Rhinology Online

ORIGINAL CONTRIBUTION

OPEN ACCESS

Effect of topical nasal steroids on intra-ocular pressure in a Nepalese population: a tertiary hospital based prospective observational study*

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Rhinology Online, Vol 6: 46 - 50, 2023

http://doi.org/10.4193/RHINOL/23.021

***Received for publication:**

August 14, 2023

Accepted: November 20, 2023

Published: November 26 , 2023

Abstract

Background: Impact of intranasal corticosteroid (INC) on intraocular pressure (IOP) has been a topic of longstanding debate with various studies showing variable results. This study aims to assess the effect of INC on IOP in the Nepalese population in a tertiary hospital of Nepal.

Methodology: This was prospective observational study conducted in a tertiary hospital from May 2021 to November 2022. IOP of patients who met our inclusion criteria were measured before and after 6 weeks of the initiation of INC. Data were collected and compiled in Microsoft Excel. The statistical test was done using SPSS version 25.

Results: A total of 48 cases were evaluated. We observed that the mean IOP difference before and after nasal steroid usage exhibited no statistically significant variance: 0.5 mean IOP in the right eye and 0.12 mean IOP in the left eye.

Conclusions: This study proposes that intranasal steroids pose a minimal risk of inducing ocular hypertension in the Nepalese population. Nonetheless, larger cohort studies with extended follow-up durations are warranted to substantiate these findings.

Key words: corticosteroid, nasal spray, rhinitis, intraocular pressure, ocular hypertension, glaucoma

Introduction

Steroids are one of the most frequently used medications in rhinology practice. Topically administered steroids confer a great role in inflammatory nasal conditions like allergic rhinitis, acute and chronic rhinosinusitis, vasomotor rhinitis, etc. [1-3].

Topical steroids are generally safe, however, not completely devoid of complications. A recent study from Netherlands Pharmacovigilance Center reported a range of adverse drug reactions related to topical intranasal corticosteroids (INC). The observed complications varied significantly, with nasal septal perforation having a reported odds ratio (ROR) of 463.23, while Cushing's syndrome had an ROR of 22.11, and Glaucoma had an ROR of 14.26, among others [4].

Ocular topical steroids are known to increase intraocular pressure by impeding the outflow of aqueous humor (5). Concerns have been raised about the potential of intranasal corticosteroids to have a similar effect and various studies have been conducted to evaluate the impact of intranasal corticosteroids on intraocular pressure. Although the majority of these studies have demonstrated no significant effect of intranasal corticosteroids on intraocular pressure, there are a few literature sources that provide evidence suggesting a possible influence on intraocular pressure [5-9]. Moreover, the responsiveness to steroids can vary individually [9].

Against this backdrop, with no similar study performed so far in Nepalese population, this study aims to assess the effect of INC on IOP in the Nepalese population.

Materials and methods

This was a prospective observational study conducted jointly in the Department of ENT and Department of Ophthalmology of Tribhuvan University Teaching Hospital (TUTH), Nepal from May 2021 to November 2022. Adult cases (>15 years) with allergic rhinitis or chronic rhinosinusitis who were prescribed with INC were included in the study. Cases using INC along with systemic steroids, non-compliant with the use of INC and those having history of glaucoma were excluded from the study. The dose of INC was 400 mcg/ day (50 mcg/puff). To avoid heterogeneity, we used Mometasone Furoate in all cases. Before starting INC, all cases were sent for IOP assessment. The second IOP assessment was done after 6 weeks. IOP pressure of >21mm Hg was considered elevated. If the IOP was found to be elevated, INC was stopped and IOP was again measured after 6 weeks. Those who have raised IOP were further evaluated by a glaucoma expert and the IOP raise was reconfirmed. This minimized the potential subjective bias in our study. The instrument that we used to confirm the IOP was Goldmann applanation tonometer (GAT) which is considered the reference standard [10] for IOP measurement. The instrument is calibrated every three months at our institution.

If there was a drop in IOP after discontinuation of steroids, the raised IOP was attributed to topical steroid use. The person who measured the IOP was blinded regarding the use of steroids. Data was collected and compiled in Microsoft Excel. The statistical test was done using SPSS version 25. The paired t-test was used to compare the mean IOP before and after using INC. A p-value of <0.05 was considered as statistically significant.

