Ministry Of Higher Education
And Scientific Research

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Designing a Campaign On Topical steroids misuse

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بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

﴿ وَقُلْ رَبِّ زِدْنِي عِلْمًا ﴾

صدق الله العظيم

List of subjects :

Dedication	4
Aim	**4**
Chapter one : introduction	**5**
Potency	**8**
Adverse effects	**10**
Study on topical steroids	**18**
Chapter tow : methodology	**19**
Chapter three : Conclusion discussion recommendations	**22**
References	25

Dedication :

We dedicate this work to our families and to the Iraqi army

Aim :

Is to make a campaign that raise awareness on topical steroids' misuse and side effects

Chapter One

Introduction

1.1 Introduction

1.1.1 Corticosteroids:

Corticosteroids are a class of steroid hormones that are produced in the adrenal cortex of vertebrates, as well as the synthetic analogues of these hormones. Two main classes of corticosteroids, glucocorticoids and mineralocorticoids , are involved in a wide range of physiologic processes, including stress response, immune response, and regulation of inflammation, carbohydrate metabolism, protein catabolism, blood electrolyte levels, and behavior.[1]

Some common naturally occurring steroid hormones are cortisol ($C_{21}H_{30}O_5$), corticosterone ($C_{21}H_{30}O_4$), cortisone ($C_{21}H_{28}O_5$) and aldosterone ($C_{21}H_{28}O_5$). (Note that aldosterone and cortisone share the same chemical formula but the structures are different.) The main corticosteroids produced by the adrenal cortex are cortisol and aldosterone. [2]

1.1.2 Topical steroids:

The introduction of topical corticosteroids (TC) by Sulzberger and Witten in 1952 is considered to be the most significant landmark in the history of therapy of dermatological disorders.[3] This historical event was gradually, followed by the introduction of a large number of newer TC molecules of varying potency rendering the therapy of various inflammatory cutaneous disorders more effective and less time consuming. Although, it is this very usefulness of the drug which has become a double edged sword and made it vulnerable to now an alarming proportion with constantly rising instances of abuse and misuse leading to serious local, systemic, and psychological side effects. Such misuse occurs more with TC of higher potency and on softer areas of the body particularly the face and genitalia. The end-users of TC are hapless patients. They tend to overuse TCs beyond the time limit set by clinicians by repeating prescriptions. Of more concern is the miss use of TCs as fairness creams. Many people become victims to the craze of beautification leading to a virtual epidemic of monomorphic acne, steroid

atrophy, steroid rosacea, telangiectasia, perioral dermatitis, striae and other manifestations of a condition which has been collectively described steroid as topical damaged facies (TSDF).[4] Children are particularly prone to develop systemic side effects when potent TCs are used on their softer skin with enhanced capacity for absorption as also the issue of weight versus body surface.[5] TCs are the choice of therapy in atopic children however, steroid-phobia among parents of such children is now a well-documented phenomenon. At the opposite end of the spectrum lies the danger of steroid addiction. While TC addiction can manifest with features of TSDF, its withdrawal is also accompanied by repeated flares of photosensitivity, erythema, papules and pustules accompanied by intense itching and burning, features of the so called "TSDF." TC misuse has thus become almost an epidemic needing immediate attention from all quarters. Side effects due to topical steroids (TS) are more prevalent than systemic reactions.The most common side effects are localized to sites of application.[6] The mechanisms responsible for their effectiveness are also responsible for their adverse effects.[7]

1.2 Potencies of topical steroids

USA SYSTEM

The USA system utilizes 7 classes, which are classified by their ability to constrict capillaries and cause skin blanching. Class I is the strongest, or super potent. Class VII is the weakest and mildest. [8]

Group I

Very potent: up to 600 times stronger than hydrocortisone

- Clobetasol propionate 0.05% (Dermovate)
- Betamethasone dipropionate 0.25% (Diprolene)
- Halobetasol propionate 0.05% (Ultravate, Halox)
- Diflorasone diacetate 0.05% (Psorcon)

