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Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Review Article

Glaucoma in general population and steroid users

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ARTICLE INFO

Article history:

Received 27-05-2023

Accepted 04-12-2023

Available online 30-09-2024

Keywords:

Glaucoma

Steroids

Diseases

Management

ABSTRACT

In recent years, several surveys have reported on the prevalence of glaucoma worldwide. One study has shown that financial stability in population has affected glaucoma. However, there have been differences in the reported prevalence rates due to methodological variations. In the Eastern part of the world, 7.8 million people had primary open angle glaucoma (POAG) with prevalence of about 2.51%. To estimate the number of people with glaucoma or at risk of the disease, they age and gender occurrence estimates have been used, along with population estimates. East Asians have more chances to have PACG than POAG compared to western people. Their analysis shows that about 11.2 million people of the age 40 years and older with glaucoma in South East Asia, with POAG in 6.48 million people and PACG affecting 2.54 million. Additionally, any primary angle-closure disease could affect around 27.6 million people. The majority of glaucoma patients in South East Asia go undiagnosed, which makes it difficult to discover and treat the condition. We consider different strategies to raise case detection rates across the nation while taking into account the limited resources and personnel at our disposal. Aim of this study was to understand prevalence of glaucoma in general populations and steroid users.

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1. Introduction

Steroids are a type of anti-inflammatory medication used for treating various systemic and ocular problems. However, the careless use of steroids, particularly in the form of eye drops, is widespread in times where it is readily found without a prescription, resulting in unwanted side effects.

One study has shown that financial stability in population has affected glaucoma.¹⁻¹⁶ In the Eastern part of the world, 7.8 million people had POAG with prevalence of about 2.51%.¹⁴ East Asians have more chances to have PACG than POAG compared to western people.¹⁷

The prolonged use of steroid preparations on the eyelid skin may result in the development of glaucoma induced by steroids. This condition is more commonly observed in patients with atopic dermatitis who apply steroid

preparations chronically, and people who have a glaucoma in their family history.^{1,18,19}

Cataracts and glaucoma are common steroidal ocular side effects. The link between chronic use of systemic steroids & increased IOP, known as ocular hypertension induced by steroid use, has first occurred in 1950. In the UK, The most common glaucoma is POAG which affects 2% of people who are above 40 years and 10% of people above 75 years of age, most specifically African-Caribbean people. PACG is less prevalent, affecting only 0.17% of people below 40 years, more specifically East Asians.²⁰ Furthermore, mostly in people of about 40 years and above had glaucoma in Nigeria, which suggests that the concentration or occurrence of glaucoma starts at earlier ages and advances more in blacks than in white people and Asians.²¹ Typically, an increase in intraocular pressure (IOP) due to topical steroid use is observed after three to

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six weeks from the initiation of treatment, and it usually normalizes within two weeks of stopping therapy.²² Chronic steroid administration in any form can neuropathy of the optic nerve and glaucoma induced by steroid due to raised IOP.

Globally, approximately 57.5 million individuals are impacted POAG, which has a prevalence rate of 2.2%.¹³

However, it is known that approximately 61-63% of the normal population are nonresponders to GC, exhibiting IOP elevations 5 mm Hg, while 33% of the normal population exhibits a moderate response of IOP increase (6 to 15 mm Hg), and 46% of the normal population is highly responsive to GC (IOP elevation > 15 mm Hg). The prevalence of SIG among all forms of secondary glaucoma is unknown.²³ On the other hand, after topical GC therapy, IOP rises significantly and may become hazardous in 46 to 92% of POAG patients.²⁴

Similar findings of a retrospective investigation examining the prevalence of blindness associated with SIG in young patients with vernal keratoconjunctivitis were recently published by Senthil and associates.²⁵ 91 (157 eyes) of the 4062 participants in the research had SIG. The remaining 34 eyes (21.6%) of the 157 eyes with SIG had OH, and 123 eyes (78.3%) had glaucomatous disk damage. Once more, there were significant glaucomatous complications at presentation: the median presenting IOP was 24.9 12.8 mm Hg, the median cup-to-disk ratio was 0.9 (0.7e0.9), and the median mean deviation of the visual field defect was 21.9 (30.2 to 10.2) dB. 29 participants (36.9%) had bilateral blindness, while 10 (6.4%) had unilateral blindness.²⁵

This review aims to inform clinicians about the pathophysiology, epidemiology of glaucoma induced by steroid, the side effects detection, and the management principles. It is crucial to make healthcare providers familiar with the hazards of prescribing steroids without careful diagnosis of the eye and the risks of blindness which are irreversible in cases of over the counter self-prescription by patients.