Results

A total of 62 cases were assessed of which 14 cases were excluded from the study owing to incompliance with medication and failure to follow up. The study population comprised of 26 males and 22 females with age ranging from 15 to 57 years. The majority of the cases (37) had allergic rhinitis. The rest had chronic rhinosinusitis (CRS) (11) of which two had nasal polyposis. The study included only two cases of CRS with nasal polyposis because the majority of cases with sinonasal polyposis had already initiated treatment involving oral steroids, along with saline/ sodium bicarbonate douching, with or without the addition of budesonide. This prior treatment could potentially have introduced confounding factors that might affect the study results. The cases with sinonasal polyposis who were selected for the study all presented with Grade I polyps bilaterally and concomitant allergic rhinitis.

Normality of the IOP data before and after the use of intranasal steroids was assessed using Saphiro Wilk test and the distribution was found to be normal. There were two cases who had raised IOP (22 mmHg) in their right eye at 6 weeks of starting intranasal steroids. On stopping the steroids, the IOP returned to the baseline. Among the patients with elevated intraocular pressure (IOP), there was a significant increase from their baseline measurements. Specifically, one patient had a baseline IOP of 15 mmHg, experiencing a rise of 7 mmHg, while the other had a baseline IOP of 18 mmHg, showing a rise of 4 mmHg. The cases with elevated IOP underwent further evaluation and were subsequently confirmed by a glaucoma specialist. The mean baseline IOP and IOP measured after 6 weeks of intranasal steroids for both eyes are shown in Table 1 and Figures 1 and 2. The difference in mean IOP before and after the use of steroids was not statistically significant.

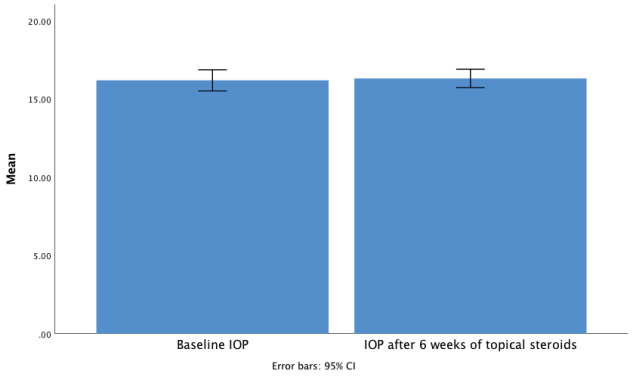

Figure 1. Comparison of mean IOP before and after using intranasal steroids in left eye.

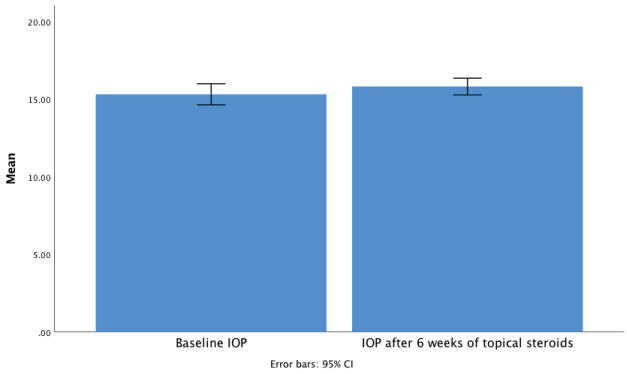

Figure 2. Comparison of mean IOP before and after using intranasal steroids in right eye.

Discussion

Intranasal corticosteroids (INCs) are highly effective in managing inflammatory nasal conditions, including allergic rhinitis, acute and chronic rhinosinusitis, and vasomotor rhinitis. This efficacy has led specialists to increasingly prescribe them for their prolonged use [1]. Nasal steroids are commonly used in the form of nasal spray which includes first-generation INCs formulations (beclomethasone dipropionate, triamcinolone acetonide, flunisolide, budesonide) and newer preparations (fluticasone propionate, mometasone furoate, fluticasone furoate, and ciclesonide) [11]. Fluticasone and mometasone are the two most

Table 1. Mean IOP before and after starting intranasal corticosteroids for both eyes.

