



INTRAOCCULAR PRESSURE; INCIDENCE OF STEROID INDUCED RISE IN LOCAL POPULATION OF NORMAL, V.K.C AND C.S.G PATIENTS.

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ABSTRACT... Objective: To assess the incidence of steroid induced rise in intra-ocular pressure in different group of patients. **Place and duration of study:** The study was conducted in the department of ophthalmology Akhtar Saeed Trust Teaching Hospital of Akhtar Saeed Medical and Dental College Lahore and Continental Medical College Lahore from Jan 2009 to Oct 2010. **Material and Methods:** Three groups were formulated in which group A comprised of normal population with no ocular disease, group B included patients with vernal keratoconjunctivitis while group C comprised of chronic simple glaucoma patients with controlled intraocular pressure. Dexamethasone 0.1% eye drops were used four times daily for four weeks and patients were evaluated weekly in terms of IOP monitoring after which they were labeled as either low or non-responders, moderate responders or high responders. **Results:** In group A 40% of the patients showed rise in IOP, group B showed 95% rise in IOP and the response in group C cases was 100%. **Conclusions:** Topical steroids result in significant rise in IOP therefore careful monitoring should be done in all patients on corticosteroids.

Key words: IOP, steroid responsiveness, VKC, ocular hypertension.

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INTRODUCTION

Steroid induced ocular hypertension is a well-documented phenomenon and is genetically determined¹. Steroid induced glaucoma is a form of open angle glaucoma, and is an adverse effect of steroid therapy if IOP remains elevated². Glaucoma, a sight threatening condition is often diagnosed late due to minimal or no symptoms in early stages. Steroid drops are commonly used for treating eye inflammation and allergy and their indiscriminate and long term use can result in steroid induced glaucoma. Steroid induced IOP elevation can occur in people of all ages although children are less frequently reported to have IOP elevation³.

Incidence of IOP elevation in patients on systemic steroids is unknown but approximately one third of individuals show moderate increase in IOP after topical use of steroids⁴. However 5-6% of normal

population develops marked rise in IOP after 4-6 weeks of steroid therapy^{5,6}, so 5% of the general population without any other risk is vulnerable to have steroid induced glaucoma after its long term use⁷. Patients of POAG have much greater potential to experience a raised IOP after topical use of steroids. Others who are at risk are first degree relatives of POAG patients,⁸ high myopes,⁹ diabetics¹⁰ and patients of rheumatoid arthritis¹¹. Patients using inhalational corticosteroids have been reported to experience significant rise in IOP on short term use, especially in patients predisposed to POAG¹². Potent steroids like dexamethasone and beta-methasone have a significant tendency to induce glaucoma¹³. Less potent steroids like fluoromethalone and medrysone are less likely to induce IOP elevation¹⁴. Topical steroids typically produce IOP elevation within 2-6 weeks but systemically administered steroids may take longer duration to elicit an IOP rise¹⁵.

Different theories have been postulated ultimately affecting the facility of outflow. It is generally agreed that IOP increase after steroid administration results from reduction in facility of outflow¹⁶. Myocilin gene formerly known as trabecular meshwork induced glucocorticoid response protein (TIGR), increased in response to elevated IOP may have a protective role in outflow pathway¹⁷. Myocilin gene mutations result in the formation of abnormal gene products which may lead to trabecular meshwork clogging and increased IOP.

MATERIAL AND METHODS

The study was conducted in the department of ophthalmology AkhtarSaeed Trust Teaching Hospital of AkhtarSaeed Medical and Dental College Lahore and Continental Medical College Lahore from Jan 2009 to Oct 2010. Study was designed to know the steroid response in terms of rise in intra-ocular pressure in three different groups of patients. Steroid used was 0.1% dexamethasone eye drops 4 times daily for 4 weeks in one eye and the other eye was used as a control. IOP was taken by Goldman applanation tonometer on day 0, 7, 14, 21 and 28.

GROUP A: 20 volunteers having normal eyes and IOP.

GROUP B: 24 patients of VKC having no history of CSG and both eyes were almost equally involved.

