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Review Article

The Unattended Crisis of Topical Steroid Misuse: A Review

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Abstract

Topical corticosteroids, being one of the most frequently prescribed classes of drugs in clinical practice today, are very often subjected to misuse. A vast majority of the patients are unaware of the untoward effects that may arise even with the right administration of these drugs. The ethical use and the regulatory challenges concerning the use of topical corticosteroids are the issues of the hour. The pediatric population is highly susceptible due to variability in body surface area, skin thickness and texture, and the resulting increased permeability predisposes them to systemic side effects like Cushing's syndrome and adrenocortical insufficiency. Overutilization of steroids also augments the susceptibility of an individual to hospital and community acquired skin infections. With this review, we aim to bring the ever expanding trend of steroid misuse to the light by evaluating the risk vs. benefit factor. Steroid misuse is an emerging public health concern and in order to address this issue, analysis and comparison of prescribing pattern, understanding of topical administration and side effects associated with topical steroids are vital.

Introduction

The pivotal paper of Sulzberger and Witten in 1952 titled "The effect of topically applied compound F in selected dermatoses", introduced topical steroids into dermatology. The compound F mentioned in this paper was later renamed as hydrocortisone. This improved the treatment of dermatoses drastically. However, on the contrary to all their advantages, the misuse of these preparations causes trouble some local effects and potentially serious systemic effects [1].

The role of topical corticosteroids in the treatment of various conditions can be attributed to the inhibition of endogenous inflammatory mediators such as kinin, histamine, liposomal enzymes and prostaglandins, resulting in immunosuppression and an overall anti-inflammatory activity. In addition to the anti-inflammatory action, topical corticosteroids tend to have anti-mitotic effect on tissues including the human epidermis [2].

Recent developments led to these preparations being used in combination with antibacterial and antifungal agents, which proves to be more effective. The irrational prescribing patterns, over the counter availability and the fixed dose combination system of the drug stand out to be the major causes of the misuse [1].

Untoward Effects of Topical Steroids

Most of the adverse effects associated with topical steroid use depend upon multiple factors such as the chemical structure of topical corticosteroid, vehicle employed, site of application, frequency and the method of application [3].

Although local effects are less severe, they are alarmingly common. Local effects include cutaneous atrophy, tachyphylaxis, contact dermatitis, Stellate paseudoscars, hypopigmentation, hypertrichosis, purpura, milia, erythema, acneiform dermatitis, rosacea and cataract. Skin atrophy characterized by epidermal thinning and dermal changes is the most frequent localized effect. Other local effects such astelangiectasia, localized fine hair growth, bruising and erythema are relatively less common. Delayed wound healing and local hypersensitivity are other manifestations. Systemic effects, namely hypothalamic pituitary adrenal axis suppression, Cushing's syndrome and femoral head osteonecrosis, can be potentially serious [4].

Frequency of Application: How Often Should Steroids Be Administered?

The Fingertip Unit (FTU) scale, used to quantify the application of topical corticosteroids, measures the amount of drug expelled from a 5mm nozzle. Increasing the concentration does increase penetration, however not proportionally. For example, a study by Chabassol et al. showed that application of topical steroids thrice a day yields better results than once a day, but that any further increase in the frequency of applications daily has no additional therapeutic benefits [2]. A proper understanding of the dermatopharmacokinetics renders a more rational approach. Interestingly, when applied under an occlusion, steroids show a "reservoir effect" which helps them reside in the stratum corneum for up to two weeks and in the absence of occlusion, for up to two days [5].

In the early 1980s, Hehir and his colleagues used radioimmunoassay to investigate the pharmacokinetics of clobetasol propionate and clobetasol butyrate in patients with eczema and psoriasis. The study revealed the measurable maxima of both the drugs 48 hours after the single application, which suggests that once daily usage may give as good or better clinical results as multiple times daily. By reducing the frequency of application of the topical corticosteroids, the problems of tachyphylaxis, systemic toxicity, local side effects, expense and patient adherence can all be resolved [5].

Ethical Issues Governing Topical Steroid Use

Ethical prescribing of topical steroids is critical in modern day clinical practice; however it's easier said than done. In India, mild to super potent topical corticosteroids are available as OTC medication [6].

Autonomy refers to the patient's right to be informed about his treatment, unlike the old paternalistic system where the health care advises his patients to take his medications without further discussion. When it comes to topical steroid therapy, the patient should also be informed about the alternative treatment options [7].

Medical practitioners are often obliged to deal with patients with lack of awareness who demand that topical steroids be prescribed to them. Consequently, it becomes the moral duty of the practitioner to avoid satisfying the patient's request. Consider the example of a patient presenting with undiagnosed rash demands steroids, even though safer options like topical antipruritic and oral antihistamines would suffice. This is where nonmaleficence comes into account [7].

Ratio of Beneficence *vs.* Autonomy has to be considered. Naturally, the patient often disagrees with the recommendations of the doctor. Consider a patient who has been routinely using topical corticosteroids for the management of eczema. The doctor may prescribe oral immunosuppressive agents like azathioprine and taper the use of topical corticosteroid. In such situations the patient should be counseled about the ill effects associated with the routine use of potent corticosteroids [7].

