STEROID INDUCED GLAUCOMA

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Steroid induced glaucoma is a type of drug induced glaucoma which results from the use of steroids in any form.

Pathophysiology

The primary cause of IOP elevation in steroid induced glaucoma is increased outflow resistance. Increased responsiveness to steroids may be facilitated by upregulation of glucocorticoid receptors on trabecular meshwork cells.

1. Steroid causes stabilization of lysosomal membranes and accumulation of polymerized glycosaminoglycans (GAGs) in the trabecular meshwork, which become hydrated, producing "biologic edema" and increased the outflow resistance.
2. Steroids have been shown to increase the expression of extracellular matrix proteins like fibronectin, glycosamioglycans and elastin.
3. Steroids also suppress phagocyctic activity which may lead to increased deposition of material in the juxtacanalicular meshwork of eyes with steroid induced glaucoma.
4. Glucocorticoids alter the trabecular meshwork cell morphology by causing an increase in nuclear size and DNA content.
5. Blockage of intertrabecular spaces by white crystals after intravitreal triamcinolone injection(actual physical obstruction).
6. Patients with increased levels of endogenous corticosteroids (e.g., Cushing syndrome) can also develop increased IOP, which generally returns to normal when the corticosteroid-producing tumor or hyperplastic tissue is excised.[1]

Risk Factors

The risk of glaucoma with the use of steroids is dose and duration dependent. A higher than average risk for steroid glaucoma is found in patients with:

1. Known case of open angle glaucoma
2. Family history of glaucoma (first degree relative)
3. Very young age (age less than six years old) or an older age
4. Type 1 Diabetes Mellitus[4]
5. A history of previous steroid induced intraocular pressure (IOP) elevation
6. Connective tissue disease[5]
7. Penetrating keratoplasty, especially in eyes with Fuchs endothelial dystrophy or keratoconus
8. High myopia[6,7]

In this subset of patients, intraocular pressures should be monitored regularly. Care should be taken to avoid corticosteroids, if possible. If corticosteroids are indicated, the judicious use of an adequate potency and duration should be considered.

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Many studies independently reported that the normal population could be divided into 3 groups based on their response to the topical administration of dexamethasone and bethamethasone:

(1) High responders, 4–6% of the population, developed an intraocular pressure (IOP) above 31 mm Hg or a rise of more than 15 mm Hg above baseline;

(2) Moderate responders, approximately one third of the population, had IOPs between 20 and 31 mm Hg, or a pressure rise of 6–15 mm Hg;

(3) Nonresponders, the remaining two thirds, had pressure increases of less than 6 mm Hg and IOPs of less than 20 mm Hg

Routes of administration

1-Topical Ocular Preparations -IOP rise may occur with corticosteroid drops or ointment applied to the eye or with steroid preparations applied to the skin of the eyelids (Figure 1).

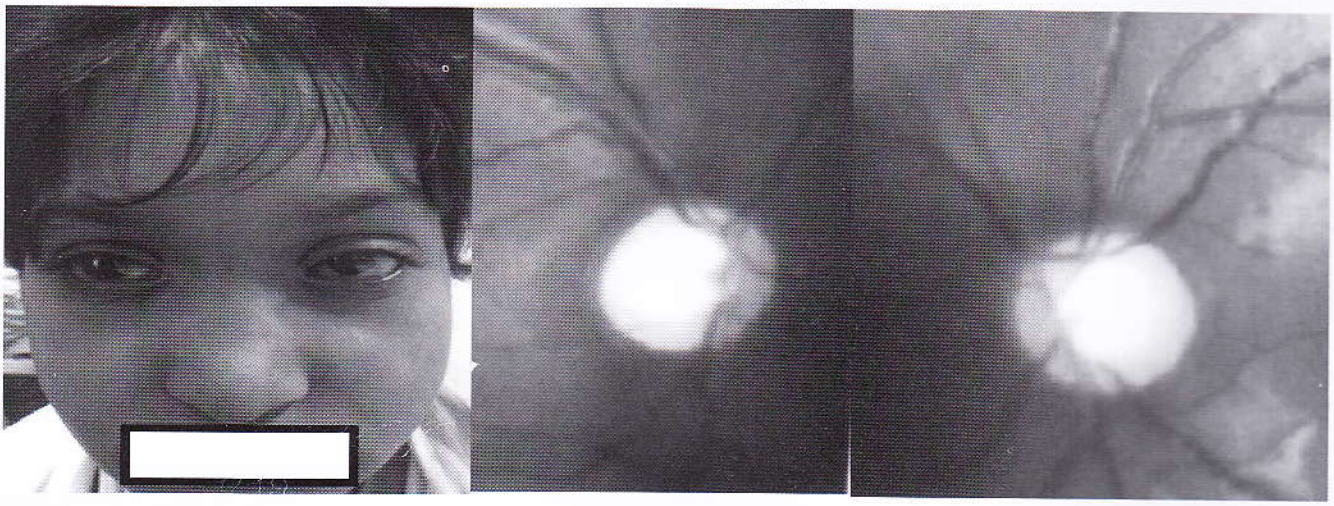

Figure 1- A child with Vernal keratoconjunctivitis OU, presented with glaucoma in both eyes following use of Dexamethasone eye drops for almost a year. She also had posterior subcapsular cataract.