GROUP C: 12 patients of bilateral CSG in whom the IOP had been under control with single drug i.e Timolol maleate 0.5 % drops twice daily.

Patients were included with the following criteria:

- (1) Corrected visual acuity 6/6.
- (2) Open angles assessed by a slit beam and also gonioscopically.
- (3) No peripheral anterior synechiae.
- (4) No significant amount of pigment in the angles.
- (5) No pseudo-exfoliation of the lens capsule.
- (6) Cup disc ratio in group C was not more than 0.6 with early glaucomatous visual field defects.

- (7) Normal discs and visual fields in group A and B.
- (8) Normal IOP by applanation tonometer in all groups.
- (9) Patients were not on oral hypotensive agents.
- (10) In group B and C patients were not on topical steroids, at least during last 4 weeks.

Pretest detailed examination for best visual acuity was done. Corneal disease, pupillary examination, lens changes, ophthalmoscopy, field studies and gonioscopy were done. Initial applanation tonometry and then weekly afterwards was done at 9-12 am.

- (1) The patients were instructed to instill drops after shaking the bottle and bottles were labeled. Other eye was treated with non-steroid drops and used as a control.
- (2) The patients were seen at weekly intervals at about the same time of day for applanation tonometry.
- (3) Steroid drops were stopped after 4 weeks and patients having positive response were checked weekly to note the IOP
- (4) The new patients were recruited in place of those who did not turn up for follow up and those patients who had poor compliance of use of drops.
- (5) - Response was termed low or no response having IOP ≤ 21 mmHg
- Moderate response where IOP was 22-30 mmHg
- High response where IOP was 31 mmHg or more

RESULTS

The features of the three groups studied are summarized in table I & II. The results of steroid provocative test in all the three groups are shown in table III and plotted in fig 1, 2 & 3.

GROUP A: Corticosteroid provocative test in 20 selected normal persons, males 14 (70%) and females 6 (30%), age ranged 16-50 years, mean IOP change ΔP in all the patients was calculated to be 7.55 ± 4.43 (Table-III). 12 patients (60%)

showed little or no response (IOP ≤ 21 mmHg table-II & fig-3). 8 patients (40%) showed positive steroid response. 01 patient (5%) showed high response (IOP 31mmHg) and 7 patients (35%) showed intermediate response (IOP 22-30 mmHg), shown in fig. 3. Mean IOP response (steroid responsiveness) is plotted, IOP verses time in fig. 1 & 2.

The second eye used as a control showed no response. Mean IOP remained at pre-test level.

GROUP B: Corticosteroid provocative test in 24 patients/eyes of patients of vernal keratoconjunctivitis having age range 12-30 years. 16 patients (66.7%) were males and 8 patients (33.7%) were females. At day 0, mean IOP was

Features	Group A	Group B	Group C
No. of patients	20	24	12
Age range (years)	16-50	12-30	40-65
10-20	2	16	-
21-30	2	8	-
31-40	10	-	-
41-50	6	-	4
51-60	-	-	5
61-70	-	-	3
Male	14	16	7
Female	6	8	5
Mean IOP	15 ± 1.52	15.54 ± 2.08	17.58 ± 1.92

Table-I. Features of the sample

15.5 ± 2.08 and mean change ΔP was 15.29 ± 4.48 at termination of study on day 28. Only one patient(4.5%) showed no response while 23 patients (95.5%) showed steroid responsiveness. Eight patients (33%) showed intermediate response and IOP was 22-30 mmHg. 15 patients (62.5%) showed marked response and IOP was >30 mmHg shown in table-II & fig. 3. Mean IOP response (steroid responsiveness) is plotted, IOP verses time scale in fig. 1 & 2.

The second eye which was used as a control showed no response. Mean IOP remained at pre-test level.