GROUP II

- Fluocinonide 0.05% (Lidex)
- Halcinonide 0.05% (Halog)
- Amcinonide 0.05% (Cyclocort)
- Desoximetasone 0.25% (Topicort)

GROUP III

- Triamcinolone acetonide 0.5% (Kenalog, Aristocort cream)
- Mometasone furoate 0.1% (Elocon, Elocom ointment)
- Fluticasone propionate 0.005% (Cutivate)
- Betamethasone dipropionate 0.05% (Diprosone)
- Halometasone 0.05%

GROUP IV

- Fluocinolone acetonide 0.01-0.2% (Synalar, Synemol, Fluonid)
- Hydrocortisone valerate 0.2% (Westcort)
- Hydrocortisone butyrate 0.1% (Locoid)

- Flurandrenolide 0.05% (Cordran)
- Triamcinolone acetonide 0.1% (Kenalog, Aristocort A ointment)
- Mometasone furoate 0.1% (Elocon cream, lotion)

GROUP V

- Fluticasone propionate 0.05% (Cutivate cream)
- Desonide 0.05% (Tridesilon, DesOwen ointment)
- Fluocinolone acetonide 0.025% (Synalar, Synemol cream)
- Hydrocortisone valerate 0.2% (Westcort cream)

GROUP VI

- Alclometasone dipropionate 0.05% (Aclovate cream, ointment)
- Triamcinolone acetonide 0.025% (Aristocort A cream, Kenalog lotion)
- Fluocinolone acetonide 0.01% (Capex shampoo, Dermasmooth)
- Desonide 0.05% (DesOwen cream, lotion)

GROUP VII

The weakest class of topical steroids. Has poor lipid permeability, and can not penetrate mucous membranes well.

- Hydrocortisone 2.5% (Hytone cream, lotion, ointment)
- Hydrocortisone 1% (Many over-the-counter brands)

1.3 Adverse effects :

1.3.1 Local side effects

These tend to occur with prolonged treatment and depend on potency of TS, its vehicle and site of application. The most common include atrophy, striae, rosacea, perioral dermatitis, acne and purpura. Hypertrichosis, pigment alteration, delayed wound healing and exacerbation of skin infections are less frequent.[7]

1.3.2 SYSTEMIC ADVERSE EFFECTS

Systemic adverse effects from TS have also been described and they are more likely to develop when highly potent TS are used for prolonged periods on thin skin (e.g. face) or on raw/inflamed surfaces.[6,7]

1.3.3 SUPPRESSION OF THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS

Hypothalamic-pituitary adrenal axis suppression is known to occur with all TS. Betamethasone dipropionate and diflorasone diacetate have an increased ability to suppress adrenal function. Around 14g/week of clobetasol propionate ointment may induce suppression in children, while 49g/week of betamethasone dipropionate reduces plasma cortisol levels. Temporary reversible suppression is seen with 49 g of superpotent TS used for 2 weeks. Children and babies have a high ratio of surface area to body volume hence are more likely develop HPA axis due to systemic absorption. Iatrogenic Cushing syndrome, corticosteroid-related Addison crises, growth retardation and death are also reported. The reactivity of the HPA axis can be assessed with the adrenocorticotropin hormone test. Recovery is time-dependent and occurs spontaneously.[6,7,9]

HYPERGLYCEMIA AND DIABETES MELLITUS

Hyperglycemia and the unmasking of latent diabetes mellitus can occur after prolonged application and high percutaneous absorption of TS, also systemically absorbed TS may precipitate or exacerbate hyperglycemia, especially in patients with preexisting hepatic disease. [9]

