

Long term use of inhaled steroids as a risk factor for ocular hypertension and glaucoma – a study in a tertiary care unit

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Abstract

Introduction: Compared to systemic steroids, inhaled steroids are much better in view of adverse reactions because of less systemic absorption. However there are indication to show that the use of inhaled steroids is a possible risk factor for ocular hypertension and glaucoma.

Materials and Methods: A total number of 100 subjects over the age of 50 years, suffering from Asthma and Chronic Obstructive Pulmonary Disease, who were prescribed inhaled steroids for the first time, were included into the study. Intra Ocular Pressure (IOP) was measured for the patients at 3, 6, and 12 month follow up.

Results: At the end of the year, the number of patients who were positive for IOP was 5. There was a significant increase of the intraocular pressure during the follow ups at 3, 6 and 12 months among the patients. The intraocular pressure significantly increased in patients with a very high dosage of over 1000 units of inhaled steroids after 1 year.

Conclusion: Prolonged administration of inhaled steroids for control of asthma can cause ocular hypertension. However, high doses of inhaled corticosteroids should be used with caution

Keywords: Glaucoma, Inhaled corticosteroid, Intra ocular hypertension

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Introduction

Glaucoma is one of the major causes of blindness and stands second only to cataract. Population surveys indicate that less than 50% of the patients with glaucomatous visual field loss had adequate diagnosis and treatment¹.

Ocular hypertension is the main risk factor for the development of primary open angle glaucoma [POAG] - the higher the pressure, the greater the risk². While the risk of glaucoma is substantial for persons with IOPs in the higher twenties, data from all studies demonstrate that risk of glaucoma increases steadily with increasing IOP, starting even with IOPs as low as 12 mm of Hg³.

In steroid glaucoma, the IOP is elevated primarily due to increased outflow resistance. Increased responsiveness to steroids may be facilitated by up regulation of glucocorticoid receptors on trabecular meshwork cells⁴. In cultured human trabecular meshwork cells, glucocorticoids increased the expression of the extracellular matrix protein fibronectin, glycosaminoglycan's, and elastin^{5,6}. Steroids also suppress phagocytic activity which may lead to observations such as increased deposition of

material in the juxtacanalicular meshwork of eyes with steroid induced glaucoma^{7,8}.

Corticosteroids are the most effective anti-inflammatory drugs in the treatment of asthma with very well-known mechanisms of effect. Both systemic and inhaled corticosteroids are used in treatment of acute and chronic asthma.

Recently inhaled steroids are being preferred for treatment of acute exacerbations of asthma as well as for long term control of asthma, wherein long term use of steroids is indicated.

Compared to systemic steroids, inhaled steroids are much better in view of adverse reactions because of less systemic absorption except in very high doses. The preference for inhaled steroids is also because of their direct access to bronchi. Although only 30-40% of drug will reach the bronchi when inhaled medication is used, it is that fraction of drug important for the treatment response with minimum adverse reactions.

It is generally known that inhaled steroids do not have the same ocular side effects as topical and oral steroids. On the other hand some studies indicate that the use of inhaled steroids is a possible risk factor for ocular hypertension and glaucoma⁹.

Very few studies have been done earlier to indicate the long term use of inhaled steroids as a risk factor for ocular hypertension and glaucoma. Hence, this study was conducted to evaluate the incidence of intraocular hypertension in patients above the age of 50 years on inhaled steroid use.

Materials and Methods

This prospective observational study was conducted by the department of Ophthalmology at Viswabharathi Medical College during the period Two years. A total number of 100 subjects over the age of 50 years, suffering from Asthma and Chronic Obstructive Pulmonary Disease, who were prescribed inhaled steroids for the first time were selected. Patients were known cases of glaucoma, those already on inhaled steroids or systemic steroids or those patients who were using topical steroids for other ophthalmic disorders were excluded from the study. Patients who were unwilling to take part in the study were also excluded.

After attaining the ethical committee clearance, all the patients and the relatives were given a detailed description of the procedure and informed consent was taken. Those who refused to give the consent were excluded from the study.

Detailed history of the disease, familial history of glaucoma was taken from the patient. Complete physical examination was done for all the patients and they were all subjected to ophthalmic examination at the beginning and at the end of 1st, 2nd and 3rd months. At every visit Intra Ocular Pressure (IOP) was measured with Goldman Applanation Tonometer (GAT) and optic disc evaluated by direct ophthalmoscopy.

At the end of the 3 months, the patients were further subjected to slit lamp examination, gonioscopy, visual field examination on Humphrey’s field analyser and direct ophthalmoscopic examination and advised to

come again in the 6th month and after 1 year at which time the visual fields were evaluated.

Results

Out of the 100 patients selected for the study, 91, 78 and 63 patients came for the follow up at the end of 3 months, 6 months and 1 year. Intraocular pressure >21 mm of Hg is taken as cut off value for the diagnosis of ocular hypertension and considered to be a positive case in this study.