	IOP	Mean	Standard deviation	Standard Error Mean	Mean difference	Paired t-test p-value
Right eye	Baseline IOP	15.31	2.34	0.33	-0.5	0.72
	IOP at 6weeks of using steroids	15.81	1.86	0.26		
Left eye	Baseline IOP	16.18	2.32	0.33	-0.12	0.652
	IOP at 6weeks of using steroids	16.31	2.02	0.29		

prescribed intranasal steroids. We used mometasone furoate 400mcg/day (50mcg/puff) for the purpose of this study to avoid heterogeneity.

Corticosteroids exert their therapeutic impact by effectively suppressing various stages of the inflammatory process and modulation of cytokines that play key roles in allergic inflammation, thereby reducing nasal blockage, rhinorrhea, sneezing and nasal itching. Nasal steroids have a direct effect on the nasal mucosa along with systemic absorption due to vascularity of nasal mucosa as well as gastrointestinal mucosa [12,13]. However, the bioavailability of commonly used nasal steroids viz. mometasone, fluticasone and budesonide are <1% thus, nasal steroids never attain serum level enough to have systemic side effects comparable to oral and parenteral steroids [12,14].

The intraocular pressure (IOP) in the eye depends on the balance between the production of aqueous humor in the ciliary process and its drainage through the trabecular meshwork to episcleral veins. In 1953, Gordon et al. for the first time found a link between systemic cortisone administration and increased IOP in patients treated for anterior uveitis [15]. However, the mechanism by which corticosteroid increases IOP is still a matter of debate [16]. Several possible explanations include- increased aqueous humor production due to altered electrolyte secretion, changes in outflow dynamics through the trabecular meshwork, and reduced drainage of aqueous humor from the eye which collectively contribute to elevated IOP, a significant risk factor for glaucoma onset and progression [9,17].

Steroid type, dose, duration, delivery method, individual susceptibility, genetics, and underlying ocular conditions might influence change in IOP of a patient [18]. Patients with risk factors like primary open-angle glaucoma, diabetes, high myopia, and connective tissue disorders, as well as those with affected first-degree relatives, are more prone to steroid-induced IOP elevation [19]. Despite low bioavailability of nasal steroids, potential ophthalmic side effects, including raised IOP, and exacerbation of existing ophthalmic conditions like glaucoma should be expected and examined [7].

To our knowledge, literature lacks the effect of INC use on IOP in Nepal. We included 48 patients with allergic rhinitis and chronic rhinosinusitis who met our inclusion criteria with normal IOP findings before the administration of nasal steroid. There has not been concrete evidence on the effect of INC in IOP in terms of duration of use. While our study assessed its effect at 6 weeks, there are studies which have followed up cases with INC ranging from 3 months [16] to 1 year [20]. On comparing IOP before administration and after 6 weeks of administration of INC, a substantial proportion (95.8%) displayed no significant changes in their baseline IOP measurements. We observed only two cases (4.2%) with abnormal IOP elevation (≥ 21 mmHg). The elevated IOP returned to baseline after discontinuing the steroids. These two cases didn't have family history of glaucoma. There was slight difference in mean baseline IOP and mean IOP after 6 weeks of administration, -0.5 on right eye and -0.12 on left eye. However, the difference was not statistically significant.

Several studies across diverse populations have established connection between intranasal steroid usage and temporary elevation of intraocular pressure (IOP) while majorities of findings from meta-analysis and systemic review have demonstrated no significant association between rise in IOP and use of INC.

The earliest report on IOP and inhaled steroids was published by Dreyer. [21] He reported inhaled beclomethasone dipropionate was linked to glaucoma in three patients. Additionally, Opatowsky et al. [8] reported two cases of elevated IOP upon administration of intranasal beclomethasone dipropionate.

Furthermore, Garbe et al. [20] reported the increased risk for ocular hypertension or open-angle glaucoma only among the patients receiving high doses of inhaled steroid for 3 or more months with an odds ratio of 1.44 while comparing with non-users. Thus, this study warrants intraocular pressure monitoring of open-angle glaucoma while prescribing high dose inhaled steroids for longer period.

Nevertheless, no heightened risk of ocular hypertension or open-angle glaucoma was observed following the high-dose utilization of nasal steroids. This observation implies that nasal steroids are administered in significantly lower doses, which may be inadequate to induce alterations in intraocular pressure (IOP).

Bui et al. [6] found that discontinuing nasal steroids potentially reduces IOP and proposed that nasal steroids could contribute to IOP elevation. They observed a mean IOP increase of 2.6 mmHg during steroid treatment. These findings emphasize the

possibility of the impact of intranasal corticosteroids on intraocular pressure (IOP).

