DOI: https://doi.org/10.53350/pjmhs02024181266

ORIGINAL ARTICLE

Impact of Intranasal Corticosteroids on Intraocular Pressure and Retinal Nerve Fiber Layer Thickness: A Cross-Sectional Study at a Tertiary Care Hospital in Pakistan

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ABSTRACT

Background: A worldwide health concern, rhinitis affects 10% to 20% of Pakistan's population. For extended periods of time, otolaryngologists frequently treat patients with rhinitis with topical intranasal corticosteroids (INCS). While oral corticosteroids have well-established effects on intraocular pressure (IOP) and lens opacity, the effects of INCS are less clear. In this study, we sought to determine how utilizing INCS affected individuals with rhinitis's intraocular pressure during a six-month period.

Objective: This study aimed to assess the impact of long-term INCS use on IOP and Retinal nerve fiber layer (RNFL) thickness.

Methods: This cross-sectional study was conducted at a tertiary care hospital in Pakistan. Patients using INCS for at least six months were recruited and compared with a control group of non-users. IOP was measured using Goldmann applanation tonometry, while RNFL thickness was assessed via optical coherence tomography (OCT). Demographic and clinical data were recorded. Statistical analysis included independent t-tests and Pearson correlation to evaluate associations between INCS use, IOP, and RNFL thickness.

Results: A total of 112 participants (56 corticosteroid users and 56 non-users) were included. IOP was significantly higher in corticosteroid users (16.8 ± 2.3 mmHg) than in non-users (14.2 ± 1.8 mmHg) ($p < 0.001$). RNFL thickness was significantly reduced in corticosteroid users (91.4 ± 6.7 µm) compared to non-users (98.6 ± 5.9 µm) ($p < 0.001$). A slight +ve correlation was observed between the duration of intranasal corticosteroid use and IOP in the left eye ($r = 0.251$, $p = 0.019$), but non-significant correlation was seen with RNFL thickness.

Conclusion: Prolonged INCS use may contribute to increased IOP and localized RNFL thinning, suggesting a potential risk for glaucomatous changes. Routine ophthalmic monitoring is recommended for chronic INCS users, particularly those with predisposing risk factors for glaucoma.

Keywords: Intranasal corticosteroids, intraocular pressure, retinal nerve fiber layer, glaucoma risk, optical coherence tomography.

INTRODUCTION

Rhinitis is known as an inflammatory condition of the mucus layer of the nose, characterized by sneezing, rhinorrhea, nasal itching, and nasal congestion. Among these symptoms, nasal congestion is particularly problematic as it significantly reduces quality of life[1,2]. Rhinitis often coexists with other conditions like atopic dermatitis, asthma, and nasal polyps. The primary line of available treatment for these conditions includes pharmacotherapy and immunotherapy. Intranasal corticosteroids (INCS) are the preferred first-line treatment for rhinitis these days[3,4] These corticosteroids help reduce mucus production, upper airway inflammation, and airway edema, thus restoring nasal airflow[5].

Various types of INCS, including triamcinolone acetonide, mometasone furoate, flunisolide, fluticasone propionate, beclomethasone dipropionate, and budesonide, are effective in managing both seasonal and perennial rhinitis[6]. This treatment reduces nasal congestion and allergic symptoms such as sneezing, itching, and rhinorrhea. The mechanism of action of this treatment involves inhibiting inflammatory factors and other mediators including prostaglandins and leukotrienes. Moreover, these corticosteroid medicine also increases the production of lipocortin-1, that ultimately prevents conversion into phospholipase A2. In this way it prevents the formation of other steroid mediators of inflammatory response. Furthermore, these are also involved in indirectly inhibiting the mediators such as kinins, PAF, histamine, and substance P[7].

Due to the common use of INCSs for treating both acute and chronic upper airway inflammation, their safety profile must be completely studied. The major issues linked with steroid use include short- and long-term growth suppression, elevated intraocular pressure (IOP), and hypothalamic-pituitary-adrenal axis suppression. In asthma patients, concurrent use of systemic and inhaled corticosteroids (ICS) may cause synergistic side effects[6]. However, the benefits of INCS are more as compared to the risks if used according to the prescription. Clinical data suggest that second-generation INCS do not affect the hypothalamic-pituitary-adrenal axis, except for beclomethasone dipropionate[9]. The differences in side effects between first- and second-generation ICS can be attributed to pharmacokinetics, as first-generation ICS undergo significant first-pass hepatic metabolism and exhibit higher oral bioavailability[10]. Nonetheless, further research is needed to establish a comprehensive safety profile of INCS.