There are four major types of glaucoma:

1. Open-angle glaucoma
2. Closed-angle glaucoma
3. Congenital glaucoma
4. Secondary glaucoma

There are various factors that can cause increased IOP, including steroidal use. However, unlike glaucoma, IOP induced by steroids can be reversed upon discontinuation. Here is a list of possible diagnoses that can cause elevated IOP:

1. Angle-closure glaucoma
2. Angle-recession glaucoma
3. Low-tension glaucoma

4. Pigmentary glaucoma
5. Plateau iris glaucoma
6. Pseudoexfoliation glaucoma
7. Uveitic glaucoma

2. Risk Factors

The risk of steroid-induced glaucoma is present for anyone who undergoes steroid therapy, and this risk escalates with the length of the treatment.

Steroid glaucoma patients with the following have a higher than average risk:

1. POAG^{26,27}
2. A relative of first degree with POAG^{28,29}
3. A history of previous steroid-induced IOP elevation
4. Type 1 diabetes mellitus³⁰
5. Very young age (age less than six years old) or an older age³¹
6. Connective tissue disease³²
7. Penetrating keratoplasty, especially Fuchs endothelial in eyes with dystrophy or keratoconus
8. High myopia³³

Earlier investigations have also suggested that connective tissue illness, high myopia,³⁴ type I diabetes,³⁵ and angle-recession glaucoma³⁶ are risk factors for steroid responsiveness.

The clear front part of the eye is filled with a fluid called aqueous humor, which is produced in the area posterior to the iris. The eyes flow aqueous humor through channels where the cornea and iris meet, which is known as the anterior chamber angle. Cornea is the clear covering on the front of the eye that lies in front of the iris, pupil, and angle.

Aqueous humor flow due to blockage or slowing down of the flow can lead to an increase IOP.

The administration of corticosteroids, commonly prescribed to treat a range of ocular and systemic conditions, may result in increased (IOP) and cause a risk to visual function, regardless of the route of administration. This risk is attributed to optic disc damage and glaucoma related to visual field loss.² There has been considerable research on and reporting of glaucoma in adults as a result of the ocular hypertensive response brought on by corticosteroids. However, there is limited knowledge regarding how people react to steroids in the paediatric population. Some previous records suggested that children may not experience as significant of an elevated IOP in response to steroids as adults do.

3. Management

The initial step in managing glaucoma caused by steroid use is to stop the use of steroids. If the medication was used for 18 months or more, the IOP can stay high far longer even after stopping therapy.³⁷ Additionally, if feasible, the

removal of repository steroids is also recommended. In situations where it is not possible to entirely discontinue steroid use, the dose should be decreased, or a milder steroid should be used as a substitute. Antiglaucoma medications may be prescribed to regulate the intraocular pressure (IOP).^{38–40}

There are three ways of managing glaucoma caused by steroid use, which include:

3.1. Medical management

treatment is similar to POAG. Medications such as beta-blockers, alpha-2 agonists, and carbonic anhydrase inhibitors may be used. Beta-blockers are typically the 1st agents for this, and prostaglandin analogues are generally not recommended for patients who develop glaucoma due to steroid use after curing uveitis.

3.2. Laser trabeculoplasty

If medical solution fails, and optic nerve damage may occur, laser trabeculoplasty might be suggested. It may also be an option for patients who experience unwanted effects from antiglaucoma medications.

3.3. Surgical management

Surgery is recommended for patients who do not respond to medical or laser therapies, or for those who are likely to have further exposure to steroids. Trabeculectomy is the most commonly used surgical procedure, although tube shunt surgeries and cyclodestructive procedures are other options.

3.4. Removing depot steroids

IOP decrease can be a result.^{41–43} In cases of intravitreal steroid-induced glaucoma, vitrectomy can also be effective in lowering IOP. However, since underlying oedema may be managed by ongoing steroid therapy, some people may need medications or surgery to manage their IOP.³¹

3.5. Routes of drug administration

IOP elevation or glaucoma may result from the topical, intraocular, periocular, oral, intravenous, inhaled, nasal, and transcutaneous delivery of exogenous GC. In a small number of rare endocrine illnesses, increased endogenous glucocorticoid production may cause SIG.³³ Additionally, the formulation of the steroid affects how well it penetrates the cornea. Steroid acetates, like DEX acetate 0.1%, are lipophilic and tend to do this better than hydrophilic derivatives like phosphates. These variables are regarded as GRa independent, and they often have a transient influence.³⁷

