

**“Incidence of Ocular Hypertension In Patients (Above 50 Years) on Inhaled Corticosteroid Use”**

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**Abstract:** Objective: To study the incidence of Ocular hypertension in patients above the age of 50 years using inhaled corticosteroids for the first time.

Materials and methods: This study was a prospective observational study. A total number of 100 subjects above 50 years age, who were prescribed inhaled corticosteroids for the first time in the Department of pulmonology for various conditions such as chronic obstructive pulmonary disease [COPD], Asthma and COPD overlap, Interstitial lung disease and Asthma (late onset) were included in the study. Patients were evaluated by taking history and by ophthalmic examination performed at the beginning and again at 1, 3 and 6 months. At every visit IOP was measured at same time of the day using Goldman Applanation Tonometer (GAT) to avoid diurnal variation. In every visit all the patients were subjected to slit lamp examination, gonioscopy, visual field examination on Humphrey's field analyzer and direct ophthalmoscopic examination.Paired t test was used to find relation between attributes. P value <0.05 will be considered statistically significant.

Results: In the present study out of 100 patients, total number of positive subjects at the end of 1 month is - 0 subjects ( 0% incidence), at the end of 3 months there are 7 positive subjects (7% incidence), overall total number of positive subjects at end of this study period of 6 months was 8 subjects ( 8% incidence).we have studied the change in IOP with usage of different dosages inhaled corticosteroids, among all the positive cases used hight to very high doses of inhaled corticosteroids. Results show a statistically significant increase in IOP with increase in duration and dosage of inhaled corticosteroids (P=0.00)

Conclusion: High doses of inhaled corticosteroids increases the risk of ocular hypertension. Higher the dose, greater the risk. Higher the duration of inhaled corticosteroid usage, greater the risk.

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I.  Introduction

Glaucoma is a chronic, progressive optic neuropathy caused by a group of ocular conditions which lead to damage to the optic nerve with loss of visual function. The most common risk factor being raised intraocular pressure (IOP).¹ This is one of the major causes of irreversible blindness in the world 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 treatment. Open angle glaucoma is a chronic progressive optic neuropathy characterized by intraocular pressure (IOP) exceeding 21mmHg without tretment (daily pressure curve), characteristic appearance of optic nerve head (cup disc ratio), visual field defects and open angles determined by gonioscopy.² Ocular hypertension is the main risk factor for the development of primary open angle glaucoma, the higher the pressure, the greater the risk.² In Ocular hypertension trestment study, the rate of developing either disc or field loss was about 10% at 5 years, similar to the incidence from population based studies.³ New evidence in the recent randomised studies is that IOP lowering decreased the incidence and progression of glaucoma compared to no treatment.³

Asthma is a complex syndrome characterized by airway hyper-responsiveness caused by a multicellular inflammatory reaction that leads to airway obstruction. Recent guidelines in the management of obstructive airway diseases advocate the early use of oral and inhaled steroids. With this current trend of extensive use of steroids, its side effects can extend to several systems of the human body and donot spare the eye either. It has been found that 4% to 6% of the population are steroid responders when on topical and systemic steroids. They are defined as those who develop IOP rise of greater than 15mmHg or with IOP greater than 31mmhg after daily topical corticosteroids us for 4-5 weeks

Many theories have been postulated on the mechanism of action of steroids in raising the intraocular pressure. Corticosteroids stabilize the lysosomal membrane, which contain hyaluronidase that depolymerizes hyaluronate. This may lead to an accumulation of polymerized glycosaminoglycans, in the trabecular...
meshwork. These polymerized glycosaminoglycans when hydrated cause an increase in the resistance to aqueous outflow. Corticosteroids have also been found to alter the trabecular meshwork genes myocilin (MYOC) and optineurin (OPTN) which in turn causes changes in the extracellular matrix. This can also cause an increased resistance to the aqueous outflow. Steroids also reduce the phagocytic action of the endothelial cells. Awareness, early diagnosis and timely treatment are required to prevent this irreversible visual loss. It is well documented that steroids can cause a raise in intraocular pressure. The modes of steroid administration most commonly studied have been oral, topical and periocular. But other modes like inhalation have been less explored. With the current trend of early usage of inhaled steroids in the management of respiratory conditions, its adverse effects are bound to rise. Inhaled steroids can be absorbed from the nasal mucosa and lungs. This bypasses the degradation by the liver by 1st pass metabolism and in turn exposes the body to longer duration of steroid action. Hence this study is aimed at finding if inhaled steroids have an effect on intraocular pressure.