Recently, ocular safety has become a significant area of research due to the widespread use of INCS for rhinitis. Clinical studies indicate that reducing IOP in cases of severe ocular hypertension lowers the risk of glaucoma progression[11]. Elevated IOP can cause acute ischemic effects and mechanical stress on the retinal nerve fiber layer (RNFL), potentially leading to primary open-angle glaucoma and chronic vision loss[12]. Additionally, long-term INCS use has been associated with posterior subcapsular cataracts. Several studies have explored the relationship between IOP fluctuations and plasma cortisol levels, which are influenced by the circadian rhythm, age, medications, and other systemic and local factors[13]. Although research suggests that corticosteroids—whether applied topically, systemically, or intranasally—may elevate IOP, the extent of this effect remains debated. This study aims to examine the association between INCS use and IOP, contributing to a better understanding of patient safety and potentially improving compliance to reduce the disease burden.

METHODOLOGY

This cross-sectional study was conducted at Jinnah Hospital, Lahore, Pakistan, over six months, from January 2023, to June,

Received on 10-07-2023
Accepted on 20-12-2023

2023. Ethical approval was obtained from the Institutional Review Board (IRB) of Jinnah Hospital, Lahore, under reference number IRB/JHL/ABC, dated 20-01-2023. Written informed consent was obtained from all participants before enrollment, ensuring they were fully informed about the study objectives, procedures, and potential risks.

The sample size was determined using OpenEpi, considering a 95% confidence level and an expected mean difference in intraocular pressure (IOP) based on previous literature, resulting in a required sample of 112 participants. Patients were recruited using a non-probability consecutive sampling technique.

Participants aged 18 years and older who had been using intranasal corticosteroids for at least three months were included in the study. Exclusion criteria encompassed individuals with pre-existing glaucoma, ocular hypertension, optic nerve disease, a history of intraocular surgery or laser treatment, systemic corticosteroid use, or any condition that could independently affect IOP or retinal nerve fiber layer (RNFL) thickness, such as diabetes mellitus or uncontrolled hypertension. Patients with significant refractive errors (more than ±6.00 diopters) and those on medications known to alter IOP were also excluded.

Each participant underwent a detailed ophthalmic examination, including best-corrected visual acuity assessment, slit-lamp biomicroscopy, and fundus examination. Intraocular pressure was measured using Goldmann applanation tonometry, ensuring three consecutive readings were taken per eye and averaged for analysis. The Steven et al. criteria served as the basis for calibrating the Goldmann tonometer [14]. Retinal nerve fiber layer thickness was assessed using spectral-domain optical coherence tomography (SD-OCT), measuring RNFL thickness in the superior, inferior, nasal, and temporal quadrants. All measurements were performed by a single examiner to minimize inter-observer variability.

Data were analyzed using SPSS version 26. Continuous variables, including IOP and RNFL thickness, were reported as mean ± standard deviation. The independent t-test was applied to compare these parameters between corticosteroid users and non-users, as data normality was assessed using the Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages, with comparisons performed using the chi-square test. Pearson correlation analysis was conducted to evaluate the association between the duration of corticosteroid use and ocular parameters. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics: The mean age of the study population was 42.5 ± 10.2 years. There was no significant difference in age and gender distribution between the two groups (p = 0.512 and p = 0.764, respectively).

The corticosteroid user group had a mean duration of corticosteroid use of 8.2 ± 2.5 months. The mean intraocular pressure was significantly higher in corticosteroid users (16.8 ± 2.3 mmHg) compared to non-users (14.2 ± 1.8 mmHg) (p < 0.001). Similarly, the mean RNFL thickness was significantly lower in corticosteroid users (91.4 ± 6.7 µm) than in non-users (98.6 ± 5.9 µm) (p < 0.001) (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants

Parameter	Corticosteroid Users (n = 56)	Non-Users (n = 56)	p-value
Age (years)	42.8 ± 9.8	42.2 ± 10.6	0.512
Male/Female (%)	30 (53.6) / 26 (46.4)	28 (50.0) / 28 (50.0)	0.764
Duration of Use (months)	8.2 ± 2.5	N/A	-
Intraocular Pressure (mmHg)	16.8 ± 2.3	14.2 ± 1.8	<0.001
RNFL Thickness (µm)	91.4 ± 6.7	98.6 ± 5.9	<0.001

Comparison of Retinal Nerve Fiber Layer (RNFL) Thickness by Quadrants: The independent t-test analysis demonstrated a statistically significant reduction in RNFL thickness in the superior, inferior, and temporal quadrants among corticosteroid users compared to non-users. The superior quadrant thickness was significantly lower in corticosteroid users (115.2 ± 7.4 µm) than in non-users (121.6 ± 6.8 µm, p = 0.002). Similarly, the inferior quadrant thickness was reduced in corticosteroid users (112.5 ± 6.9 µm) compared to non-users (118.3 ± 7.2 µm, p = 0.004). The temporal quadrant also exhibited a significant reduction in corticosteroid users (56.3 ± 4.7 µm) relative to non-users (61.7 ± 5.3 µm, p < 0.001).