3.6. Types of steroids

1. Topical ocular preparations: IOP may rise after using steroid preparations on the skin of the eyelids or applying corticosteroid drops or ointments to the eyes, per studies.⁴⁴ The steroid potency as well as the frequency and duration of administration appear to be related to the risk of elevated IOP. For instance, stronger steroids such as dexamethasone and prednisolone have a higher likelihood of increasing IOP compared to less potent steroids like fluoromethalone, hydrocortisone, and rimexolone.⁴⁵ Topical application causes three-fourths of all cases of SIG and is substantially more common for GC-induced OH or glaucoma than systemic administration.^{37,46} Numerous ocular illnesses are treated with topical GCs, and many surgical and laser treatments include them in the postoperative regimen.^{47,48} In contrast to more recent topical CS like loteprednol etabonate, difluprednate, or rimexolone, older GC like DEX, prednisolone, betamethasone, clobetasone, and fluorometholone are considerably more likely to cause IOP elevation.^{44,49–54} In patients on DEX compared to those receiving fluorometholone treatment, the IOP elevation with older GC may vary from 6 mm Hg to 22 mm Hg.^{55,56} The use of topical DEX (QID for 4 weeks) as a provocation test to identify steroid responders before intravitreal (IVT) steroid implantation has resulted as a result.⁴²
2. Periocular: subconjunctival, sub-Tenon, and retrobulbar injections are routes of steroid delivery that may result in an increased IOP.⁵⁷ The subject's reaction to treatment that is topical steroid, is not always indicative of the potential for an IOP response from periocular steroid treatment. However, the likelihood of IOP elevation in response to periocular steroids significantly higher than that of ophthalmic steroids that are topical. Typically, increased IOP post periocular steroid treatment happens within a few months, although it may occur as early as within 7 days for some instances. IOP levels reduce to normal by the sixth to 6th to 9th month after the injection.⁵⁸
3. Intravitreal: intravitreal administration of corticosteroids typically involves triamcinolone, fluocinolone, and dexamethasone. Dexamethasone is a more potent steroid and is often administered at a dosage of 0.4–0.8 mg with a shorter duration of action. Triamcinolone, on the other hand, is often administered at a dosage of 4 mg and has time of action extending up to 3 months.⁵⁹
4. Dermatologic: glaucoma induced by steroids may develop as a result of applying steroid preparations to the skin of the eyelids. This increase in IOP is most commonly seen with chronic use, particularly in people with glaucoma in their family and with atopic

dermatitis.¹

5. Systemic and non-ocular targeted: Steroidal medications administered through oral or intravenous routes were found to increase intraocular pressure, as do non-ocular targeted localized steroids like intranasal, inhaled, and intra-articular administration.⁶⁰ The degree of increase is likely to be linked to the patient's IOP reaction to topical steroids.^{61,62}

3.7. Exclusion criteria

1. Single functional eye
2. Diabetes mellitus
3. History of surgery on same eye or contralateral eye
4. Uveitis, endothelial dystrophy
5. Significant refractive disease (High Myopia or Hypermetropia)

4. Discussion

Studies have shown³ that children under 6 and old people are actually more prone to developing glaucoma caused by steroids than adults.^{10,33} Research has shown that over 20% of paediatric patients given steroids for various medical reasons develop glaucoma caused by it.^{4,5} While the occurrence of glaucoma is similar among different age groups, studies have shown that glaucoma can be more severe, develop earlier, and progress more rapidly paediatric patients when compared to adults.^{6,7} Even though the long use and often unselective steroid use can result in an elevated IOP and loss of vision due to glaucoma, it is not uncommon to observe considerable elevation in IOP by hours of consuming steroid medication, particularly in susceptible individuals.⁸ In paediatric patients, mostly used form of steroid used leading to steroid-induced glaucoma is through the use of topical steroids, typically prescribed for managing uveitis or vernal conjunctivitis. However, this may not be a reversible in certain cases. According to Kelly et al.,⁶³ 5.7% of black persons and 2.2% of white people over the age of 40 have glaucoma, respectively. Even while the incidence of the condition is similar in all age groups, glaucoma in children tends to be more severe, to manifest earlier, and to proceed more quickly than in adults.⁵

4.7% of children with glaucoma were found to have steroid-induced glaucoma in a tertiary hospital in India, and two-thirds of them had substantial visual impairment from glaucomatous optic neuropathy in one or both eyes.¹⁰ This was discovered in a sizable group of kids, some of whom had been using steroids carelessly for up to eight years before receiving an advanced glaucoma diagnosis, in spite of being monitored by ophthalmologists. Dexamethasone or betamethasone were the medications most frequently used by kids that had caused advanced glaucomatous visual field loss, and they were readily accessible in pharmacies without

a valid doctor's prescription. According to estimates, India sells 20 times as many topical drugs as the US. Many topical corticosteroids are now less expensive thanks to government rules, which allow kids to use them unchecked for symptomatic relief of ocular allergies without the proper medical supervision. In 45% of adolescents with steroid-induced glaucoma, filtering surgery was also required, demonstrating the advanced and treatment-resistant nature of this iatrogenic glaucoma.