The risk of IOP rise increases with duration of use and may be directly correlated to its anti-inflammatory effect. For example, dexamethasone and prednisolone increase the IOP more frequently than fluoromethalone, hydrocortisone, and rimexolone. Fluoromethalone has poor intraocular penetration with fewer tendencies towards IOP elevation.

According to study [8], inhaled fluticasone at the regular dose used over a short period (6-24 months) was not associated with a significant effect on CCT and IOP measured with noncontact devices in asthmatic children between 5 and 15 years, without a family history of glaucoma.

2. Periocular- This route of steroid delivery includes subconjunctival, sub-tenon's, or retrobulbar injections. Sometimes, it is necessary to excise the depot of steroids in order to control the intraocular pressures

3. Intravitreal IOP elevation develops in about half the patients that receive intravitreal triamcinolone, usually developing between two to four weeks after the injection Smithen *et al*[9] found that 40.4% of patients receiving triamcinolone show a pressure rise to greater than 24 mmHg over at an average of 100 days after treatment.

4. Dermatologic Steroid induced glaucoma may develop after application of steroid preparations applied to the skin of the eyelids. This elevation occurs most frequently with chronic use, such as in patients with atopic dermatitis.

5. Systemic Steroids by mouth (PO) can elevate the IOP as well. The elevation appears to be correlated to the patient's IOP response to topical steroids. Though not common, elevation of IOP has also been noted with the use of inhalational and nasal corticosteroids as well as after intra-articular steroid injections.

Treatment

1-Monitoring of IOP

A baseline measurement of IOP should be taken prior to commencement of corticosteroid therapy. Patients on topical therapy should then have their IOP measured again 2 weeks after initiation of treatment, then every 4 weeks for 2–3 months, then 6-monthly if therapy is to continue.

2-Cessation of corticosteroid treatment

It is ideal to ensure that the suspected corticosteroid is responsible for the glaucoma and if glaucoma is established (and especially if progressive), use of the corticosteroid should be stopped. The chronic corticosteroid response resolves in 1–4 weeks, whereas the rare acute response may resolve within a few days of steroid cessation.[10]

3-Alternative corticosteroid formulations

Topical treatments can be changed to preparations such as fluoromethalone 0.1% or rimexolone 1%, which are claimed to have less effect on IOP[11] or in certain situations to nonsteroidal anti-inflammatory drugs (NSAIDs).

4-Irreversible steroid-induced ocular hypertension/glaucoma

In about 3% of cases, and in particular when there is a family history of glaucoma and/or chronic use of steroid (at least 4 years), the ocular hypertensive response has been shown to be irreversible.[12,13] The management of such cases is no different from that for POAG.

Medical antiglaucomatous therapy

Beta-blockers Topical beta-blockers can be used to control corticosteroid-induced glaucoma, preferably following cessation of steroid therapy and are a popular first-line agent for the condition.

Prostaglandin analogues Concomitant latanoprost has been shown to be as effective as cessation of therapy in controlling the IOP rise associated with corticosteroids so can be useful if steroid treatment must be continued. However, latanoprost has been reported to induce uveitisand is relatively contraindicated in eyes with uveitic glaucoma.

Alpha agonists Brimonidine can be useful in many patients with steroid-induced glaucoma, although there have been reports of brimonidine-induced uveitis in a minority of patients.

Carbonic anhydrase inhibitors Over longer periods, the side effect profile of acetazolamide tends to make it poorly tolerated and it is contraindicated in certain patients, such as those with renal impairment. However, topical carbonic anhydrase inhibitors (dorzolamide and brinzolamide) are of use in the control of IOP due to corticosteroid-induced glaucoma.

Miotics Corticosteroid-induced glaucoma has appeared to be relatively refractory to miotics while the steroid has still been used. Furthermore, in addition to being less popular than more modern agents, miotics are also contraindicated in inflamed eyes (ie those that may require topical steroid therapy) since they can exacerbate the formation of posterior synechiae.

Filtration surgery

Trabeculectomy remains an effective treatment for glaucoma in those patients who have a persistently

raised IOP following cessation of corticosteroid therapy and are refractory to medical therapy.[14] However, as always, the adverse consequences of trabeculectomy or other forms of drainage surgery should be considered in relation to the potential benefits.

Future Therapies

Glucocorticoid receptor blockers have been proposed as useful potential therapeutic agents for treating corticosteroid-induced glaucoma like Anecortave acetate(an analog of cortisol acetate) and Mifepristone (RU 486-6, a peripheral progesterone blocker with antiglucocorticoid properties),which is still under research area.

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