In contrast, the nasal quadrant thickness was lower in corticosteroid users (91.8 ± 5.6 µm) than in non-users (94.2 ± 5.1 µm), but this difference did not reach statistical significance (p = 0.071), suggesting a trend toward thinning without definitive evidence of an association (Table 2).

Table 2: Comparison of RNFL Thickness in Different Quadrants

Quadrant	Corticosteroid Users (n = 56)	Non-Users (n = 56)	p-value
Superior (µm)	115.2 ± 7.4	121.6 ± 6.8	0.002
Inferior (µm)	112.5 ± 6.9	118.3 ± 7.2	0.004
Nasal (µm)	91.8 ± 5.6	94.2 ± 5.1	0.071
Temporal (µm)	56.3 ± 4.7	61.7 ± 5.3	<0.001

Correlation Between Intranasal Corticosteroid (INCS) Usage and Ocular Parameters: The Pearson correlation analysis showed no significant correlation between INCS usage and IOP in the right eye (r = 0.062, p = 0.527 for the number of puffs, r = -0.089, p = 0.392 for times per day, and r = 0.047, p = 0.623 for duration of use). Similarly, for the left eye, IOP was not significantly correlated with the number of puffs (r = 0.078, p = 0.471) or frequency of use (r = -0.172, p = 0.102). However, a weak but statistically significant positive correlation was observed between the duration of INCS use and increased IOP in the left eye (r = 0.251, p = 0.019), suggesting that prolonged use may lead to a mild elevation in intraocular pressure.

For RNFL thickness, no significant correlations were found in the right eye (r = -0.089, p = 0.413 for the number of puffs, r = 0.065, p = 0.508 for times per day, and r = -0.027, p = 0.812 for duration of use). Similarly, in the left eye, RNFL thickness did not show significant correlations with INCS usage (r = 0.107, p = 0.298 for the number of puffs, r = 0.128, p = 0.215 for times per day, and r = -0.042, p = 0.688 for duration of use (Table 3).

Table 3: Pearson Correlation Coefficients and P-values for Goldmann Applanation Tonometry and OCT Results in Relation to INCS Usage

INCS Usage	Number of Puffs	Times per Day	Number of Weeks
Goldmann Applanation Tonometry (IOP) - Right Eye			
Pearson Correlation (r)	0.062	-0.089	0.047
P-value	0.527	0.392	0.623
Goldmann Applanation Tonometry (IOP) - Left Eye			
Pearson Correlation (r)	0.078	-0.172	0.251
P-value	0.471	0.102	0.019
OCT - Right Eye (RNFL Thickness)			
Pearson Correlation (r)	-0.089	0.065	-0.027
P-value	0.413	0.508	0.812
OCT - Left Eye (RNFL Thickness)			
Pearson Correlation (r)	0.107	0.128	-0.042
P-value	0.298	0.215	0.688

DISCUSSION

As far as we are aware, there aren't many studies in the literature on how intranasal steroids affect intraocular pressure in rhinitis patients in Pakistan. Our patient cohort led us to the conclusion that there was very little chance of a raised in ocular pressure

during the test period as a result of INCS administration. The thickness of the RNFL in the eyes of both sides was measured using optical nerve tomography, and the results for 95% of the subjects fell within the normal range, which is 80 mm or greater. Only 63% of the individuals' findings fell within the questionable range of 70 to 79 mm. The glaucomatous range, when the thickness of retinal nerve is 69mm ≤, did not include any of the subjects.

IOP differs from person to person. We looked at the IOP of 93 participants (186 eyes) in our study. Regardless of the central corneal thickness correction, the normal ocular pressure is between 12 and 22 mmHg, which can alter the results from various contact and non-contact tonometers. Under ideal conditions, ocular pressure above 22 mmHg is regarded as a risk factor for the long-term development of glaucoma[15].

