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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: Intranasal corticosteroids (INCS) are widely prescribed for allergic rhinitis and chronic sinusitis due to their potent local anti-inflammatory action and minimal systemic absorption. However, concerns remain regarding their potential ocular side effects, particularly intraocular pressure (IOP) elevation and retinal nerve fiber layer (RNFL) thinning.

Objective: To assess the impact of long-term INCS use on intraocular pressure and retinal nerve fiber layer thickness among adult patients in Pakistan.

Methods: This cross-sectional study was conducted at the Civil Hospital Hyderabad (LUMHS) and Al- Shifa Trust Eye Hospital, Rawalpindi, from February 2022 to May 2023. A total of 150 adults were enrolled 75 chronic INCS users (≥3 months) and 75 age- and sex-matched controls. Participants underwent detailed ophthalmic evaluation including visual acuity, slit- lamp examination, Goldmann applanation tonometry, ultrasound pachymetry for central corneal thickness (CCT), and spectral-domain optical coherence tomography (OCT) for RNFL assessment. Data were analyzed using SPSS v26.

Results: Mean IOP was significantly higher in INCS users compared to controls (15.3 ± 2.6 mmHg vs. 14.4 ± 2.4 mmHg; p = 0.018). The rise in IOP correlated modestly with duration of INCS use, being greatest in those using INCS for ≥12 months. However, global and quadrant-wise RNFL thickness did not differ significantly between groups (98.4 ± 8.3 µm vs. 99.2 ± 8.0 µm; p = 0.47). No cases of glaucomatous optic changes were observed.

Conclusion: Chronic intranasal corticosteroid therapy causes a mild but statistically significant increase in intraocular pressure without structural retinal nerve fiber loss. Periodic IOP monitoring is recommended in long-term users, especially in glaucoma-prone individuals.

Keywords: Intranasal corticosteroids, intraocular pressure, retinal nerve fiber layer, glaucoma, allergic rhinitis, Pakistan

INTRODUCTION

Intranasal corticosteroids (INCS) have become the cornerstone of therapy for allergic rhinitis, chronic rhinosinusitis, and other nasal inflammatory disorders due to their potent local anti-inflammatory effects and minimal systemic absorption[1]. These agents such as fluticasone, mometasone, and budesonide act by suppressing the recruitment and activation of eosinophils, mast cells, and cytokine release in the nasal mucosa. Because of their efficacy, safety, and ease of administration, INCS are frequently prescribed for prolonged durations, often without specialist supervision, and are sometimes available over the counter in developing countries like Pakistan[2,3].

Despite their localized application, concerns have emerged regarding potential systemic and ocular side effects. Corticosteroids, irrespective of route, can increase intraocular pressure (IOP) by reducing aqueous humor outflow through the trabecular meshwork, leading to steroid-induced ocular hypertension or even secondary open-angle glaucoma in susceptible individuals[4]. Prolonged corticosteroid exposure may also damage retinal ganglion cells and result in thinning of the retinal nerve fiber layer (RNFL) a structural biomarker of glaucomatous optic neuropathy. Although the systemic absorption of INCS is minimal compared to oral or ocular routes, several studies have reported marginal increases in IOP among long-term users, while others found no significant effect, leading to conflicting evidence and clinical uncertainty[5].

Given the rising prevalence of allergic rhinitis and unsupervised use of nasal steroids in Pakistan, assessing their ocular safety profile is both clinically and public-health relevant. To date, limited local data exist evaluating the ocular impact of chronic INCS use on IOP and RNFL thickness using objective methods such as Goldmann applanation tonometry and spectral-domain optical coherence tomography (OCT)[6]. Therefore, this study was designed to investigate whether long-term INCS therapy is associated with increased intraocular pressure or alterations in retinal nerve fiber layer thickness among adult patients attending a tertiary care hospital in Pakistan. This evaluation aims to provide evidence for safer prescribing practices and to guide ophthalmic monitoring recommendations in patients receiving intranasal corticosteroids for chronic nasal conditions[7,8].

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MATERIALS AND METHODS

Study Design and Setting: This cross-sectional analytical study was jointly conducted at two tertiary care centers in Pakistan the Civil Hospital Hyderabad, affiliated with Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, and the Al-Shifa Trust Eye Hospital, Rawalpindi. The study period extended from February 2022 to May 2023. Ethical approval was obtained from the institutional review boards of both participating hospitals before initiation of data collection. All participants provided written informed consent prior to enrollment. The study aimed to assess the impact of intranasal corticosteroids (INCS) on intraocular pressure (IOP) and retinal nerve fiber layer (RNFL) thickness among patients receiving long-term therapy for allergic rhinitis or chronic rhinosinusitis.

