

Systemic toxicity of topical corticosteroids

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Corticosteroids are known to cause many ocular and systemic side effects when administered by oral or parenteral routes. Corticosteroid induced systemic toxicity secondary to topical steroid eye drops is rare. A 6-week-old, male infant was brought to our tertiary eye care center with bilateral congenital cataracts. The child underwent phacoaspiration with primary posterior capsulotomy without intraocular lens implantation in both eyes at an interval of 6 weeks. Child was initiated on topical betamethsone 0.1% eight times a day, tobramycin 0.3% six times a day, homatropine 2% twice a day, and carboxymethylcellulose 0.5% four times a day. Two and four weeks later he underwent surgical membranectomy in the right and left eye respectively

followed by frequent use of topical steroids, initially given 1 hourly and then tapered weekly in the follow-up period. The patient showed increase in intraocular pressure and gain in body weight along with development of cushingoid habitus nearly 6 to 8 weeks after starting topical steroids. These side effects started weaning off following the reduction in dose of topical steroids, suggesting the role of the corticosteroid-related systemic side effects. This case highlights the serious systemic side effects secondary to increased frequency and duration of topical corticosteroid use in infancy. Hence, dosage of topical steroids should be adjusted in its therapeutic range to prevent their ocular and systemic side effects. Therefore, close monitoring is advocated for children using topical corticosteroids to prevent serious ocular and systemic side effects.

Key words: Cushingoid habitus, side effects of corticosteroids, topical corticosteroids

Corticosteroids are known to cause many systemic side effects when administered by oral and parenteral routes.^[1] These include excess weight gain, cushingoid habitus, osteopenia, gastritis, avascular necrosis of femur head, excess body hair growth, premature closure of bony epiphysis, etc.^[2] Ocular side effects such as glaucoma and cataract associated with topical and systemic corticosteroid use are well-recognized.^[3] Systemic toxicity associated with the use of topical corticosteroid eye drops is rare.

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Case Report

A 6-week-old boy was presented to our tertiary eye care center with bilateral white reflex. On examination, both eye congenital cataracts were noted. Ocular ultrasonography was suggestive of normal posterior segment and short axial lengths (16.20 and 16.35mm) in right and left eye, respectively. There was microphthalmos in both eyes. Horizontal corneal diameters were 9 mm in both eyes. Anthropometry and systemic examination was unremarkable. Peripartum history was normal with normal birth weight. There was no evidence of congenital rubella infection. The patient subsequently underwent phacoaspiration with primary posterior capsulotomy without intraocular lens implantation right eye followed by the left eye at an interval of 6 weeks. Patient was started on topical betamethasone 0.1% eight times, tobramycin 0.3% six times, and homatropine 2% two times a day. Excess postoperative inflammation in the form of anterior chamber reaction and fibrin was noted in the immediate postoperative period. Three weeks after right eye surgery revealed visual axis obscuration due to formation of membrane in the pupillary area leading to a smaller pupillary aperture. Right eye required pupilloplasty to clear the visual axis. Following the pupilloplasty, the dose of topical betamethasone 0.1% was increased to 12 times a day in the immediate postoperative period to prevent excess inflammation and subsequent visual axis obscuration. Two weeks later, left eye cataract surgery was performed and was started on intense topical steroids to prevent pupillary membrane formation as was the case in the right eye. At 3-weeks follow-up, examination under anesthesia (inhalational anesthetic, Sevoflurane was used) revealed elevated intraocular pressure (IOP) (with Perkins handheld applanation tonometer) of 30 and 28 mmHg in the right and left eye, respectively. The child subsequently required pupilloplasty in both the eyes due to recurrent visual axis obscuration and was initiated on similar treatment regimen along with antiglaucoma agents. Physical examination at 6 weeks follow-up showed cushingoid habitus with a moon face, buffalo hump at the back of neck, and truncal obesity was noted due to excess centripetal fat deposition mainly in buccal, neck, and trunk regions [Fig. 1a]. Body weight had increased from 3.2 Kg (-3.5Z) to 4.2 Kg (-3.1 Z) during the treatment period of 6 weeks. Weight gain in this period was similar to the age-related weight gain for the child; however, there was altered body fat distribution. Cumulative dose of topical steroid was 0.5 mg/Kg body weight during this period.