Recent studies have brought attention to the harmful effects of inappropriate use of corticosteroids in children, particularly for conditions like vernal keratoconjunctivitis, which have been demonstrated to be responsible for a significant percentage of cases of childhood glaucoma.^{4,10} Sen et al. discovered that over 3% of the children in their research had steroid-induced glaucoma and that over 15% had been using topical steroids without a doctor's prescription.¹¹ The study also found that parents and kids were not given enough information about the possible side effects of prolonged steroid use and the necessity of routine eye pressure monitoring. When treatment is halted early, children with little to no optic nerve damage have shown reversal of the ocular hypertensive response. However, two or more years of continuous topical steroid use has resulted in substantial aqueous outflow resistance, visual impairment, and glaucomatous disc damage, all of which call for surgical intervention. Surprisingly, in Indian studies, a significant percentage of children appeared with blindness in one or both eyes, highlighting the need for ophthalmologists to take proactive steps to halt this unsettling trend.

In developed countries, the incidence of childhood blindness ranges from 0.03% to 0.12%, with glaucoma accounting for 4-5% of cases. Although the prevalence of steroid-induced glaucoma in the general population is unknown, it is most likely a negligible portion of children's instances of vision impairment. As a result, it might not be regarded as a pressing public health concern, but Sen et al. describe that when children get glaucoma from using steroids, it can cause serious visual impairment and place a heavy burden on caregivers.¹¹ There is little data on the economic costs of childhood blindness and steroid-induced glaucoma, but the latter was projected to cost India \$22.2 billion in losses in 1997. Therefore, it is crucial to use steroids judiciously and monitor children closely when they are receiving steroid therapy.¹²

It is critical for primary eye care clinicians to look into non-steroidal modalities for treating vernal keratoconjunctivitis given the potential risks associated with prolonged steroid therapy in children. Effective steroid-sparing therapies such as tacrolimus and cyclosporine should be considered for managing allergic eye disorders. Ophthalmologists may be increasingly using non-steroid treatment to treat minor conditions like ocular allergies,

even though there isn't any published research on the evolving pattern of steroid-induced glaucoma in kids with allergic conjunctivitis and uveitis. However, modern methods of administering steroids, like intravitreal steroids for persistent uveitis, inhaled steroids for asthmatic bronchitis, and topical steroids for skin conditions, are still used in children. Therefore, it is essential that experts in related fields, as well as ophthalmologists, are aware of any potential side effects of steroids on the eyes.

There is an urgent need to inform the people about the possible negative effects of steroid use on the eye in any form. There should be rules in place to stop pharmacists from dispensing steroids without a legitimate and authorized prescription from the treating physician. To stop the over-the-counter sale of these possibly harmful medications, it should become necessary for those dispensing steroids to have current, updated prescriptions from doctors. The harmful effects of steroids on the eyes should be made known to doctors from all specialties, and patients receiving long-term treatment should be referred to ophthalmologists to be monitored for severe side effects like glaucoma. Children's steroid-induced glaucoma is a side effect that should be completely prevented.

5. Conclusion

Finally, it should be noted that glaucoma affects millions of people in India, the majority of whom go undiagnosed. Even though many studies have been performed, since Glaucoma is most of the time gone undetected among general population and among steroid users because of lack of awareness and other systematic diseases due to old age population affected by glaucoma, a particular significant statement cannot be made without much more precised data and history taking of the people undergoing the study. Numerous studies have estimated that 11.2 million Indians aged 40 and older have glaucoma, with 6.48 million suffering from primary open-angle glaucoma and 2.54 million from primary angle-closure glaucoma. Additionally, any primary angle-closure disease could affect around 27.6 million people. Systemic and ocular steroid use can raise intraocular pressure and seriously jeopardize vision function, resulting in steroid-induced glaucoma. Monitoring the use of steroids is essential, as is educating medical professionals about the risks involved in giving them without paying attention to the eye. The recognition of side effects and the principles of management are essential to prevent irreversible blindness.

6. Source of Funding

None.

7. Conflict of Interest


None.


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Cite this article: Saha K, Bandyopadhyay A. Glaucoma in general population and steroid users. *Indian J Clin Exp Ophthalmol* 2024;10(3):435–440.