At the end of the year, the number of patients who were positive for IOP was 5 (5% of the total and 7.9% among the people who came in for follow up after 1 year). 4 out of 78 patients who came after 6 months had positive (Table 1).

Table 1: Number of IOP positive cases during follow up

	3 Months	6 Months	1 Year
Total No. of Subjects	91	78	63
Positive Cases	3	4	5
Incidence of Ocular HTN	3.3%	5.1%	7.9%

There was a significant increase of the intraocular pressure during the follow ups at 3, 6 and 12 months among the patients (Table 2).

Table 2: IOP in the eyes at base line and final at the follow ups

Time	Baseline IOP (Right Eye)	Final IOP (Right Eye)	Baseline IOP (Left Eye)	Final IOP (Left Eye)
3 months	12.8±1.78	15.18±2.65*	12.82±1.77	15.18±2.65*
6 months	12.86±1.78	15.12±2.77*	12.86±1.77	15.12±2.77*
12 months	12.79±1.80	16.23±3.24*	12.80±1.8	16.23±3.24*

*p value < 0.0001

The intraocular pressure significantly increased in patients with a very high dosage of over 1000 units of inhaled steroids after 1 year. Though there was a slight increase in the lower dosages between the first and final follow up, this increase was not significant (Table 3).

Table 3: IOP in the eyes at base line and final at the follow ups after 1 year

Dosage	Baseline IOP (Right Eye)	Final IOP (Right Eye)	Baseline IOP (Left Eye)	Final IOP (Left Eye)
< 500	13.41±1.70	15.53±2.29	13.06±2.01	15.53±1.94
500 - 1000	12.53±1.68	14.70±2.037	12.85±1.63	15.1 ±2.40
> 1000	14.8±1.79	20.4±5.18*	14.8±2.28	22±4.70*

*p value < 0.0001

It is observed that positive family history of glaucoma played an important role in the development of raised IOP after steroid treatment. In this study 3 out of 5 positive subjects had positive family history. All the subjects with positive family history have developed ocular hypertension in early part of study period.

Discussion

Intranasal steroids are used to effectively treat patients with asthma and COPD. Absorption from nasal and gastrointestinal mucosa are the ways that intranasal steroids can enter the blood stream. Direct pass occurs via nasal mucosa without first-pass metabolism, so this can excessively injure the end organs. On the other hand, steroids absorbed from the gastrointestinal system undergo degradation in the liver, so less active metabolites can reach the end organs¹⁰. It has been reported that the amount of steroids absorbed from the nasal passages is minimal in comparison to the amount of steroids absorbed from the gastrointestinal tract¹¹.

A rise in intraocular pressure (IOP) can occur as an adverse effect of corticosteroid therapy. If the ocular hypertensive effect is of sufficient magnitude, for an adequate duration, damage to the optic nerve (steroid-induced glaucoma) may ensue¹². A corticosteroid-induced IOP rise has been shown to occur with various methods of steroid administration (see *Methods of administration*, below), but is most commonly identified as a complication of topical corticosteroid application with drugs such as dexamethasone or prednisolone. In responsive patients, the IOP typically rises after several weeks of continual corticosteroid therapy and returns to normal following cessation of such therapy¹³.

In our study we followed up patients for 12 months. The incidence of ocular hypertension at the end of 3 months was 3.3%, at the end of 6 months, 5.1% and at the end of one year it was 7.9%. The incidence of ocular hypertension is doubled at the end of 1 year when compared to incidence at 3 months of therapy. We found that the longer the duration of corticosteroids, greater the risk.

The present study was in accordance to another study by Suzana et al in 2003 at Croatia showing ocular hypertension incidence at 13.4% over 4 year period¹⁴. In a cross sectional study by Mitchell P et al an incidence of 7.4% was reported¹⁵. In a case controlled study by Garbe et al it was concluded that small but increased risk of ocular hypertension on long term inhaled steroid therapy.

High doses of inhaled steroids prescribed regularly for 3 or more months were at an increased risk with an OR of 1.44 (95% confidence interval, 1.01-2.06)⁹.

It has been reported in the literature that these ocular adverse effects may be the result of systemic absorption of corticosteroids and also of poor inhalation techniques, which can lead to direct penetration of corticosteroids into the eye, which possibly occurred in our patients.

At the end of 3 months, three subjects who developed ocular hypertension, the inhaled steroid dosage was reduced. In spite of this, they had persistent ocular hypertension and were put on ocular hypotensive medication to prevent progression to glaucoma.

Correlation was also found between the use of inhaled corticosteroids and the occurrence of elevated IOP in subjects with a positive family history of glaucoma, which was also found in other population studies.

In our study 3 patients had a positive family history of glaucoma. The other 2 patients did not mention any positive family history of glaucoma. These subjects might not be aware of the disease in their families.

Conclusion

Prolonged administration of inhaled steroids for control of asthma can cause ocular hypertension. However, high doses of inhaled corticosteroids should be used with caution in individuals with a positive family history of glaucoma. Frequent ophthalmologist consultation is required because of the increased risk of the development of glaucoma.

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