GROUP C: Corticosteroid provocative test in 12 patients/eyes of CSG having age range 40-65 years. 7 patients (58.1%) were males and 5 patients (41.9%) were females. At day 0, mean IOP was 17.5 ± 1.92 and mean change ΔP was 15.42 ± 4.48. At day 28,3 patients (25%) showed intermediate response with IOP 22-30 mmHg while 9 patients (75%) showed marked response with IOP >30 mmHg as shown in table-II & fig.3. Mean IOP response (steroid responsiveness) is plotted, IOP verses time scale in fig.1 & 2.

Second eye which was used as a control showed no response. Mean IOP remained at pre-test level.

DISCUSSION

Corticosteroid induced ocular hypertension is defined as the rise in IOP of ≥ 6 mmHg following use of steroids. Long term raised IOP results in glaucomatous changes similar to POAG and patients using topical steroids for different reasons

Features	Group A	Group B	Group C
Frequency	QID	QID	QID
Duration	4 week	4 week	4 week
Parameter	Final IOP	Final IOP	Final IOP
Type of responder			
No or low (= 21 mmHg)	12 Eyes (60%)	1 Eyes (4.5%)	-
Moderate (22-30 mmHg)	07 Eyes (35%)	8 Eyes (33%)	3 Eyes (25 %)
High (=31 mmHg)	01 Eyes (05%)	15 Eyes (62.5%)	9 Eyes (75%)

Table-II. Response to topical steroid drops

			Day 28			
	Day 0 (P1)	Day 7	Day 14	Day 21	(P2)	ΔP (P2-P1)
Group A	15 ± 1.52	15.85 ± 1.42	19.35 ± 4.35	21.25 ± 4.35	21.25 ± 4.35	7.55 ± 4.43
Group B	15.54 ± 2.04	20.33 ± 4.64	24.79 ± 4.34	27.7 ± 4.68	30.25 ± 4.48	15.29 ± 4.48
Group C	17.58 ± 1.92	20.75 ± 2.7	25.75 ± 3.95	29.83 ± 3.71	33 ± 4.11	15.42 ± 4.11