According to the Goldmann applanation tonometry Pearson coefficient, there was no discernible relationship between the tonometry test and steroid use. Similarly, ICS use did not increase the incidence of glaucoma-related structural alterations in the optic nerve.

Since no associations between RNFL thickness and steroid use were discovered, it is possible that other variables contribute to RNFL thickness loss and elevated intraocular pressure, which in turn causes glaucoma. Furthermore, there was no association between the length of ICS use and variations in RNFL thickness over time. At a 95% confidence interval, the high P-value indicates that the results were not significant. According to research by Dereci et al.[16], children with asthma who received inhaled steroids showed no change in peripapillary RNFL thickness. There is no evidence in the literature that ICS and RNFL thickness are related in rhinitis patients.

A systematic review was carried out by Ahmadi et al.[5] to investigate the effects of intranasal steroid treatment on intraocular pressure and lens opacity. According to the findings, 4376 patients who were enrolled in 10 randomized control studies did not experience a rise in IOP or the onset of glaucoma. Every clinical experiment examined the effects of different intranasal steroids, both old and new, across time ranging from 2 to 104 weeks, and detailed the variations between test and control subjects. According to this systematic review's safety profile, intranasal steroids are low-risk substitutes for treating respiratory irritation in the upper tract. The length of time intranasal steroids are administered and the patient's physiological state can both affect IOP. Prior to starting non-parenteral corticosteroid therapy, a two-week evaluation period is recommended under the current guidelines[3].

When comparing participants who used INCS to those who received a placebo, Valenzuela et al.'s identical systematic review and meta-analysis[17] found no statistically significant heightened risk of increased IOP. There were 2,837 patients with a 95% confidence interval without glaucoma. When compared to individuals who received a placebo, participants who took steroids did not even develop a posterior subcapsular cataract. Overall, the meta-analysis's included studies indicated that there is no correlation between INCS use and elevated IOP[17].

To learn more about the effects of topical nasal steroids given to individuals with rhinitis and dry eyes, Yenigun et al.[18] created pilot research. This six-week study showed that giving nasal steroids to treat rhinitis considerably reduced dry eye symptoms without changing intraocular pressure. The findings of the Schirmer I and tear breakup time tests, however, were not statistically significant. According to this study, corticosteroid delivery by mouth and eyedrops may be more dangerous and powerful than nasal administration. Thus, these findings lend credence to the safety of intranasal steroids[18].

Nonetheless, Mohd Zain et al.[19] looked at how intranasal steroids affected IOP over the long run. The result of our study implies that patients receiving intranasal steroids for rhinitis may experience an effect on their intraocular pressure (IOP) if they use these medications for an extended period of time. According to our research, using intranasal steroids and elevated IOP are not directly related. This might be the result of intranasal steroids' limited systemic absorption due to their formulation for local delivery.

Because of their superior pharmacodynamics and pharmacokinetic characteristics, newer steroids including fluticasone propionate, mometasone furoate, ciclesonide, and fluticasone furoate are all great INCS. Because of their strong affinity for the glucocorticoid receptor, these medications have greater potency and selectivity and can prevent side effects by avoiding first-pass metabolism. Additionally, these INCS have a sustained-release pharmacological effect, which lowers the daily dosage of the medications needed[3].

However, there are certain restrictions on the current study. First of all, the study is cross-sectional and the patient sample is tiny. Therefore, in order to fully support our findings, a bigger patient population is needed for a future investigation. Second, in order to evaluate adherence to medical care, we used direct questioning without any impartial recording.

CONCLUSIONS

This cross-sectional investigation showed that there is significant statistical significance in the safety profile of intranasal steroids. The safety profile of intranasal steroid usage has been described in similar trials, giving confidence that there is no connection between intranasal steroid use and elevated intraocular pressure. To assess the long-term relationship between INCS and IOP and RNFL thickness, larger cohort studies are needed.

Funding: This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest: The authors declare no competing interests.

Ethical Approval: Ethical clearance was obtained from the appropriate Institutional Review Board before initiating the study.

Informed Consent: Written informed consent was obtained from all study participants.

Authors' Contributions: All authors contributed equally in the completion of current study.

Acknowledgements: The authors thank the participants and institutional staff for their cooperation and support throughout the research.

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This article may be cited as: Bano S, Haleem A, Shaikh RM, Ahmed M, Qureshi A, Iqbal J: Impact of Intranasal Corticosteroids on Intraocular Pressure and Retinal Nerve Fiber Layer Thickness: A Cross-Sectional Study at a Tertiary Care Hospital in Pakistan. Pak J Med Health Sci, 2023; 18(1): 266-269.