II. Material And Methods

This was a prospective observational study conducted in patients, who were prescribed inhaled corticosteroids for the first time for various conditions such as chronic obstructive pulmonary disease [COPD], Asthma and COPD overlap, Interstitial lung disease and Asthma (late onset) were included in the study. All the subjects were enrolled from Department of Pulmonology, at Alluri Sitarama Raju Academy of Medical Sciences, Eluru. A total number of 100 subjects above 50 years age were included in the study.

Study Design: Prospective observational study

Study Location: This was conducted at Alluri Sitaramaraju Academy of medical Sciences, Eluru, Andhra Pradesh, a tertiary care teaching hospital

Study Duration: December 2016 to July 2018

Sample size: 100 patients.

Inclusion criteria:
1. Subjects above the age of 50 years
2. COPD, Asthma and COPD overlap, Interstitial lung disease and Asthma (late onset) patients
3. Using inhaled corticosteroids for the first time

Exclusion criteria:
1. Subjects who are already on inhaled corticosteroids
2. Subjects on systemic steroids
3. Patients using topical steroids for any ophthalmic disorders
4. Known case of glaucoma
5. Patients with family history of glaucoma
6. Corneal disorders which can affect Applanation Tonometry reading.
7. Uncooperative subjects

Procedure methodology
Institutional review board clearance (ethical committee) was obtained and informed consent was taken from all the subjects.

Brief description of the procedure was given to the patients as study informed sheets. Family history of glaucoma was obtained by asking the patients whether they had any first degree relatives with glaucoma, to exclude these patients from the study. Personal history of any smoking and alcohol intake was taken.

Patients were evaluated by taking history and by ophthalmic examination performed at the beginning and again at 1, 3 and 6 months. At every visit IOP was measured at same time of the day using Goldman Applanation Tonometer (GAT) to avoid diurnal variation.

In every visit all the patients were subjected to slit lamp examination, gonioscopy, visual field examination on Humphrey’s field analyzer and direct ophthalmoscopic examination at Alluri Sitarama Raju Academy of Medical Sciences, Eluru. The observations were noted in subjects who were continuing use of inhaled steroids for their persistent COPD, Asthma and COPD overlap, Interstitial lung disease and asthma (late onset) came for further follow ups. Every visit their IOP was measured. Optic disc evaluation was done clinically by a single person using direct ophthalmoscopy and by using green filter in slitlamp biomicroscopy. Visual fields examination was done at every visit and observations were noted.
III. Intraocular Pressure

Procedure was explained in detail to patient. Topical anaesthetic and fluorescein was instilled. The tonometer prism is maximally illuminated by cobalt light and the slit lamp is turned to 60°. Patient was aligned on the slit lamp. The probe was advanced and the tip must touch the central cornea gently while looking through the slit lamp eyepiece just prior to the tip making contact. Semi-circular mires are then observed through the eye piece, monocular through left eyepiece. The knob of the tonometer was adjusted so that inner margins of both the semi-circular mires meet and start pulsating. This is the end point where the reading is taken.

Adequate thickness of the circles is very important as thicker or thinner circle may lead to falsely high or low readings. The number in the dial was multiplied by 10 to get IOP in mm of Hg. When checking IOP, measurements for both eyes, the method used (Goldmann applanation tonometry is considered the standard), and the time of the measurement is to be recorded. A difference between contralateral eyes of 3 mm Hg or more indicates greater suspicion of glaucoma. In most circumstances, the measurements should be repeated on at least two to three occasions before deciding on a treatment plan. The measurement should be made at different times of the day to check for diurnal variation. A diurnal variation of 8 mm Hg or more indicates an increased risk for glaucoma whereas 2 to 4 mm is the normal variation.