ATROPHY-THE COMMONEST SIDE EFFECT

Skin atrophy is the commonest side effect, reported to be cause by all TS. Epstein Et Al. first reported it from use of topical triamcinolone acetonide [9].Atrophic changes can affect both epidermis and dermis. Microscopic degenerative changes in epidermis and evident following 3-14 days of treatment. Initially epidermis becomes thin due to reduction in epidermal cell size, which reflects a decreased metabolic activity. After prolonged exposure there is a decrease in cell layers, that is,stratum granulosum disappears and stratum corneum becomes thin.Synthesis of stratum corneum lipids and keratohyalin granules and formation of corneodesmosomes (required for structural integrity of stratum corneum) and suppressed. Inhibitors of the function of melanocytes may occur, giving rise to localized hypopigmentation. [6,7] TS induces resorption of mucopolyysaccharide ground substance in the dermis. Repeated use in the same area causes epidermal thinning and changes in connective tissue of dermis leading to lax, transparent, wrinkled and shiny skin lone with striae, fragility, hypopigmentation and prominence of underlying veins. The loss connective tissue support from dermal vasculature results in erythema, telangiectasia and purpura.[6] Degree of slin atrophy is influenced by age, body site ,potency and presence of occlusion of collagen synthesis. Dermal atrophy is caused by decreased fibroblast growth and reduced synthesis of collagen, acid mucopolysaccharides and simulation of human dermal microvascular endothelial cells. Intertriginous areas are particularly susceptible due to thinning skin, increased moisture, elevated temperature and partial occlusion provided by the skin in these sites.[9] The atrophy is reversible on stoppage of TS, but the normalization may take months.[10]

1.3.6 STRIAE

Striae due to TS use need to be distinguished from those that occur due to excessive weight gain and pregnancy.[9]

1.3.7 CONTACT ALLERGY

Contact hypersensitivity to TS may cause persistence or worsening of skin diseases. It is rare, but its risk increases with prolonged exposure. Nonfluorinated TS (e.g, hydrocortisone hydrocortisone-17-butyrate, and budesonide) result in a higher prevalence of contact allergy in comparison with fluorinated compounds.

Binding to the amino acid arginine is probably required for development of contact allergy.[9]

Contact sensitivity can develop not only to constituents (e.g. lanolin, preservatives such as parabens and antibiotics) of the preparation, but also to the steroid molecule. Sensitivity to more than one TS is common. Risk factors for development of contact sensitivity include history of multiple patch test positivity to non-TS allergen, treatment resistant eczema, leg ulcers, stasis dermatitis, perineal dermatitis and chronic actinic dermatitis. It presents as chronic dermatitis not responding to locally applied steroids or rarely, as acute eczema, urticaria, acute local edema, immediate-type reaction, or id eruption like spread over the body.[6,7,11]

1.3.7 INFECTIONS

Mucocutaneous infections (tinea versicolor, onychomycosis due to ***Trichophyton*** and ***Candida*** species, dermatophytosis) are common during treatment with TS, occurring early in the therapy. The incidence varies between 16% and 43%. When dermatophyte infections are treated with TS, the symptoms and signs improve transiently, giving rise to tinea incognito. TS suppress the normal cutaneous immune response to dermatophytes leading to enchantment of fungal infections. An immune mediated phenomenon called "tinea pseudoimbricata" is a particular type of tinea incognito which has been described by one of the authors.[12] Pruritus in scabies improves by TS but infestation persists unless scabicidal treatment is given. Granuloma gluteale infantum a persistent reddish-purple, granulomatous, papulonodular eruption seen on buttocks, thighs or inguinal fold in children, is a well-known consequence of diaper dermatitis being treated with TS, caused by impairment of immune response to ***Candida*** by TS.[6]

Similar effects on mitigation or prolongation of herpes simplex, molluscum contagiosum and scabies infection have also been reported; hence TS should not be used in presence of these infections. TS also facilitate proliferation of ***Propionibacterium acnes*** and ***Demodex folliculoroum*** leading to acne-rosacea like condition. Reactivation of Kaposi sarcoma has also been reported.[9,13]

1.3.8 ACNEIFORM ERUPTIONS

Systemic corticosteroid therapy, in some cases intravenous or inhaled TS are known to induce acneiform lesions. The eruption consists of small and uniformly sized (monomorphic) inflammatory papules and pustules with few or no comedones, located predominantly on trunk and extremities, with less involvement of the face. In the case of inhaled steroids, lesions occur in and around nose or

mouth. Anti-inflammatory effects of TS may initially suppress inflammatory lesions and erythema, but flare-ups occur on stopping TS. The eruption subsequently resolves after discontinuation of the TS.