A more recent cross-sectional study by Mohd Zain et al. [5] documented a slightly elevated IOP in patients with allergic rhinitis undergoing chronic treatment with intranasal glucocorticoids. However, the observed IOP difference was minimal (1.30 mmHg) and within the normal range. Man et al. [22] on the other hand, conducted a similar study where patients used fluticasone propionate for six weeks postoperatively, observing no elevation of IOP. Similarly, a placebo-controlled study involving non-glaucoma patients with seasonal allergic rhinitis taking nasal fluticasone for a year also indicated no increased risk of glaucoma.

A Randomized Control Trial (RCT) conducted by Bross-Sariano et al. [16] revealed slight rise in IOP on mometasone intranasal spray administered group (right eye P value 0.092 and left eye P value 0.117) while comparing placebo administered group and mometasone intranasal steroid spray administered group after 1-year follow-up. However, the finding was not statistically significant. Another RCT conducted by Yuen et al. [13] also observed statistically insignificant results when comparing the alteration in intraocular pressure (IOP) between patients with ocular hypertension/controlled glaucoma who received either a placebo or intranasal beclomethasone spray for a duration of 6 weeks.

A meta-analysis and systematic review conducted by Vinokurtseva et al. [23] evaluating 65 studies revealed that there was no statistically significant elevated IOP in participants who used INCs, and inhaled corticosteroids compared to control over 45,457 person-years of follow-up. Overall, the studies included in the meta-analysis suggested that the use of intranasal and inhaled corticosteroid does not lead to an increase in the incidence of ocular hypertension and glaucoma.

A similar systematic review and meta-analysis conducted by Ahmadi et al. [24] showed that there was no increase in IOP or development of glaucoma in 4376 patients included in 10 RCTs, exposed to a range of intranasal steroids from 2-104 weeks, between controls and INCs users. Thus, the study concluded that there is a low risk of rise in IOP by use of INCs in the management of upper airway inflammatory diseases.

Findings from our study are consistent with the evidence from the studies demonstrating no association between use of INC and rise in IOP. Strong association shown in some studies can be attributed to the use of older generation steroids, which have higher bioavailability and systemic effects. Although there are consistent evidence suggesting a lack of robust association between an increase in IOP and the use of INC, it is important to acknowledge the occurrence of IOP elevation in a small subset of individuals. Consequently, there is a compelling need for more extensive studies involving a larger sample size and randomized controlled trials to provide a more conclusive understanding.

While our study offers valuable insights into the correlation between intranasal steroids and IOP elevation in the Nepalese population, it's important to acknowledge certain limitations. The relatively small sample size and single hospital-based study could impact the generalizability of our findings. Our study also lacks assessing optic disc finding to evaluate glaucomatous disc changes. Additionally, we relied on the patients' verbal confirmation of the compliance to the medical therapy, lacking objective documentation of the adherence to the therapy.

Conclusions

Our study suggests that intranasal steroids have a low risk of causing ocular hypertension or glaucoma in the Nepalese population. However, some cases may develop elevated IOP after using intranasal steroids and should be screened for glaucoma. Patients with pre-existing ocular hypertension or glaucoma should be monitored more frequently when using intranasal steroids. The observed reversible IOP elevation emphasizes the importance of monitoring and timely intervention. Further studies with larger cohorts and extended follow-up durations are essential to comprehensively understand the relationship and guide clinical practices.

Abbreviations

INC: Intranasal corticosteroid; IOP: Intraocular pressure; CRS: Chronic Rhinosinusitis; RCT: Randomized Control Trial; TUTH: Tribhuvan University Teaching Hospital.

Acknowledgments

None.

Funding

Not applicable.

Authorship contribution

Conceptualization: BG, SB, SMB, PG, UG, RG; Data Curation: BG, SB, RG, ST, NMT, BP; Methodology: BG, PG, UG; Formal analysis: BG, ST; Writing-original draft: BG, SMB, SB, RG; Review and editing: BG, SMB, PG, UG.

Ethics approval and consent to participate

Verbal consent was obtained from participants, and approval was received from the Institutional Review Committee (IRC) prior to the commencement of the study. Consent documentation can be provided on request.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that they have no competing interests.

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