Sources of Error:
1. Errors due to Improper Technique.
2. Corneal Astigmatism = 1 mm Hg error for every 4 D astigmatism.
3. Take average of two readings and then align the tonometer with the axis
4. State of Corneal Hydration: Edematous thick corneas underestimates IOP
5. Central Corneal Thickness–The impact of central corneal thickness (CCT) on applanation tonometry was first discussed by Goldmann. Ocular hypertension treatment study (OHTS) group published report that CCT was an important independent risk factor for progression from ocular hypertension to early glaucoma. Thin corneas lead to an underestimation, Thick corneas lead to an overestimation. If 550 microns is taken as normal corneal thickness, for every 70 microns difference IOP is adjusted by 5 mm Hg.
6. Refractive Surgery, Calibration Errors, Errors due to repeated measurements, intra observer and inter observer variability.
7. Too much dye overestimates IOP, Too little dye underestimates IOP.

Statistical Analysis
- Descriptive statistics of attributes were analyzed
- Paired t-test was used to find relation between attributes. P value < 0.05 will be considered statistically significant.
- SPSS software used.

IV. Result

This study included a total number of 100 subjects who were prescribed inhaled corticosteroids for the first time in the department of pulmonology for various conditions like Chronic obstructive pulmonary disease [COPD], Asthma and COPD overlap, Asthma (late onset), Interstitial lung disease. All the subjects were above 50 years age group.

Results were analyzed at baseline and at the end of 1 month, 3 months and 6 months. Patients who came for all the three follow ups were included in the study.

Intraocular pressure >21 mmHg is taken as cut off value for the diagnosis of ocular hypertension and considered to be positive cases in this study.

<table>
<thead>
<tr>
<th>Table 1: Frequency of age</th>
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<tbody>
<tr>
<td>AGE</td>
</tr>
<tr>
<td>50-55 years</td>
</tr>
<tr>
<td>55-60 years</td>
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<tr>
<td>&gt;60 years</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Frequency distribution of various clinical conditions included from pulmonology department</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIAGNOSIS</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease [COPD]</td>
</tr>
<tr>
<td>Asthma and COPD overlap</td>
</tr>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
</tr>
</tbody>
</table>
In the present study out of 100 patients, total number of positive subjects at the end of 1 month is - 0 subjects (0% incidence), at the end of 3 months there are 7 positive subjects (7% incidence), overall total number of positive subjects at end of this study period of 6 months was 8 subjects (8% incidence).

In the present study, the change of IOP after inhaled steroid therapy with different dosages from low dose to very high dose was studied. Out of 8 total positive cases, 6 cases had used only very high doses of corticosteroids (>1000 mcg) whereas other 2 cases had used high doses of corticosteroids (>750 mcg) irrespective of steroid type.

Notably none of these subjects had either optic disc changes or visual field defects.

### Table 4: Age distribution and change in IOP in both RE and LE

<table>
<thead>
<tr>
<th>AGE</th>
<th>RIGHT EYE</th>
<th></th>
<th>P VALUE</th>
<th>LEFT EYE</th>
<th></th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN BASELINE IOP</td>
<td>FINAL BASELINE IOP</td>
<td></td>
<td>MEAN BASELINE IOP</td>
<td>FINAL BASELINE IOP</td>
<td></td>
</tr>
<tr>
<td>50-55 years</td>
<td>12.82 ± 1.57</td>
<td>15.64 ± 2.70</td>
<td>0.00</td>
<td>12.77 ± 1.74</td>
<td>15.77 ± 2.70</td>
<td>0.000</td>
</tr>
<tr>
<td>55-60 years</td>
<td>12.53 ± 1.78</td>
<td>15.79 ± 2.07</td>
<td>0.00</td>
<td>12.74 ± 1.77</td>
<td>15.26 ± 2.05</td>
<td>0.000</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>13.56 ± 2.01</td>
<td>18.78 ± 4.45</td>
<td>0.00</td>
<td>14.22 ± 1.52</td>
<td>18.56 ± 4.94</td>
<td>0.000</td>
</tr>
</tbody>
</table>

In right eye, age between 50 - 55, 55 - 60, 60 - 65 years, the mean baseline IOP was 12.82 ± 1.57, 12.53 ± 1.78, 13.56 ± 2.01 and mean final IOP was 15.64 ± 2.70, 15.79 ± 2.07, 18.78 ± 4.45 respectively. It shows a significant difference between baseline and final IOP with increase in age of the patient. (P = 0.00)