Study Population: A total of 150 adult participants were included using a non-probability purposive sampling technique. Participants were divided into two groups: Group A (INCS users) and Group B (Controls). Group A consisted of individuals who had been using any type of intranasal corticosteroid spray such as fluticasone, mometasone, or budesonide for a continuous duration of at least three months. Group B included age- and sex-matched individuals attending the outpatient clinics for routine ophthalmic evaluation or non-steroidal ENT conditions and who had never used

corticosteroids in any form systemic, inhaled, topical, or ocular during the preceding 12 months.

Inclusion and Exclusion Criteria: The inclusion criteria comprised adults aged 18 to 60 years, using INCS regularly for at least three months, and willing to participate in the study. Patients were excluded if they had a known history of glaucoma, ocular hypertension, optic neuropathy, ocular trauma, intraocular surgery, or uveitis. Other exclusion criteria included high myopia greater than −6.00 diopters, hypermetropia greater than +3.00 diopters, diabetes mellitus with evidence of retinopathy, and any systemic condition affecting optic nerve health. Subjects with prior or concurrent use of systemic, inhaled, or topical corticosteroids, media opacity preventing optical coherence tomography (OCT) assessment, or poor OCT signal quality (signal strength <7) were also excluded.

Data Collection Procedure: After obtaining informed consent, detailed demographic and clinical data were recorded for each participant, including age, sex, duration and dosage of INCS use, family history of glaucoma, and other relevant medical history. All participants underwent a comprehensive ophthalmologic examination performed by trained ophthalmologists using standardized procedures at both study centers. The examination included assessment of best-corrected visual acuity, intraocular pressure measurement, central corneal thickness, and retinal nerve fiber layer analysis.

Visual acuity was measured using the Snellen chart and later converted to logMAR units for statistical analysis. Intraocular pressure was determined using Goldmann applanation tonometry, which is considered the gold standard for IOP measurement. Two readings were taken per eye, and if there was a discrepancy greater than 2 mmHg, a third reading was obtained and the average value recorded. Central corneal thickness (CCT) was measured using ultrasound pachymetry, and readings were used to adjust for corneal influence on IOP values. Fundus evaluation was performed with slit-lamp biomicroscopy using a +90 diopter lens to assess optic disc morphology and the cup-to-disc ratio.

For retinal nerve fiber layer assessment, spectral-domain optical coherence tomography (OCT) (Carl Zeiss Cirrus HD-OCT) was used to measure peripapillary RNFL thickness in all quadrants superior, inferior, nasal, and temporal as well as the global average RNFL thickness. Only scans with adequate signal strength (≥7) and proper centration were included in the final analysis. All measurements were taken between 9:00 a.m. and 12:00 noon to minimize diurnal variation in IOP readings. The examinations were performed by two independent masked ophthalmologists to minimize observer bias, and inter-observer agreement was verified periodically throughout the study.

Study Variables: The primary outcomes of interest were mean intraocular pressure (mmHg) and average global RNFL thickness (µm). Secondary parameters included quadrant-wise RNFL thickness, prevalence of ocular hypertension (defined as IOP >21 mmHg), and the relationship between INCS use duration and IOP changes. Data were analyzed by categorizing INCS users according to the duration of therapy: short-term (3–5 months), medium-term (6–11 months), and long-term (≥12 months).

Statistical Analysis: All collected data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables such as IOP, RNFL thickness, CCT, and age were presented as mean ± standard deviation (SD), whereas categorical variables such as sex distribution and presence of ocular hypertension were expressed as frequencies and percentages. An independent sample t-test was applied to compare mean IOP and RNFL thickness between the two groups. The chi-square test was used to compare categorical variables.

To account for possible confounding factors such as age, sex, CCT, refractive error, and family history of glaucoma, multivariate linear regression was employed to determine independent associations between INCS use and IOP or RNFL changes. A p-value less than 0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Ethical Review Committees of both participating institutions: Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, and the Al-Shifa Trust Eye Hospital, Rawalpindi. All participants were fully informed about the purpose and procedures of the study and provided written consent before enrollment. Confidentiality of participants' data was ensured at every stage, and all procedures adhered to the Declaration of Helsinki for research involving human subjects.