Other systemic causes and endocrine abnormalities were ruled out by appropriate investigations. Ultrasound abdomen did not reveal any adrenal mass. On evaluation, it was found that serum adrenocorticotropic hormone (ACTH) levels were suppressed (ACTH level <0.1 pg/mL; reference 5–27 pg/mL). As ACTH levels were low, ACTH-dependent causes of Cushing's syndrome (pituitary hypersecretion, ectopic ACTH tumor) were unlikely. In view of the aforementioned characteristic clinical features, prolonged use of topical steroids and suppressed ACTH level; a diagnosis of exogenous steroid toxicity was considered and topical steroids were gradually tapered. The patient was started on dorzolamide (0.1%) and timolol (0.5%) combination twice a day for control of IOP. He was added on topical nepafenac sodium (0.1%) suspension, while topical steroids were tapered. All systemic features subsequently subsided and intraocular pressure also normalized. At 3 months follow-up there were no cushingoid

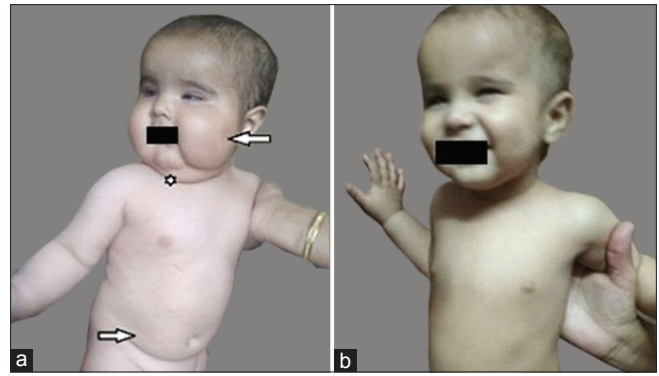


Figure 1: (a) Clinical photograph of the child showing typical Moon face and centripetal deposition of fat especially in buccal, neck, and trunk areas (b) Clinical photograph of the child showing resolution of cushingoid features

features and normalization of ACTH level at 10 pg/mL (5–27 pg/mL) [Fig. 1b]. Weight and height at 6 months of age was 5.5 kg (-3.3 Z) and 60 cm (-2.8 Z), respectively. In view of temporal association with topical steroids and reversal of all corticosteroid toxicity symptoms and laboratory parameters final diagnosis of iatrogenic Cushing's syndrome secondary to ocular steroids was proffered.

Discussion

As studied by Becker's and Armaly: in normal population, nearly 60–70% individuals are mild, 25–30% are intermediate, and nearly 5% are high steroid responders.^[3,4] Use of corticosteroids by any route can lead to rise in intraocular pressure.^[5] The ocular response to steroid induced rise in intraocular pressure is typically found after 4–6 weeks of topical use and the effect goes down subsequently with stoppage of steroid use. Infants are at higher risk of development of systemic toxicity secondary to topical ocular corticosteroid use.^[6] The membranes in the eyes of newborns and infants are thin; so drug absorption and corneal permeation may be more rapid in these groups leading to systemic side effects.^[6] Moreover, ocular corticosteroids do not undergo portal metabolism; hence, frequent ocular steroid use may result in severe systemic side effects compared to the oral route.^[7] Ozerdem *et al.* reported systemic toxicity in an 11-year-old patient due to use of topical eye drops and pericocular steroid injections.^[8] Our case typically showed increase in intraocular pressure and increase in body weight along with development of cushingoid habitus nearly 6–8 weeks after starting frequent topical steroids. Moreover, these side-effects started weaning off following the reduction in the dose of topical steroids; suggesting the role of the corticosteroid-related side effects. Although few case reports suggesting systemic side effects of topical ocular steroids in older children have been reported, to the best of our knowledge systemic corticosteroid toxicity secondary to topical steroid eye drop has not been reported so far in infants.^[6,8–10]

Conclusion

This is the first case report of systemic steroid toxicity secondary to use of topical ocular corticosteroid in infants. Hence, it is very important to observe pediatric patients especially infants on topical steroids drops for signs

of development of systemic toxicity, to which they are particularly very susceptible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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