Table-III. Results of steroid provocative test

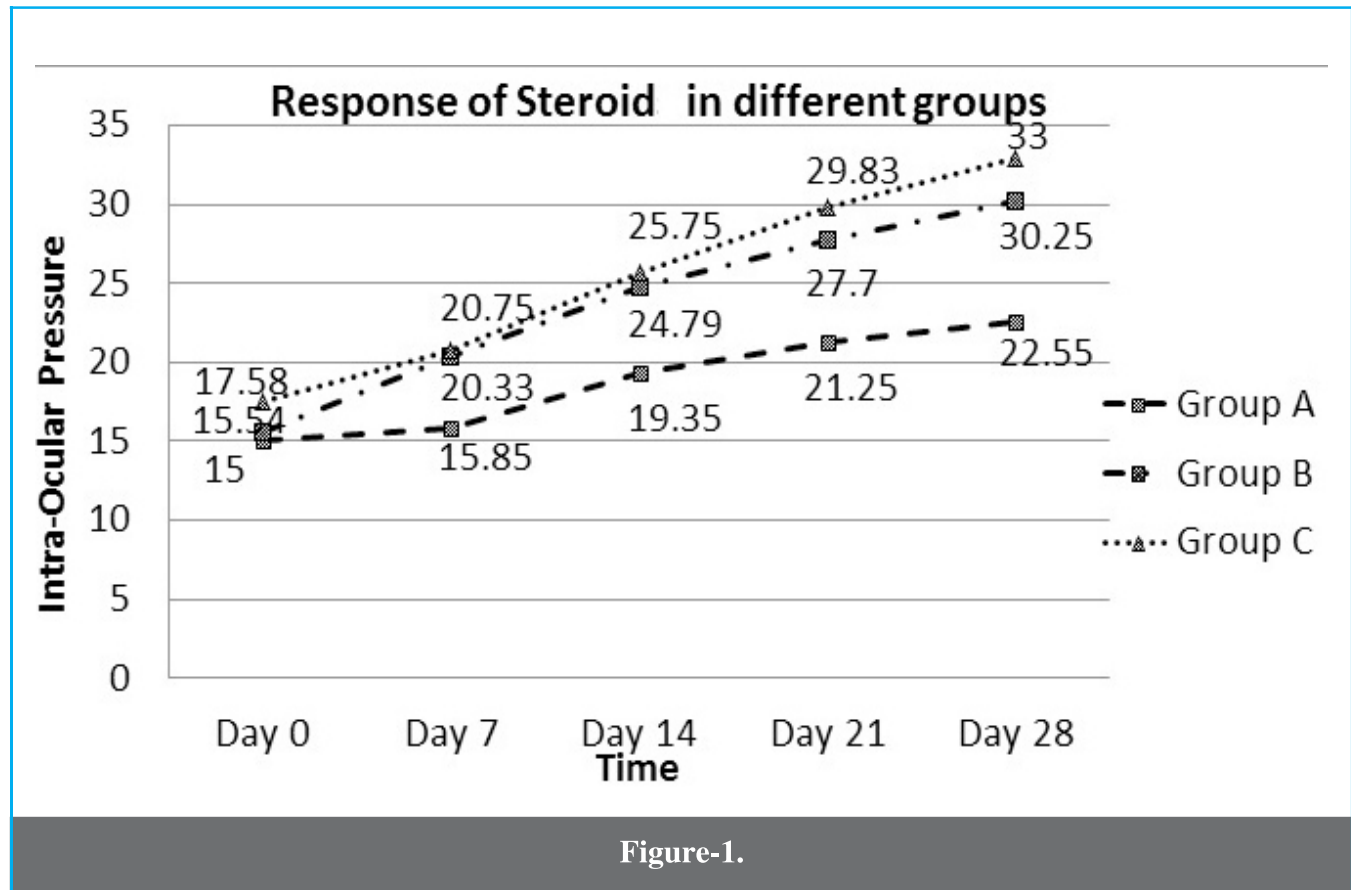


Figure-1.

or diseases as in vernal keratoconjunctivitis develop rise in IOP leading to glaucomatous changes without any notice as the rise in IOP is gradual and very few symptoms exist¹⁸. Although the elevation of IOP beyond normal values is not necessary for the occurrence of glaucomatous damage but it is thought to be a major risk factor¹⁹.

The high IOP due to steroids can occur within a week or can be delayed for months but in susceptible cases IOP gradually increases within 2-4 weeks, as in our case not all normal persons

responded to topical steroids but only 30%, while known cases of CSG and their offsprings always showed marked response.

Becker and Hahn have suggested and explained the response on genetic basis. Homozygous responsiveness state is represented by cases of chronic simple glaucoma and that the heterozygous or carrier state, in which only one responsive gene is present. Becker and Hahn found 95% of the offsprings of patients with glaucoma showing significant change in IOP after

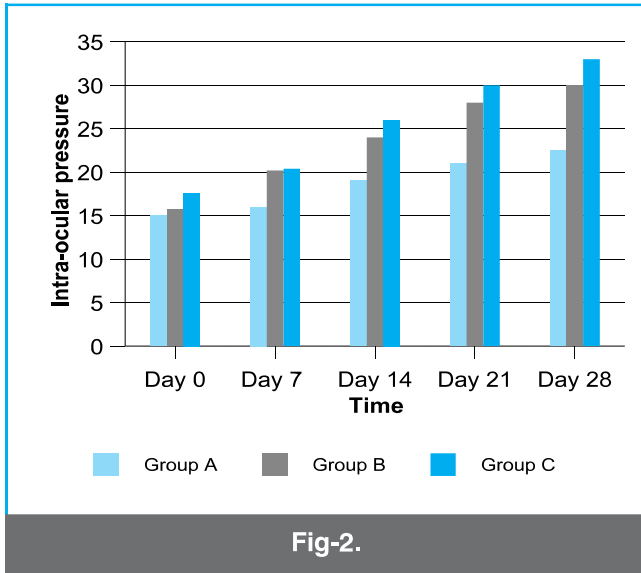


Fig-2.