In left eye, age between 50 - 55, 55 - 60, 60 - 65 years, mean baseline IOP was 12.77 ± 1.74, 12.74 ± 1.77, 14.22 ± 1.52 and mean final IOP was 15.77 ± 2.70, 15.26 ± 2.05, 18.56 ± 4.94 respectively. It shows a significant difference between mean baseline IOP and mean final IOP with increase in age of the patient. (P = 0.000)

**FIGURE 1:** Age distribution and change in IOP RE

**FIGURE 2:** Age distribution and change in IOP LE
Table 5: Influence of duration of steroid usage on change of IOP in both RE and LE

<table>
<thead>
<tr>
<th>Duration</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN BASELINE IOP</td>
<td>MEAN FINAL IOP</td>
</tr>
<tr>
<td>1MONTH</td>
<td>12.848 ± 1.763</td>
<td>15.010 ± 2.256</td>
</tr>
<tr>
<td>3MONTHS</td>
<td>12.848 ± 1.763</td>
<td>15.353 ± 2.897</td>
</tr>
<tr>
<td>6MONTHS</td>
<td>12.848 ± 1.763</td>
<td>16.282 ± 3.103</td>
</tr>
</tbody>
</table>

Table 5 represents in right eye the mean of baseline IOP at 1, 3 and 6 months was 12.848 ± 1.763 and mean of final IOP in right eye at 1, 3 and 6 months was 15.010 ± 2.256, 15.353 ± 2.897, 16.282 ± 3.103 respectively. It shows a significant rise in IOP with increase in duration of corticosteroid usage. (P = 0.000)

In left eye, the mean of baseline IOP in 1, 3 and 6 months was 13.02 ± 1.786 and mean final IOP in at 1, 3 and 6 months was 15.32 ± 2.382, 15.76 ± 2.930, 16.08 ± 3.215 respectively. With increase in duration of steroid usage there was significant rise in baseline and final IOP. (P = 0.000).

Table 6: Influence of steroid dosage on change of IOP in both RE and LE

<table>
<thead>
<tr>
<th>DOSAGE</th>
<th>RIGHT EYE</th>
<th>LEFT EYE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN BASELINE IOP</td>
<td>MEAN FINAL IOP</td>
</tr>
<tr>
<td>&lt;500mcg</td>
<td>12.87 ± 1.69</td>
<td>15.62 ± 1.92</td>
</tr>
<tr>
<td>500-1000mcg</td>
<td>12.5 ± 1.68</td>
<td>15.86 ± 2.67</td>
</tr>
<tr>
<td>&gt;1000mcg</td>
<td>14.4 ± 1.77</td>
<td>22.25 ± 4.71</td>
</tr>
</tbody>
</table>

Table 6. In right eye steroid dosage < 500, 500 - 1000, > 1000mcg mean baseline IOP was 12.87 ± 1.69, 12.5 ± 1.68, 14.4 ± 1.77 and mean final IOP was 15.62 ± 1.92, 15.86 ± 2.67, 22.25 ± 4.71 respectively. (P value = 0.00)

In left eye with steroid dosage < 500, 500 - 1000, > 1000mcg mean baseline IOP was 12.92 ± 1.84, 12.86 ± 1.58, 14.5 ± 2.07 and mean final IOP was 15.0 ± 1.70, 16.09 ± 2.58, 22.5 ± 5.52 respectively. It shows significant rise in IOP with increase in dosage of steroids. (P = 0.00)
“Incidence Of Ocular Hypertension In Patients (Above 50 Years) On Inhaled Corticosteroid Use”

![FIGURE 5: Influence of Steroid dosage on change of IOP RE](image1)

![FIGURE 6: Influence of Steroid dosage on change of IOP LE](image2)

Visual Field Interpretation

| DURATION | RIGHT EYE | | | LEFT EYE | | |
|----------|-----------|----------------------|----------------------|----------------------|----------------------|
|          | MEAN BASELINE MD | MEAN FINAL MD | P VALUE | MEAN BASELINE MD | MEAN FINAL MD | P VALUE |
| 1MOONTH  | -0.6 ± 0.98 | -0.4 ± 0.93 | 0.791 | 0.1 ± 0.98 | 0.11 ± 0.96 | 0.889 |
| 3MONTHS  | -0.6 ± 0.98 | 0.13 ± 1.02 | 0.115 | 0.1 ± 0.98 | 0.19 ± 1.01 | 0.424 |
| 6MONTHS  | -0.6 ± 0.98 | 0.11 ± 1.11 | 0.21 | 0.1 ± 0.98 | 0.24 ± 1.08 | 0.242 |

