9;329(24):1822.
9. Bross-Soriano D, Hanenberg-Milver C, Schimelmitz-Idi J, Arrieta-Gomez JR, Astorga Del Toro R, Bravo-Escobar G. Effects of three nasal topical steroids in the intraocular pressure compartment. Otolaryngology—*Head and Neck Surgery*. 2004 Feb;130(2):187-91.
10. Bergmann J, Witmer MT, Slonim CB. The relationship of intranasal steroids to intraocular pressure. Current allergy and asthma reports. 2009 Jul 1;9(4):311-5.
11. Garbe E, LeLorier J, Boivin JF, Suissa S. Inhaled and nasal glucocorticoids and the risks of ocular hypertension or open-angle glaucoma. *JAMA* 1997;277(9):722-7.
12. Bui CM, Chen H, Shyr Y, Joos KM. Discontinuing nasal steroids might lower intraocular pressure in glaucoma. *Journal of allergy and clinical immunology*. 2005 Nov 30;116(5):1042-7.
13. Carnahan MC, Goldstein DA. Ocular complications of topical, peri-ocular, and systemic corticosteroids. *Current opinion in ophthalmology*. 2000 Dec 1;11(6):478-83.