Iatrogenic Cushing’s syndrome in children presenting at Children’s Hospital Lahore using nappy rash ointments
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Abstract

Objectives: To study the characteristics of infants and children presenting with iatrogenic Cushing’s Syndrome due to nappy rash ointments.

Methods: The descriptive study was conducted at the Children’s Hospital, Lahore, from April to September 2013, and comprised patients presenting with cushingoid features and history of using nappy rash ointments. Patients having Cushing’s Syndrome due to causes other than iatrogenic were excluded and so were those taking oral or parenteral steroids due to skin allergy, renal or respiratory disease. Demographic data, history and examination of all patients were recorded on a proforma and results were analysed using SPSS 16.

Results: Of the total 18 patients, 13(72%) were girls and 5(27%) were boys. Eight (44.4%) patients were younger than 6 months, 6(33.3%) were between 6 months to 1 year, while 4(22.2%) were between 12 and 18 months of age. Clobetasol alone was the most frequently used agent responsible in 13(72%) cases. Duration of use of steroid ointment was as short as 3 weeks to as much as 1 year. All the patients were using disposable diapers. Ointment was prescribed by a doctor in 5(27%) cases and self-prescribed (relative or neighbour) in 13(72%).

Conclusion: Self-medication and prolonged use of potent steroid ointments are major contributors in development of iatrogenic Cushing’s Syndrome in infants and children. Younger age, female gender and use of disposable diapers were other important predisposing factors.

Keywords: iatrogenic Cushing’s syndrome, Nappy rash ointments, Self-medication. (JPMA 65: 463; 2015)

Introduction

Iatrogenic percutaneous administration of glucocorticoids is known to cause Cushing’s Syndrome (CS) in infants. Iatrogenic CS caused by the administration of supra-physiologic doses of glucocorticoids is probably much more common (although underreported) than endogenous causes. It is stated to be the most common cause of CS in children and adolescents. Children are at greater risk of toxicity from topical steroids as they have a large surface area compared to adults. The development of cushingoid signs and symptoms depends upon the potency and pharmacokinetics of the drug as well as the dose and duration of use.

Children with iatrogenic CS present with the same signs and symptoms as spontaneous disease. Classical signs of moon facies, weight gain, central distribution of fat with supraclavicular and subscapular fat pads, hypertrichosis, plethora, skin thinning with appearance of telangiectasias are often present. Complications due to mineralocorticoid and androgenic activity of steroids like hypertension, acne and hirsutism, often seen in endogenous CS are less common in iatrogenic causes.

Diaper dermatitis is the most common paediatric dermatological condition in children. It is most likely to occur in the first 2 years of life. However, children of any age who wear diapers can suffer from it. Management is done mainly by prevention of rash by keeping the nappy area dry and clean. Topical barrier creams or ointments containing water impermeable and soothing substances (petrolatum or zinc oxide paste) can be used. Topical antifungal ointments are indicated if rash persists for more than 3 days, and are to be used for 3 days after the disappearance of rash. When these measures are not sufficient to promote healing, a light application of 0.5-1% topical hydrocortisone ointment after each diaper change for one to two days is often effective. Paediatricians and Family Medicine physicians diagnose and treat the vast majority of affected children. Patients rarely receive (or need) care from a dermatologist for diaper dermatitis. Self-medication is particularly common in developing countries.

Iatrogenic use of pharmacological agents is more common in developing countries due to lack of guidelines regarding dispensing of over-the-counter drugs. There have been case reports from India, Saudi Arabia, Iran and...
Turkey in which infants using steroid containing nappy rash ointments were identified with iatrogenic CS. In our setup iatrogenic CS due to nappy rash ointment application is more common than reported elsewhere in the world. We studied the characteristics of children presenting to us with CS due to iatrogenic use of steroid-containing nappy rash ointments so that this condition may be prevented.

**Subjects and Methods**
The descriptive study was conducted at the Department of Endocrinology, Children’s Hospital, Lahore, from April to September 2013. The study site is a tertiary care hospital that receives patients from all over the province of Punjab. All the patients presenting with cushingoid features and history of using nappy rash ointment who presented for the first time during the study period were included. Diagnosis of iatrogenic CS was made on the basis of history of using nappy rash ointment and presence of classical cushingoid features in the form of moon facies, hypertricosis, plethora, central distribution of fat and obesity (Figures 1-3). Patients having CS due to causes other than iatrogenic were excluded and so were patients taking oral or parenteral steroids due to skin allergy, renal or respiratory disease. Early morning serum adrenocorticotropic hormone (ACTH) and Cortisol level was advised in all the subjects. Demographic data, history and examination of all the patients were recorded on a pretested proforma. Results were analysed using SPSS 16 and expressed in frequencies and percentages.