Table 7. In right eye, the mean of baseline mean deviation at 1, 3 and 6 months was -0.6 ± 0.98 and mean of final mean deviation at 1, 3 and 6 months was -0.4 ± 0.93, 0.13 ± 1.02, 0.11 ± 1.11 respectively. P value at 1, 3 and 6 months was 0.791, 0.115 and 0.21 respectively. P value is not < 0.5%, which shows that P value is not significant.

In left eye, the mean baseline mean deviation in LE at 1, 3 and 6 months was 0.1 ± 0.98 and mean final mean deviation at 1, 3 and 6 months was 0.11 ± 0.96, 0.19 ± 1.01, 0.24 ± 1.08 respectively. P value at 1, 3 and 6 months was 0.889, 0.424, 0.242 respectively. P is not < 0.5%, which shows that P value is not significant.

![FIGURE 7: Mean deviation RE](image3)
**Incidence Of Ocular Hypertension In Patients (Above 50 Years) On Inhaled Corticosteroid Use**

![Figure 8: Mean deviation LE](image1)

Table 8: Pattern standard deviation (PSD) RE and LE

<table>
<thead>
<tr>
<th>DURATION</th>
<th>RIGHT EYE</th>
<th>LEFT EYE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN BASELINE PSD</td>
<td>MEAN FINAL PSD</td>
</tr>
<tr>
<td>1MONTH</td>
<td>2.71 ± 1.9</td>
<td>2.69 ± 1.91</td>
</tr>
<tr>
<td>3MONTHS</td>
<td>2.71 ± 1.9</td>
<td>2.78 ± 1.92</td>
</tr>
<tr>
<td>6MONTHS</td>
<td>2.71 ± 1.9</td>
<td>2.75 ± 1.93</td>
</tr>
</tbody>
</table>

Table 8 in right eye, the mean baseline pattern standard deviation in RE at 1, 3 and 6 months was 2.71 ± 1.9 and mean final pattern standard deviation at 1, 3 and 6 months was 2.69 ± 1.91, 2.78 ± 1.92, 2.75 ± 1.93 respectively. P value at 1, 3 and 6 months was 0.942, 0.798, 0.887 respectively. P value was >0.5%, which shows that P value is not significant.

In left eye, mean baseline pattern standard deviation at 1, 3 and 6 months was 2.65 ± 1.86 and mean final pattern standard deviation at 1, 3 and 6 months was 2.81 ± 1.9, 2.74 ±1.86, 2.8 ± 1.88 respectively. P value at 1, 3 and 6 months was 0.568, 0.73, 0.577 respectively. P value is >0.5%, which shows that P value was not significant.

**FIGURE 9: Pattern standard deviation (PSD) RE**

![Figure 9](image2)

**FIGURE 10: Pattern standard deviation (PSD) LE**

![Figure 10](image3)
V. Discussion

Glaucoma, is the second leading cause of blindness; worldwide about 66.8 million people were suffering from visual impairment from glaucoma and 6.8 million suffering from blindness. Ocular hypertension is the main risk factor for the development of primary open angle glaucoma [POAG] - the higher the pressure, the greater the risk.

Bronchial asthma is a chronic inflammatory disease of the respiratory pathways. Both inhaled and systemic corticosteroids are used in treatment of asthma. Inhaled corticosteroids are the basic anti-inflammatory agents for asthma and their use has led to revolutionary changes in the treatment of chronic asthma. Studies have proved that patients with moderate to severe chronic obstructive pulmonary disease [COPD] also benefit from long term use of inhaled steroids.

The present study was in accordance to another study by Suzanaet al in 2003 at Croatia showing ocular hypertension incidence at 13.4% over 4 year period. In present study, incidence of ocular hypertension was 8% over a study period of 18 months from Dec 2016 to July 2018. Incidence of ocular hypertension at the end of 1.3 and 6 months was 0%, 7% and 8% respectively (table 3). The incidence of the present study is less when compared to the above study which can be explained by the shorter duration of follow ups. If the study period can be extended for more duration, there could be a rise in incidence rate.