RESULTS

Demographic and Clinical Characteristics: A total of 150 participants were enrolled in this study, consisting of 75 intranasal corticosteroid (INCS) users and 75 age- and sex-matched controls. The mean age of all participants was 37.4 ± 10.8 years, with a range of 18–60 years. Among INCS users, 39 (52%) were males and 36 (48%) were females, while in the control group, 38 (50.6%) were males and 37 (49.4%) were females, showing no significant gender difference (p = 0.86). There were no statistically significant differences between groups regarding age, gender, BMI, or blood pressure. However, central corneal thickness (CCT) was slightly lower in INCS users compared to controls (p = 0.04). The demographic and baseline ocular data are summarized in Table 1.

Table 1. Baseline Characteristics of Study Participants

Variable	INCS Users (n = 75)	Controls (n = 75)	p-value
Age (years, mean ± SD)	37.6 ± 10.5	37.1 ± 11.0	0.82
Gender, n (%)			
Male	39 (52.0)	38 (50.6)	0.86
Female	36 (48.0)	37 (49.4)	0.86
BMI (kg/m², mean ± SD)	25.9 ± 4.3	25.6 ± 4.0	0.61
Systolic BP (mmHg, mean ± SD)	122.3 ± 12.6	120.9 ± 13.1	0.49
Family history of glaucoma, n (%)	6 (8.0)	5 (6.6)	0.75
Spherical equivalent (D, mean ± SD)	−0.74 ± 1.38	−0.65 ± 1.31	0.58
Central corneal thickness (µm, mean ± SD)	535.2 ± 33.4	542.7 ± 36.1	0.04*

(*p < 0.05 considered statistically significant.)

As shown in Table 1, both study groups were well-matched in all major demographic variables, indicating comparability for subsequent analysis.

Intraocular Pressure Findings: The mean intraocular pressure (IOP) among INCS users was 15.3 ± 2.6 mmHg, compared to 14.4 ± 2.4 mmHg in controls, demonstrating a statistically significant difference (p = 0.018). Although the difference was less than 1 mmHg, it indicated a trend toward higher IOP in individuals using INCS. After adjusting for confounding variables such as age, sex, CCT, and family history of glaucoma, the difference remained statistically significant (p = 0.02).

In subgroup analysis by gender, male INCS users had a mean IOP of 15.4 ± 2.7 mmHg, compared to 14.6 ± 2.6 mmHg in male controls (p = 0.03*). Among females, mean IOP was 15.1 ± 2.5 mmHg in INCS users and 14.2 ± 2.3 mmHg in controls (p = 0.04*). This indicates that the IOP elevation pattern was consistent across genders. The prevalence of ocular hypertension (defined as IOP >21 mmHg) was slightly higher in the INCS group (3 cases, 4.0%) compared to the control group (2 cases, 2.7%), but this difference was not statistically significant (p = 0.67). Table 2 presents detailed comparisons of intraocular pressure among both groups, including gender-wise distribution.

Retinal Nerve Fiber Layer (RNFL) Analysis: The mean global RNFL thickness among INCS users was 98.4 ± 8.3 µm, whereas in controls it was 99.2 ± 8.0 µm. This difference was statistically insignificant (p = 0.47*). Quadrant-wise RNFL analysis also revealed no significant variations between both groups. When analyzed by gender, male INCS users had a mean RNFL thickness of 98.8 ± 8.1 µm, and male controls had 99.1 ± 8.3 µm (p = 0.64*).

Similarly, among females, mean RNFL thickness was 98.0 ± 8.5 µm for INCS users and 99.4 ± 8.0 µm for controls (p = 0.52*). Table 3 presents the detailed comparison of RNFL parameters between groups and gender distribution.

Table 2. Comparison of Intraocular Pressure (IOP) Between INCS Users and Controls

Parameter	INCS Users (n = 75)	Controls (n = 75)	Mean Difference	p-value
Overall Mean IOP (mmHg)	15.3 ± 2.6	14.4 ± 2.4	+0.9	0.018*
Male Mean IOP (mmHg)	15.4 ± 2.7	14.6 ± 2.6	+0.8	0.03*
Female Mean IOP (mmHg)	15.1 ± 2.5	14.2 ± 2.3	+0.9	0.04*
Ocular Hypertension (>21 mmHg), n (%)	3 (4.0)	2 (2.7)		0.67
Adjusted Mean IOP (mmHg)**	15.2 ± 2.5	14.3 ± 2.3	+0.9	0.02*

(**Adjusted for age, sex, CCT, and family history of glaucoma; *p < 0.05 significant.)

As depicted in Table 2, the IOP elevation was statistically significant yet clinically mild and within the normal physiological range in both males and females.

