



"INHALED CORTICOSTEROID: EFFECT ON INTRAOCULAR PRESSURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND BRONCHIAL ASTHMA PATIENTS"

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ABSTRACT

Aim: The purpose of this study was to determine whether a commonly prescribed inhaled corticosteroid treatment induce a clinically meaningful elevation in intraocular pressure, when administered in bronchial asthma and chronic obstructive pulmonary disease COPD patients.

Material And Method: In this analytical cross sectional study of 300 eyes of 150 patients (75 cases and 75 controls) were enrolled for study. Subjects were evaluated in tertiary care centre, Bhopal Memorial Hospital and Research Centre, Bhopal, M.P. India. Both the eyes of all the patients and comparison group/controls meeting the inclusion criteria were examined for the study. Cases were taken from department of pulmonary medicine BMHRC, who were on inhaled corticosteroid for more than 3 months as a treatment for either COPD or bronchial asthma. Sources of /comparison group/controls were patients attending department of ophthalmology for general eye check-up. All patients were evaluated for visual acuity, intraocular pressure, Gonioscopy, central corneal thickness and slit lamp examination.

Results: Mean Intraocular pressure (mmHg) among cases & controls was compared. Mean Intraocular Pressure was higher among cases i.e 18.79 ± 4.85 as compare to controls who had 15.00 ± 2.57 mmHg intraocular pressure. There was statistically highly significant difference in Mean Intraocular pressure (mmHg) among cases & controls. ($P=0.001$)

Conclusion: This study concluded that the use of inhaled corticosteroid leads to significant increase in intraocular pressure.

KEYWORDS : Inhaled corticosteroids, Intra Ocular Pressure, CCT, Gonioscopy.

INTRODUCTION:

Glaucoma is a 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 is raised Intra Ocular Pressure (IOP). This is one of the major causes of irreversible blindness in the world.¹

With the current trend of extensive use of steroids, its side effects do not spare the eye either. Recent guidelines in the management of bronchial asthma² and COPD^{3,4} advocate the use of oral and inhalation steroids. It has been found that 4% to 6% of the populations are steroid responders when on topical and systemic steroids are used. They are defined as those who develop IOP rise greater than 22 mmHg after daily topical/systemic steroid use for 4 to 6 weeks⁵. This can lead to optic disc changes and vision loss. There are very few reports on the effect of inhaled steroids on intraocular pressures.

An early diagnosis of glaucoma and ocular hypertension is required for timely treatment to prevent irreversible visual loss.

MATERIALS AND METHOD:

This was an analytical cross sectional study. Here 150 patients (75 cases + 75 controls = 300 eyes) were enrolled. Study was done in Department of Ophthalmology of Bhopal Memorial Hospital and Research Centre, Bhopal M.P. Both the eyes of all the patients and controls/comparison group meeting the inclusion criteria were evaluated after obtaining informed consent.

Inclusion criteria for case included, patients aged 18 to 60 years of both sexes, with no history of glaucoma and who were on inhaled corticosteroids for more than 3 months as a treatment for bronchial asthma and COPD. The duration of study was 2 years.

Controls/comparison group were the patients who presented in eye OPD for general eye check-up and fulfilled the inclusion criteria for control and that were normal subjects with no history of glaucoma (age 18 to 60 years). Controls were not on

any type of steroid therapy (systemic, topical, periocular, inhalation) for at least last 3 months.

Exclusion criteria for both cases and controls included patients with history of previous intraocular surgery or refractive surgery, blindness in either eye or any kind of refractive error (high myopia & hypermetropia). Patients potentially unavailable for follow up visit were also excluded from study.

Patients underwent a comprehensive ophthalmic evaluation that included the following

- Best corrected visual acuity for near and distance vision by Snellen's chart
- Slit lamp examination of both the eyes.
- Color vision using Ishihara's chart
- Measurement of IOP by Applanation tonometer and corrected by central corneal thickness. The average of 3 readings was taken.

This method indirectly measures the IOP by gauging how much force it takes to flatten the cornea over a fixed surface area. Before beginning the procedure patients were explained about the procedure. Local anaesthetic (propracain eye drop) was installed in eyes, cornea was stained by fluorescein using fluorescein strip. The tonometer mounted on the slit lamp microscope illuminated with beam is guided so that it gently touches the corneal apex and 3 reading were taken. Other ocular examination included-

- Gonioscopy to rule out any angle anomaly and angle closure.
- Fundus examination to evaluate the optic nerve and retinal nerve fiber layer.
- Gonioscopy by three mirror lens.
- Fundus examination by 90 D lens.

RESULTS:

Total 300 patients were selected for the study. Out of 300, 150 were cases who were on inhaled corticosteroids and 150 (controls) were not taking corticosteroids. Out of 300 patients, 174(58.0%) were male and 126(42.0%) were female.

Mean age of cases was 51.91 years and of controls was 45.23 years respectively.