Mitchell et al. performed a cross-sectional population based study in 3654 patients with Inhaled corticosteroids [ICS] aged 49–97 years. Open-angle glaucoma was diagnosed in 108 subjects, and elevated intraocular pressure was found in 160 subjects. In persons with a glaucoma family history, there was a strong association between inhaled corticosteroid use and presence of either glaucoma or elevated intraocular pressure (odds ratio [OR], 2.6; 95% confidence interval, 1.2–5.8). The risk increased with higher doses (OR, 6.3; 95% CI, 1.0–38.6) for persons who used more than four puffs per day. These findings were not explained by concurrent use of oral or ocular corticosteroids. In persons without a family history of glaucoma, no association was found between use of inhaled corticosteroids and glaucoma or elevated intraocular pressure. Hence they suggested that patients with a glaucoma family history who were on inhaled corticosteroids need frequent review by an ophthalmologist.

Garbe et al. in a case-control study (9793 cases and 38,325 controls) found a greater risk of glaucoma among patients who used high-dose inhaled corticosteroid (budesonide >1600μg/day) for longer than 3 months (OR: 1.44; 95% CI: 1.01–2.06). However, this study is limited by its design and the non-standardized diagnosis of glaucoma. Prolonged administration of high doses of inhaled glucocorticoids increases the risk of ocular hypertension or open-angle glaucoma. This finding suggests that in these patients intraocular pressure monitoring may be warranted.

The present study had excluded patients with history of glaucoma and positive family history of glaucoma. Since positive family history is a risk factor for primary open angle glaucoma (POAG) and ocular hypertension, the cause for increased intraocular pressure (IOP) could not be differentiated whether it was due to positive family history of glaucoma or due to the usage of inhaled corticosteroids. In other population studies association was found between the use of inhaled corticosteroids and the occurrence of elevated intraocular pressure in subjects with a positive family history of glaucoma. Some of these patients might not be aware of their disease in the family.

In present study, out of 8 patients with elevated intraocular pressure, 6 patients were on very high doses of inhaled corticosteroids (>1000 mcg), the other 2 were on high doses of inhaled corticosteroids (i.e. 500 - 1000 mcg). All these patients have negative history of glaucoma and negative family history of glaucoma. Maybe these patients might have family history of glaucoma which was unknown. Mean baseline IOP was compared to mean final IOP in 3 groups, which were categorized based on dosage of inhaled corticosteroids. The mean of final IOP showed a statistically significant increase with increase in dosage on inhaled corticosteroid usage.

According to Mitchell et al study, high doses of inhaled corticosteroids should be used with caution in individuals with a positive family history of glaucoma. Hence, they suggested these patients to have regular follow up for every 6 months.

Another study also suggested regular follow up for the patients on inhaled corticosteroids as they effect on IOP with duration and dosage of inhaled corticosteroid usage.

Opatsowskiet al. Three patients showed a possible ocular hypertensive response to beclomethasone dipropionate by nasal spray or inhalation. In two patients, the intraocular pressure returned to pre-treatment levels after discontinuing of nasal corticosteroid spray. One patient required medication to control intraocular pressure with continued inhaled corticosteroid. One patient later demonstrated an ocular hypertensive response to oral steroids.

Corticosteroids by nasal spray or inhalation may cause ocular hypertension in susceptible patients. The authors recommend surveillance of intraocular pressure in patients using these medications.
Gonzalez et al., in a study a total of 2291 cases were identified. For comparison, a total of 13,445 age-matched controls were selected. The mean age was (75±4.2 years). The adjusted rate ratio for glaucoma was 1.05 (95% CI 0.91-1.20) with inhaled corticosteroid use in the preceding 30 days. There was no dose-related effect of inhaled corticosteroids on the risk of glaucoma or raised intraocular pressure requiring treatment. Continuous use of high-dose inhaled corticosteroids for 3 or more months was not associated with an increased risk of glaucoma.