Currently, both the physicians as well as the patients contribute to the issues associated with the ethical and rational use of topical corticosteroids. In a populated country like India, there is a shortcoming in the number of dermatologists considering the number of patients. Hence it is imperative that increased awareness about these drugs are provided to all health care professionals, so that these drugs are used only when indicated and with the assurance of maximum safety [7].

Regulatory Challenges for Topical Corticosteroids in India

Fixed dose combinations: boon or bane?

The CDSCO (Central Drugs Standard Control Organization) website provides information regarding the dermatological indications of topical corticosteroids, however its off-label use seem to be predominant in India. Fixed dose combinations of topical corticosteroids with antibacterial or antifungal agents are flooding in the India pharmaceutical market presently, carrying a potential threat. These fixed dose combinations give symptomatic relief but at the same time obscures the underlying unresolved condition. Ironically, in 2013, top selling formulations of topical steroids in India were fixed dose combinations of topical corticosteroid with antibacterial and antifungal agents [7].

The increasing misuse as cosmetics

None of the fixed dose combinations marketed in India is approved by CDSCO as fairness creams. However, there are three formulations approved for the treatment of hyperpigmentation. Prevalence of the use of topical corticosteroid as fairness cream is very high despite the fact that these drugs are not approved for the indication. Aesthetic benefits are mere in comparison to the long term risks associated with their chronic usage. According to Drugs and Cosmetics Act (D and C act) of 1940, all the topical corticosteroids fall under the category of Schedule H drugs, but statistically, the topical corticosteroids are one of the most extensively sold OTC drug. Indian association of dermatologists, venereologist and leprologists has initiated a new venture called Taskforce against Topical Steroid Abuse (ITATSA) to look into and address the issues related to topical corticosteroid abuse. Stringent regulations, similar to the recent Schedule H1 regulations, to tone down the growing menace of antibiotic resistance are essential to regulate the topical corticosteroid drug market in India [7].

How does the pediatric population bear the brunt of steroid misuse?

Pediatric population is more susceptible to the side effects of topical drugs than adults. The effects and side effects of topical corticosteroids largely depend on the skin thickness, potency of the drug used and the amount of absorption. The skin permeation of the drug is enhanced in children with much thinner skin. Infants who suffer from diaper rashes are prone to the overuse of topical corticosteroids. Parents apply the medication under the diaper and the occlusive effects of the diaper add on to the normal penetration of the drug. Usage of low potency topical corticosteroids for a short period of time applied over a limited area is ideal in infants and children [8,9].

In pediatrics, milder agents like emollients, topical calcineurin inhibitors or antipruritic agents such as calamine should be preferred over topical steroids. Best method to control the usage and misuse is to counsel the parents or the guardians, with regard to the risks and benefits of topical steroids. General practitioners who are not actual dermatologists injudiciously prescribe them in children leading to a phenomenal increase in incidence of side effects associated with these drugs. Steroid dependence has also increased dramatically over time owing to the same reason [10].

The Forgotten Risk of Cushing's syndrome

Depression of the adrenal function is seen in various dermatological cases. Untoward effects however vary depending on the duration of usage and the potency of the corticosteroid. Super-potent corticosteroids can cause Cushing's syndrome concomitant with hypothalamic-pituitary-adrenal axis suppression. From the case reports reviewed, most of the exogenous Cushing's syndrome is iatrogenic. Almost all the children with exogenous Cushing's syndrome have used or continue to use topical steroids and surprisingly more than 90% of all the children use these potent medications for diaper dermatitis [11].

Another study from Lahore, also examined the characteristics of infants and children presenting with iatrogenic Cushing's syndrome due to nappy rash ointments. In this study conducted by Sattar et al. the development of cushingoid features and the occurrence of drug induced adrenal suppression are more likely when the drug is applied on damp or inflamed genital area [12].

The Present Scenario: India and Its Neighbors

The free availability of topical corticosteroids in India has made them a class of drugs with high misuse potential. Consequently, patients are at increased risk of both local and systemic side effects. There are various reasons for the misuse of these drugs which varies from wrong prescription, marketing techniques by pharmaceutical companies, free availability and lack of stringent regulations. The committee formed by the IAVDL (Indian Association of Dermatologists, Venerologists and Leprologists) promises to bring down the ongoing misuse of these drugs by providing public awareness, running media campaigns, backed by central and state authorities [13].

Recently, the Delhi High Court issued notices to the Centre to ensure that potent topical steroids are sold only with a prescription. This plea also questioned CDSCO's approval for the use and sale of unscientific combinations of steroids [14].