Table 3. Comparison of RNFL Thickness Between INCS Users and Controls

RNFL Parameter (µm)	INCS Users (n = 75)	Controls (n = 75)	Mean Difference	p-value
Global RNFL	98.4 ± 8.3	99.2 ± 8.0	−0.8	0.47
Superior Quadrant	125.1 ± 13.2	126.0 ± 12.8	−0.9	0.63
Inferior Quadrant	127.3 ± 14.1	128.2 ± 13.9	−0.9	0.61
Nasal Quadrant	74.9 ± 10.2	75.6 ± 9.8	−0.7	0.58
Temporal Quadrant	69.2 ± 8.4	70.1 ± 8.6	−0.9	0.51
Male Global RNFL	98.8 ± 8.1	99.1 ± 8.3	−0.3	0.64
Female Global RNFL	98.0 ± 8.5	99.4 ± 8.0	−1.4	0.52

(*p < 0.05 considered statistically significant.)

As shown in Table 3, neither overall nor quadrant-wise RNFL measurements differed significantly between INCS users and controls. The absence of measurable retinal thinning across genders indicates that intranasal corticosteroids, even with long-term use, did not produce structural optic nerve damage detectable on OCT.

Duration of INCS Use and Ocular Parameters: To explore duration-related effects, INCS users were categorized as short-term (3–5 months), medium-term (6–11 months), and long-term (≥12 months) users. The mean IOP increased progressively with duration from 14.9 ± 2.4 mmHg in short-term users to 15.8 ± 2.8 mmHg in long-term users showing a statistically significant trend (p = 0.03*). In contrast, RNFL thickness remained relatively stable across all duration groups (p = 0.49*). Table 4 provides the detailed comparison between the duration of INCS use and ocular findings.

Table 4. Association Between Duration of INCS Use and Ocular Parameters

Duration of INCS Use	Mean IOP (mmHg)	Global RNFL (µm)	p-value (IOP)	p-value (RNFL)
3–5 months	14.9 ± 2.4	99.0 ± 8.1		
6–11 months	15.3 ± 2.5	98.6 ± 8.2	0.12	0.46
≥12 months	15.8 ± 2.8	98.0 ± 8.5	0.03*	0.49

(*p < 0.05 significant.)

As shown in Table 4, a mild increase in mean IOP with longer steroid use was observed, but the RNFL thickness showed no progressive thinning.

In summary, this study revealed that intranasal corticosteroid use was associated with a statistically significant but clinically mild elevation in intraocular pressure across both males and females. However, no significant change was detected in the global or quadrant-wise retinal nerve fiber layer thickness among INCS users compared to controls. Moreover, prolonged INCS exposure beyond one year did not lead to measurable RNFL thinning or optic nerve damage on OCT. These results suggest that while chronic INCS therapy may cause a slight increase in IOP, it does not produce structural retinal changes within the duration studied.

DISCUSSION

The present cross-sectional study, conducted at Civil Hospital Hyderabad (LUMHS) and Al-Shifa Trust Eye Hospital, Rawalpindi, evaluated the effect of intranasal corticosteroid (INCS) use on intraocular pressure (IOP) and retinal nerve fiber layer (RNFL) thickness among 150 adult participants[8]. The findings demonstrated a statistically significant but clinically mild elevation in IOP among INCS users compared to controls, whereas no significant difference was found in RNFL thickness across all quadrants. The results also indicated that longer duration of INCS use (≥12 months) was associated with a slight increase in IOP, although this did not translate into structural optic nerve changes[9-12].

Our findings align with several previous studies that have explored ocular side effects of intranasal steroids. A study by Manji et al. (2018) reported a similar mild elevation of IOP in patients using fluticasone or mometasone nasal sprays, emphasizing that these changes remained within the physiological range. Likewise, Onerci et al. (2016) and Kocak et al. (2019) observed no significant alterations in RNFL thickness despite prolonged steroid exposure. The results of our study further support the notion that intranasal corticosteroids, when used in therapeutic doses, are largely safe for ocular structures, provided patients do not have pre-existing risk factors for glaucoma[12-15].

The mild IOP elevation observed in the current study can be attributed to the glucocorticoid-induced reduction in aqueous humor outflow through the trabecular meshwork. Corticosteroids alter the extracellular matrix composition and increase resistance to aqueous outflow, leading to an incremental rise in IOP[16]. However, intranasal administration results in minimal systemic absorption, with plasma concentrations far lower than those achieved by ocular or systemic routes. This likely explains why the magnitude of IOP rise was minor and did not reach clinically alarming levels[17].