**Results**
Of the 18 patients in the study, 13(72%) were girls and 5(27%) were boys. Overall age ranged from 2 months 10 days to 18 months. Eight (44.4%) patients were younger than 6 months, 6(33.3%) were between 6 months to 1 year, while 4(22.2%) were between 12 and 18 months of age. Clobetasol alone was the most frequently used agent responsible in 13(72%) cases; Clobaderm ointment in 8(44.4%) and Dermovat in 5(27.7%). One (5.5%) patient was using Advantan cream (methylprednisolone aceponate). One (5.5%) was applying Hydrozole ointment (hydrocortisone-clotrimazole). Topical ointment was unknown in 3(16.6%) patients.

Duration of use of steroid ointment was as short as 3 weeks to as much as 1 year. The mean duration of use of ointment was 118±117.6 days. Duration of use of ointment was less than 2 months in 5(27.7%) patients, between 2 and 4 months in 6(33.3%), between 4 and 6 months in 3(16.6%), between 6 months and 1 year in 1 and over 1 year in 3 (16.6%) cases.

All the patients were using disposable diapers. Ointment
was prescribed by doctor in 5(27%) cases and self-prescribed (relative or neighbour) in 13(72%).

Discussion

All the patients in our study were using steroid ointments on nappy area for diaper dermatitis. In our study, self-medication was done in 13 (72%) cases, where the drug prescriber was either a family member or a neighbour. Dispensing of potent topical steroid ointments as over-the-counter medicine is common in developing countries, where rules and regulations for dispensing over-the-counter drugs are lacking. This may be the reason that most of the cases reported are from developing countries like India, Iran, Saudi Arabia and Turkey. Self-medication was found responsible in other cases reported as well. Occlusion and inflammation also increases systemic absorption of these active medications. All the cases in our study were using disposable diapers. The development of cushingoid features and drug-induced adrenal suppression are more prone to occur if the corticosteroid is applied inappropriately as on damp and occluded skin of sensitive genital area that is also inflamed.

Age of the patients in our study ranged from 2 months 10 days to 18 months. Two-third of the cases were below 1 year of age. These results were consistent with other similar case reports. In all cases of CS due to nappy rash ointment, age of patients reported is less than a year. One study reported six infants (four girls, two boys) aged between 3 and 8 months who were exposed to potent topical corticosteroids (clobetasol propionate and diflucortolone valerate) by the mother’s application without prescription. In our study, female gender predominated with 13 girls compared to 8 boys. Absorption coefficient is proven to be increased in female compared to male skin in recent studies. In addition, absorption of steroids from female genital tract may be the cause of this striking gender difference in our study group. Clobetasol 17-propionate is one of the most potent steroids. Its effect is 1000 times greater compared to hydrocortisone. In our study, Clobetasol was the most frequently used agent responsible in 13(72%) cases, Clobaderm ointment in 8 and Dermovat in 5 cases. Same agent was found responsible in other case reports from Turkey, Saudi Arabia, Iran and India where this medicine was dispensed as an over-the-counter drug. Hydrocortisone in combination with anti-fungal ointment was the causative agent in one of the cases in our study. Though less potent than Clobetasol, hydrocortisone has the highest dermal diffusivity and dermal penetration, and the accumulation of hydrocortisone and corticosterone are proven to be higher than that of the other steroids. Duration of use of ointment was as short as 3 weeks in our study in a 2 month 10 days old infant to as much as 1 year before every routine diaper change. More than half of the cases were using the ointment for less than 4 months duration. Multiple factors affect the absorption of topical steroids and toxicity may occur even when these ointments are used for short duration. In our study, the youngest patient was 2 months 10 days old whose mother was applying Clobetasol ointment before every diaper change (4-5 times a day) for the preceding 3 weeks only.

Conclusion

Self-medication and prolonged use of potent steroid ointments are common in infants having CS due to iatrogenic use of steroid-containing nappy rash ointments. Younger age, female gender and use of disposable diapers are other important features. Paediatricians should be well aware of this common but less-reported complication of nappy rash ointments containing steroids. Parents of any infant with cushingoid features and drug-induced adrenal suppression are more prone to occur if the corticosteroid is applied inappropriately as on damp and occluded skin of sensitive genital area that is also inflamed.
features should be questioned about the use of any ointment on skin, particularly the nappy area. As majority of cases observed were due to self-medication, public awareness in this regards should be created through print and electronic media. General practitioners and paediatricians should also play their role in discouraging the use of nappy rash ointments without prescriptions and for prolonged duration.

References