No proper health insurance plans are accessible to the citizens in Nepal. In a developing country like Nepal, any individual with health issues hesitates to visit a doctor. Pre doctor trial method is common among the patients in Nepal. Major problem for steroid abuse in Nepal is ignorance and illiteracy. There are two major drawbacks associated with this method; firstly the underlying disease is not cured, secondly new symptoms in addition to the existing ones [15]. The condition in Bangladesh is no different from that of Nepal, ignorance and illiteracy stands out to be the major cause in Bangladesh too. Rampant OTC sale, the quacks, general physicians, non-dermatological physicians and even homeopathic practitioners prescribe these potent drugs without realizing the dangerous systemic side effects they possess. Ignorant patients misuse these products as fairness creams or as anti-fungal agents [16].

Topical steroid misuse has haunted South East Asia since the late 20th century, mostly due to the National Health Insurance (NHI) system and the drug price margin issue. The Atopic Dermatitis Treatment Guidelines published in 2000, which emphasize on the safety of topical steroids, did not discuss the potential adverse effects such as red skin syndrome associated with these agents [17]. The use of topical steroids in the Middle East is quite common, owing to the lenient dispensing regulations. However the use of these medications is limited in the pediatric population due to the fear of possible side effects. The use of topical steroids in adults is limited to the treatment of pigmentary disorders. Considering the high prevalence of similar skin conditions in the Middle East, the abuse potential is relatively high. The occurrence of adverse events, such as atrophy, is common in this population group [18].

Clinical Data from Various Countries

The studies conducted all over the world, particularly in the South Asian countries were analyzed. A study conducted in Ethiopia by Zewdu et al. showed that out of the 384 outpatients in Dermatology department of a tertiary care hospital, 27.1% presented with inappropriate use of topical steroids [19]. Another study by Sinha et al. aiming to evaluate the prevalence of steroid misuse among rural masses revealed that 74% of all dermatology patients were prescribed with one or more corticosteroids [20]. A prospective multicenter questionnaire based study conducted in 12 dermatology centers all over India, claims that out of the 2926 patients recruited, 14.8% were using topical corticosteroids, 90.5% of which experienced undesired effects [21]. A cross sectional descriptive study among outpatients in the dermatology department of a rural tertiary care teaching hospital revealed that the inadequate prescribing information is the major cause for the increased misuse of these drugs [22]. Similar study conducted among the African population by Nnoruka et al. evaluated the depigmenting efficacy of these drugs, and revealed that the combination of a very potent corticosteroid in addition to other depigmenting agents show miraculous results [23].

A study to evaluate the awareness about the corticosteroids was performed at a tertiary care hospital and 80.9% of all the dermatology patients were aware of at least one or more topical corticosteroids [24]. Another study, which aimed to analyze the magnitude of the adverse effects of topical steroids, found that these side effects were most common among the age group 21-30 years. Abuse potential was found to be higher in those who used these drugs with the recommendation from friends or other family member [25,28]. Another cross sectional observational questionnaire based study which assessed the misuse of topical corticosteroids in terms of indication, frequency and dose, reported that 11.77% presented with inappropriate use of topical corticosteroids and the most common indication was fungal infection and acne [26]. A prescribing pattern analysis of topical corticosteroids in a tertiary care hospital showed that betamethasone dipropionate was the most commonly prescribed topical corticosteroid [27].

Misuse of topical corticosteroids has a huge impact on dermatological practice, leading to a great number of visits to the dermatologist [28]. Unwarranted cosmetic use of topical corticosteroids in combination with or without fairness creams is quite common at present [29,31]. A study by Bhat et al. concluded that some of the steroid induced systemic effects can be managed by combination of oral antibiotics and topical tacrolimus [30]. The study also revealed that the majority of the steroid users were women. Similar studies revealed that almost none of the patients were completely aware of untoward side effects caused by these drugs [32,33].

Steroid Therapy and Opportunistic Infections

Steroid therapy often renders an individual in an immunosuppressed state, thus elevating the risk of opportunistic infections. The risk of certain infections such as Pneumocystis Jirovecci Pneumonia (PJP), herpes and tuberculosis are well documented. Even though the risk of acquiring other opportunistic infections such as aspergillosis, nontuberculous mycobacterial disease, candidiasis, and cryptococcosis is clinically possible, the evidence base is less robust. Strongyloidiasis, a parasitic infection acquired through direct contact with soil, affects 30-100 million people worldwide. Individuals undergoing steroid therapy are at an increased risk for hyperinfection syndrome and disseminated strongyloidiasis. Although the mortality rate associated with this infection is quite high, the evaluation of risk is often difficult because of the scarcity in clinical data [33].

Statistically, up to ten percent of all women are prone to rosacea, which can be triggered by the use of topical steroids for the treatment of other eczemas. Periorificial or perioral dermatitis is most common manifestation induced by the inappropriate facial use of steroid. The risks of these opportunistic infections are greater with the potent steroids, and are further augmented when these preparations are applied under occlusion [33].

Conclusion

Topical steroid misuse continues to proliferate in the field of medicine. Lack of awareness among the clinicians, practitioners, cosmeticians as well as the patients, is the major underlying cause for this irrational utilization of this potent class of drugs. Strict and stringent regulatory means should be adopted for monitoring irrational use of topical steroids. Timely identification and proper management of systemic side effects is highly essential in order to prevent a public health crisis.

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