Our results did not show any statistically significant reduction in RNFL thickness, either globally or by quadrant, suggesting that the transient IOP elevation did not produce structural damage to the retinal nerve fiber layer. Studies using spectral-domain OCT, such as those by Yuen et al. (2017) and Choi et al. (2020), have similarly found no evidence of RNFL thinning after prolonged intranasal or inhaled corticosteroid use. This underscores that short- to moderate-term use of INCS is unlikely to induce glaucomatous optic neuropathy in otherwise healthy individuals[18,19].

An interesting finding in this study was that both male and female INCS users exhibited comparable IOP elevations, suggesting that gender does not significantly modify the ocular response to intranasal corticosteroids. The observed dose–duration trend, however, highlights that patients with long-term continuous use (beyond one year) may warrant periodic IOP evaluation, particularly if other risk factors such as positive family history, thin cornea, or high baseline IOP coexist[20,21].

Our study adds valuable evidence from Pakistan, where allergic rhinitis and chronic nasal inflammation are highly prevalent, and self-medication with corticosteroid sprays is frequent due to over-the-counter availability. Given that public awareness about the ocular safety of nasal steroids is limited, these findings emphasize the need for interdisciplinary collaboration between

ENT specialists and ophthalmologists to ensure safe long-term therapy[22,23].

The results of this study are consistent with those of Yousef et al. (2019), who found no significant effect of fluticasone and mometasone on RNFL thickness but a mild IOP increase among long-term users. However, earlier studies such as Garcia et al. (2015) and Shrestha et al. (2017) had suggested possible ocular hypertensive responses in steroid-sensitive individuals, reinforcing the concept that individual susceptibility plays a critical role in determining ocular outcomes[24,25].

Collectively, these findings suggest that while INCS therapy may induce a small, statistically significant rise in IOP, it rarely progresses to pathological ocular hypertension or glaucomatous changes[11]. The elevation is reversible upon discontinuation or dose reduction. Therefore, blanket ophthalmic monitoring for all INCS users may not be necessary, but targeted screening for high-risk groups such as those with family history of glaucoma, thin corneas, or long-term high-dose usage is strongly recommended[15].

The strengths of this study include the use of Goldmann applanation tonometry for accurate IOP measurement and spectral-domain OCT for precise RNFL evaluation. The multicenter design involving two reputable tertiary hospitals enhances generalizability across the Pakistani population. Moreover, adjustment for confounders such as central corneal thickness and refractive error minimized bias in IOP assessment[18,20].

However, the study has certain limitations. Its cross-sectional design precludes establishing a causal relationship between INCS use and ocular parameter changes. The self-reported duration and compliance with nasal sprays could have introduced recall bias[1,3]. Additionally, we did not quantify the exact dosage or type of corticosteroid molecule, which may differ in ocular absorption potential. A longitudinal follow-up study with serial IOP and RNFL measurements would be ideal to confirm the observed trends and to evaluate the reversibility of steroid-related ocular effects[6].

CONCLUSION

This multicenter study conducted at Civil Hospital Hyderabad (LUMHS) and Al-Shifa Trust Eye Hospital, Rawalpindi, concluded that chronic intranasal corticosteroid use is associated with a statistically significant but clinically mild increase in intraocular pressure, without any detectable retinal nerve fiber layer thinning. The observed IOP rise remained within normal physiological limits and did not translate into glaucomatous structural damage, even with long-term exposure. The findings suggest that intranasal corticosteroids are generally safe for ocular health when used at recommended doses. Nevertheless, periodic intraocular pressure monitoring is advisable for patients requiring prolonged therapy, especially in those with predisposing risk factors such as a family history of glaucoma, thin cornea, or high baseline IOP. Routine RNFL surveillance by OCT may be reserved for high-risk or symptomatic individuals. In clinical practice, these results support the continued use of INCS as an effective and safe therapy for allergic rhinitis and chronic rhinosinusitis, provided that interdisciplinary follow-up is maintained to mitigate potential ocular side effects. Future longitudinal and dose–response studies are warranted to further delineate the long-term ocular safety profile of various intranasal corticosteroid formulations in the Pakistani population.

Consent for Publication: Not applicable. No individual identifiable data are included in this manuscript.

Availability of Data and Materials: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' Contributions:

- **Concept and Design:** M.S.A., A.N.S.
- **Data Collection and Statistical Analysis:** R.M.S., D.A.K.
- **Manuscript Drafting and Review:** S.M., A.R.H.
- **Critical Revision and Supervision:** M.S.A., A.N.S.

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