Mean Intraocular Pressure was higher among cases i.e. 18.79±4.85 as compare to controls who had 15.00±2.57 mmHg intraocular pressure. There was statistically highly significant difference in Mean Intraocular pressure (mmHg) among cases & controls. (P=0.001)

Mean Intraocular pressure (mmHg) according to gender was compared which showed, Mean Intraocular Pressure was higher among males i.e. 18.79±4.85 as compare to females who had 15.00±2.57 mmHg intraocular pressure. There was statistically highly significant difference in Mean Intraocular Pressure (mmHg) according to gender. (P=0.001)

Mean Intraocular pressure (mmHg) was compared according to age, which showed that Mean IOP was highest among 41-60 year old patients i.e 18.02±4.55 mmHg and it was comparatively less among 20-40 and more than 60 year old patients. There was statistically highly significant difference in Mean Intraocular pressure (mmHg) according to age. (P=0.001)

Mean Intraocular pressure (mmHg) was also compared, according to duration of corticosteroid use among cases. Mean IOP was highest among patients with 169-240 months use of corticosteroids i.e 20.75±5.49 mmHg and least with duration of 241-288 months i.e 14.50±3.69 mmHg.

Statistical Analysis:

Table 1: Demographic Distribution Of Patients According To Use Of Corticosteroids (case & Controls) And Gender.

Gender	Cases N(%)	Controls N(%)	Total N(%)
Male	98(32.7%)	76(25.3%)	174(58.0%)
Female	52(17.3%)	74(24.7%)	126(42.0%)
Total	150(50.0%)	150(50.0%)	300(100.0%)
Chi Square Value	6.623		
Significance 'p' Value	0.010(S)		

Table 1 reveals demographic distribution of patients according to use of corticosteroids (case & controls) and gender. Total 300 glaucoma patients were selected for the study. Out of 300, 150 were cases who were taking corticosteroids and 150 were not taking corticosteroids. Out of 300 patients, 174(58.0%) were male and 126(42.0%) were female.

Table 2: Demographic Distribution Of Cases & Controls According To Age.

Age groups	Cases N (%)	Controls N (%)	Total N (%)
20-40 Year	18(6.0%)	64(21.3%)	82(27.3%)
41-60 Year	117(39.0%)	54(18.0%)	171(57.0%)
>60 Year	15(5.0%)	32(10.7%)	47(15.7%)
Total	150(50.0%)	150(50.0%)	300(100.0%)
Mean Age (Year)	51.91 Year	45.23 Year	48.56 Year
Chi Square Value	55.164		
Significance 'p' Value	0.001(HS)		

Table 2 reveals demographic distribution of cases & controls according to age. Out of 300 patients, maximum 171(57.0%) were 41-60 year old. 82(27.3%) were 20-40 year and 47(15.7%) were more than 60 year old. Mean age of cases was 51.91 Year and of controls was 45.23 Year respectively. There was statistically significant difference in distribution of glaucoma patients according to age. (P=0.001)

Table 3: Duration Of Use Of Corticosteroids Among Cases.

Duration(Month)	Number	Percentage
1-48 months	100	66.7%
49-96 months	26	17.3%
97-144 months	8	5.3%
145-168 months	0	0.0%
169-240 months	12	8.0%
241-288 months	4	2.7%
Total	150	100.0%
Mean Duration(months)	59.85 (3month to 288 months)	

Table 3 reveals Duration of use of corticosteroids among cases. Most of the cases were using corticosteroids since 1-48 month i.e 66.7% and 4(2.7%) were using since 241-288 months. Mean duration of use of corticosteroids was 59, 85 month and its range was from 3 month to 288 months.

Table 4: Mean Intraocular Pressure (mmHg) Among Cases & Controls.

Groups	Intraocular Pressure (mmHg)		
	Number	Mean	SD
Cases	150	18.79	4.854
Controls	150	15.00	2.578
Student 't' Test Value	8.453		
Significance 'p' Value	0.001(HS)		

Table 4 reveals Mean Intraocular pressure (mmHg) among cases & controls. Mean Intraocular Pressure was higher among cases i.e 18.79±4.85 as compare to controls who had 15.00± 2.57 mmHg intraocular pressure. There was statistically highly significant difference in Mean Intraocular pressure (mmHg) among cases & controls. (P=0.001)

Table 5: Mean Intraocular Pressure (mmHg) According To Gender.

Gender	Intraocular Pressure (mmhg)		
	Number	Mean	SD
Male	174	17.49	4.912
Female	126	16.08	3.176
Student 't' Test Value	2.821		
Significance 'p' Value	0.005(S)		

Table 5 reveals Mean Intraocular pressure (mmHg) according to gender. Mean Intraocular Pressure was higher among males i.e 18.79±4.85 as compare to females who had 15.00± 2.57 mmHg intraocular pressure. There was statistically highly significant difference in Mean Intraocular pressure (mmHg) according to gender. (P=0.001)

Table 6: Mean Intraocular Pressure (mmHg) According To Age.