The present study showed statistically significant association between the use of inhaled corticosteroids and the occurrence of elevated intraocular pressure in elderly subjects, which was also found in other population studies. Table 1 represents the frequency distribution of age. Based on age, patients were categorized into 3 groups (50-55 years, 55-60 years, >60 years). Frequency distribution of age between these 3 groups were calculated as 54, 38 and 8 respectively. In present study most of the patients included were between 50-55 years of age. This also showed a significant increase in IOP with increase in duration and dosage of inhaled corticosteroids usage.

Moss EB et al. conducted a randomized, double-masked, placebo-controlled trial which included 22 adults with well-controlled open-angle glaucoma or ocular hypertension. Consenting participants were randomized to a 6-week course of twice-daily fluticasone propionate 250-500 μg metered-dose inhaler or saline placebo metered-dose inhaler. Biweekly clinic visits included masked Goldmann applanation tonometry and assessment to identify adverse effects. Primary outcome was mean intraocular pressure (IOP) at week 6. Secondary outcomes included IOP elevation of >20% at 2 consecutive visits, adherence, side effects, and logMAR visual acuity. A total of 10 patients in each arm completed the study. There were no statistically significant differences in IOP between groups at baseline (14.3±3.0 and 15.6±3.6 mm Hg in steroid and placebo groups, respectively, P=0.39) or at week 6 (14.7±2.4 and 14.8±3.8 mm Hg in steroid and placebo groups, respectively, P=0.92). Adherence was >80% for all participants. There were no statistically significant differences in IOP between groups at any secondary measures. One patient in the steroid group met the secondary end point of >20% elevation in IOP (IOP increased from baseline of 9 to 11 mm Hg at weeks 2 and 4). The limitation of this study was the IOP distribution in this small sample. With a greater-than-expected SD, the analysis was, in retrospect, underpowered to detect a difference of r3.2 mm Hg between groups.14

In the present study, with the increase in the duration of inhaled corticosteroid usage, the mean of final IOP showed a statistically significant increase when compared to the mean of baseline IOP in both eyes at 1, 3 and 6 months. Here glaucoma history and family history of glaucoma patients were excluded, since it may alter the accurate findings of IOP increase in patients using inhaled corticosteroids.

Samiyet et al. conducted a large prospective study to evaluate the risk of raised intraocular pressure in patients receiving inhaled corticosteroids. A total of 187 patients (99 men and 88 women) with no documented history of glaucoma who were about to begin inhaled steroid therapy for various pulmonary conditions were enrolled. Of the 187, 183 were followed at 12 weeks. No significant rise in intraocular pressure was observed. No patient had a rise in intraocular pressure greater than 4 mm Hg. However, six cases of increased intraocular pressure associated with combined nasal and inhaled steroid use in non-glaucomatous patients have been reported.15

Although isolated case reports indicate a definite risk of glaucoma in the presence of inhaled steroid therapy, the risk appears to be small.15

Similarly, a large case-control study in 1997, suggested that the presence of nasal steroid use in patients with newly diagnosed glaucoma or Ocular hypertension versus nonglaucomatous patients was not statistically significant (odds ratio, 1.02; 95% CI, 0.59-1.77). However, the number of patients taking continuous high-dose nasal steroids was too small for statistical analysis. In 1998, a small prospective study of 26 non-glaucomatous patients revealed no evidence of Ocular hypertension or cataracts after prolonged use of nasal steroids after endoscopic sinus surgery (mean follow-up, 8.8 ± 3.6 months; range, 3-19 months).

Kenan Dagdelen et al. in a study included 109 eyes from 62 POAG patients, 50 eyes from 30 OH patients, and 101 eyes from 53 healthy volunteers. Data gained by OCT were compared with perimetry indexes. ONH, RNFL and macula analysis were performed for all subjects. Rim area, disc area, average cup/disc (C/D) ratio, vertical C/D ratio, cup volume data were recorded during ONH analysis. Average RNFL thickness and the thickness of four quadrants (superior, inferior, nasal and temporal) was established in microns.