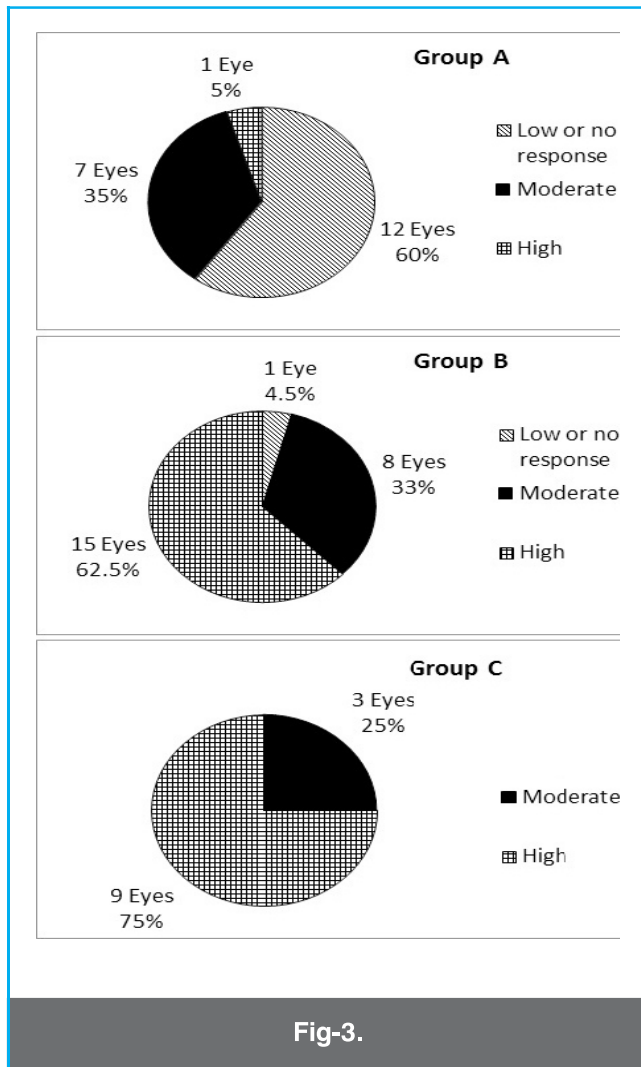


Fig-3.

3 weeks of topical Betamethasone treatment and suggested that glaucoma is transmitted as a recessive character with a prevalence of the gene in the population of about 0.2, then approximately 4% of the population should be homozygous, 32% should be heterozygous carriers and 64% would be normal.

In our study, in group A , 40% showed positive response but only 5% showed marked response to be predicted as homozygous and 60% showed no or little response. In group B, 95.5% showed steroid responsiveness, 33% of them showed moderate response and 62.5% showed marked response. This response is very similar to patients of chronic simple glaucoma which is suggestive of that patients of VKC might be having similar genes like chronic simple glaucoma patients determining the steroid responsiveness. In group C, all the patients (100%) showed steroid response, 75% of them showed marked response (IOP >30 mmHg) and 25% showed moderate response (IOP 22-30 mmHg). Several workers in the past showed similar results, Becker and Hahn-92%,²⁰ Armaly-92%²¹ and Kitzawa-100%²².

CONCLUSIONS

- In general population 40% are steroid responders though only 5% are high responders.
- Almost all patients of chronic simple glaucoma and VKC are steroid responders and 60-75% are high responders.
- Strong topical steroids should be avoided in patients of chronic simple glaucoma and VKC as far as possible.
- Careful monitoring should be done in all patients on corticosteroids especially in VKC and glaucoma.
- Steroid therapy must be used with intermittent drug holidays and never on continuous basis.
- Before administering depot steroid in any disease, topical steroid provocative test can be performed for 2-3 weeks to judge the steroid responsiveness.

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PREVIOUS RELATED STUDY

Muhammad Kamran Saeed, Sameer Shahid Ameen, Muhammad Tahir Ibrahim, Umar Ijaz, Kashif Hanif. RAISED INTRAOCULAR PRESSURE; FREQUENCY AFTER Nd: YAG LASER CAPSULOTOMY. (Original) Prof Med Jour 16(3) 410-413 Jul, Aug, Sep, 2009.