Age Groups	Intraocular Pressure (mmHg)		
	Number	Mean	SD
20-40 Year	82	15.39	3.026
41-60 Year	171	18.02	4.557
>60 Year	47	15.45	4.190
Total	300	16.90	4.320
ANOVA 'F' Value	14.608		
Significance 'p' Value	0.001(HS)		

Table 6 reveals Mean Intraocular pressure (mmHg) according to age. Mean IOP was highest among 41-60 year old patients i.e 18.02±4.55 mmHg and it was comparatively less among 20-40 and more than 60 year old patients. There was statistically highly significant difference in Mean Intraocular pressure (mmHg) according to age. (P=0.001)

Table 7: Mean Intraocular Pressure (mmHg) According To

Duration Of Corticosteroid Use Among Cases.

Duration(Month)	Number	Intraocular Pressure (mmHg)	
		Mean	SD
1-48 months	100	18.70	5.032
49-96 months	26	19.12	4.274
97-144 months	8	18.13	2.588
169-240 months	12	20.75	5.496
241-288 months	4	14.50	3.697
TOTAL	150	18.79	4.854
ANOVA F Value	1.359		
Significance 'p' Value	0.251(NS)		

Table 7 reveals Mean Intraocular pressure (mmHg) according to duration of corticosteroid use among cases. Mean IOP was highest among patients with 169-240 months use of corticosteroids i.e 20.75 ± 5.49 mmHg and least with duration of 241-288 months i.e 14.50 ± 3.69 mmHg. There was statistically no significant difference in Mean Intraocular Pressure (mmHg) according to age. (P=0.251)

DISCUSSION:

Inhaled corticosteroids are currently the most commonly used medication for the management of COPD and asthma patients. Steroid can cause an elevation of IOP whether they are administered topically or systemically over along period of time.

Corticosteroids decrease outflow by inhibiting degradation of extracellular matrix material in the trabecular meshwork (TM), which leads to excessive accumulation of material within the outflow pathway and it causes increase in outflow resistance⁶. Two types of extracellular deposition have been described in TM of steroid-induced glaucoma patients, first is the fingerprint-like deposition of material in uveal meshwork and second one is, accumulation of fine fibrillar material in the juxtacanalicular region⁷.

In their study, Francois^{8,9} and Armaly¹⁰ suggested that the response might be due to an alteration of the metabolism of mucopolysaccharides, leading to its accumulation in the TM. In two different studies Wordinger⁷ et al and Tripathi¹¹, proposed that corticosteroids, which stabilize lysosomal membranes, could reduce the release of lysosomal hyaluronidase, this resulting in a relative inhibition of hyaluronate depolymerisation. The subsequent accumulation of mucopolysaccharide could cause retention of water (biological oedema) and subsequent narrowing of the trabecular spaces. Glucocorticoids have been shown to alter TM cell morphology by causing an increase in nuclear size and DNA content^{7,11}. A further study of Wilson K has shown that steroids also induce proliferation and activation of the endoplasmic reticulum, golgi apparatus and increase deposition of extracellular matrix material¹².

The amount of glycosaminoglycans, elastin and fibronectin have been shown to increase in tissue culture preparations in response to dexamethasone treatment while the level of tissue plasminogen activator, stromelysin¹³ and the activity of several TM metalloproteases^{7,14} have been shown to fall. Excessive accumulation of glycosaminoglycans has been identified in human trabecular meshwork specimens obtained from steroid-responders¹⁵.

Dexamethasone treatment has also been shown to inhibit TM cell arachadonic acid metabolism¹⁶ and reduce phagocytic activity^{17,7}. TM cells have phagocytic properties the function of which is to clear the outflow channels of debris. A steroid induced inhibition of phagocytosis within the meshwork could result in accumulation of channel debris and decreased facility of outflow¹⁸ so contributing to steroid induced glaucoma.

Garbe E et al.¹⁹, conducted a retrospective study, at the Hadassah University Hospital, Jerusalem, Israel, in which they found that, usage of high dose inhaled steroids for more than a period of 3 months causes an elevation of intraocular pressure. The study was conducted on the enrollees in a universal health insurance program for all elderly above 66 years of age.

Optowsky I et al.²⁰, also found Intraocular Pressure elevation associated with inhalation and nasal corticosteroids and recommended the routine surveillance of IOP in patients using long term inhalational and nasal steroids.

Mitchell Pet.al.⁵, studied the correlation of corticosteroids and family history and risk of glaucoma. According to study there was correlation only between persons with family history of glaucoma and increase of IOP with usage of inhaled steroids for more than 3 months.

CONCLUSION:

The result of this study shows that long term use of inhaled corticosteroid leads to raised intra ocular pressure and the patients on inhaled steroids must be regularly monitored/evaluated for glaucoma work up.

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