In total, nine macular quadrants involving the foveal region mentioned in the Early Treatment Diabetic Treatment Study (ETDRS) template were measured, and average macular thickness and macular volume data were recorded during macula analysis. Differences between groups were evaluated with the one-way ANOVA test. Tukey’s multiple comparison test was performed to detect difference between groups. Receiver-operating characteristic (ROC) analysis was done for early stage POAG patients to establish sensitivity and specificity of chosen parameters in early stage POAG. Area under the receiver operating characteristic (AUC) values were calculated to compare ROC areas. In this study statistically significant differences were found in all ONH parameters, except optic disc area. Neuroretinal rim area was identified as the parameter with the highest difference between groups (F=21.72, P<0.05). The highest correlation between ONH parameters and perimetry
was observed at neuroretinal rim region (r=0.487). Inferior RNFL thickness was established as the parameter with the highest difference between groups among RNFL parameters. In the mean of all glaucoma patients, the highest correlation between data handled with OCT and mean deviation was observed in RNFL thickness. Average macular thickness was detected as the parameter with the highest difference between groups among macular parameters. The highest correlation between macula parameters and perimetry indexes was observed between average macular thickness and perimeter indexes (r=0.514).16

Kenan Dagdelenet al concluded that although the assessment of ONH and the analysis of macular thickness are important in diagnosis and treatment, RNFL assessment is the most valuable parameter.16

Johnson LN et al. performed a retrospective study of participants with glaucoma or glaucoma suspect having 2 or more OCTs during a 6-year period. The rates of change in Stratus OCT fast RNFL thickness scan and fast optic disc scan data were compared between ICS users and nonuser controls using random coefficient models. A total of 170 participants met the inclusion criteria, of whom 42 (25%) were ICS users and 128 (75%) were controls. The mean duration of follow-up was 3.2 years. There were no significant differences in the mean rates of change in superior RNFL (-0.8874 μm/y ICS users; -0.8592 μm/y controls; p=0.943), nasal RNFL (-0.0529 μm/y ICS users; -0.3577 μm/y controls; p=0.419), inferior RNFL (0.2703 μm/y ICS users; -0.1910 μm/y controls; p=0.165), and temporal RNFL (-0.3618 μm/y ICS users; -0.3612 μm/y controls; p=0.998) between ICS users and controls. There were no significant differences in the mean rates of change in horizontal cup/disc ratio (-0.0047 μm/y ICS users; 0.0002 μm/y controls; p=0.212) and vertical cup/disc ratio (0.0013 μm/y ICS users; 0.0029 μm/y; p=0.717) between ICS users and controls.17

According to Johnson LN et al study no significant difference in the rates of RNFL or optic nerve cup/disc ratio progression among individuals with glaucoma or glaucoma suspect following short-term ICS use.15

In present study optic disc evaluation and visual field examination was done at every visit. Optic disc evaluation was done by a single person using direct ophthalmoscopy and by using green filter in slit lamp biomicroscopy. No optic disc changes relevant to open angle glaucoma was observed, this study had focused mostly in the measurement of retinal nerve fiber layer thickness (RNFL) clinically. In almost all the cases the retinal nerve fiber layer (RNFL) was noted healthy. In the above study, they used Stratus OCT fast RNFL thickness scan and fast optic disc scan data to measure changes in the optic disc and retinal nerve fiber layer thickness. In present study, retinal nerve fiber layer thickness and optic disc evaluation was done clinically at every visit. No statistically significant changes were noted.

Visual field examination was done using Humphrey’s visual field analyzer, SITA standard at every visit in both eyes. The present study had analyzed the visual fields by taking mean deviation (MD) and pattern standard deviation (PSD) into consideration. The mean of mean deviation and pattern standard deviation was calculated at baseline, 1, 3 and 6 months in right eye and left eye. The mean of baseline MD and PSD was compared with the mean of MD and PSD at 1, 3, and 6 months and P value was calculated. P value is > 0.5% for both mean deviation (MD) and pattern standard deviation (PSD) in both eyes which showed that there was no progression in visual fields in subjects taking inhaled corticosteroids during 6 months follow up, by considering the global indices of visual filed mean deviation (MD) and pattern standard deviation patters (PSD). (Table 7 and 8 and FIGURE: 7.8 and 9.10).

VI. Conclusion
Incidence of ocular hypertension increases with increase in duration of inhaled corticosteroid usage.
Increase in dosage of inhaled corticosteroids also play a significant role in the incidence of ocular hypertension. Age also acts as a risk factor in patients using inhaled corticosteroids.
Patient on inhaled corticosteroids should undergo regular ophthalmology examination, to check for any progression of the disease.

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