Topical steroids induce comedone formation by rendering follicular epithelium more responsive to comedogenesis. They also lead to increased concentration of free fatty acids in skin surface lipids and increased numbers of bacteria in the pilosebaceous duct. Free fatty acids, formed in pilosebaceous ducts by breakdown of triglycerides in the sebaceous secretion, may contribute to comedogenesis.[14,15]

1.3.9 ROSACEA

Topical steroids induced rosacea is seen in middle-aged woman, presenting with papules and pustules. These are initially controlled with low potency TS, but lesions may reappear and require continued use of higher potency TS.[9]

1.3.10 PERIORAL DERMATITIS

Perioral dermatitis occurs in females on the face and is caused by long term use of potent TS on face. It presents as follicular papules and pustules on an erythematous base seen in a perioral distribution, with sparing of skin adjacent to the vermilion border. It is also seen in men and children.[9]

1.3.11 HYPERTRICHOSIS

Steroids promote vellus hair growth by unknown mechanism. Local and disseminated hypertrichosis due to TS is rare, seen commonly with systemic steroids. Even months after withdrawal of TS the darker hairs may persist.[9]

1.3.12 HYPER/HYPOPIGMENTATION

Hypopigmentation after topical use is quite common, but not noticed frequently in very light skinned individuals. People with Type IV to VI are particularly affected. TS probably interfere with the melanin synthesis by smaller melanocytes, causing patchy areas of hypopigmentation which are reversible after discontinuation of steroids. Hyperpigmentation after intralesional steroids has been well-documented.[9]

1.3.13 PURPURA, STELLATE PSEUDOSCARS, AND ULCERATIONS

These develop after severe steroid induced dermal atrophy and loss of intercellular substance, causing blood vessels to lose their dermal matrix support. The resulting fragility of dermal vessels leads to purpuric, irregularly shaped, hypopigmented,

depressed pseudoscars over extremities. Continued misuse of TS can also lead to ulceration.[9]

1.3.14 TACHYPHYLAXIS

Tachyphylaxis is characterized by decreasing efficacy of TS during continued treatment. It occurs commonly in psoriasis patients.[13] It may reflect patient noncompliance, normal variance in disease severity unrelated to therapy, or inability of TS to completely clear the disease. Withdrawal of TS is followed by a disease flare. As the tissue becomes less sensitive (tachyphylaxis), increasingly potent preparations are required to achieve comparable effects, leading to more severe side effects.[9] Tachyphylaxis can be quantified by vasoconstrictor assay and inhibition of fibroblast proliferation.[6,7]

1.3.15 REBOUND PHENOMENON

Withdrawal of potent TS applied to the extensive area of psoriasis for a prolonged period may result in a relapse or a papulopustular flare and may even precipitate unstable or severe generalized pustular psoriasis. This is especially likely when steroids are used in large quantities or applied under occlusion. vascular effect of TS is vasoconstriction of superficial small vessels, followed by rebound vasodilatation which may become fixed after prolonged treatment and may be more conspicuous, as a result, of dermal and epidermal atrophy. Similarly, abrupt withdrawal can cause eczema flares.[6,7]

1.3.16 STEROID ADDICTION

Steroid addiction is known to occur after inadvertent application of potent TS usually on the face.[9] Patients with steroid addiction have acne, rosacea, perioral dermatitis, or telangiectasia and continue its use, fearing that there may be flare of their condition on steroid withdrawal. Three phases have been described:

(1) Initial treatment improves pustulation, pruritus, erythema and scaling;

(2) with continued use, local immunosuppression increases microbial growth and

(3) on treatment withdrawal, rebound flares of itching, redness, postulation and scaling are seen.[7] “Red burning skin syndrome” may be the presentation in some cases.[9]

1.3.17 TOPICAL STEROID-DEPENDENT FACE

Misuse of TS on the face is seen all over India and its incidence appears to be increasing rapidly. TSDF has also been described under various names like steroid addiction, dermatitis rosaceaformis steroidica and red face syndrome. In this condition after long term application of TS on the face, there is severe rebound erythema, burning and scaling on the face on attempting to stop the application of TS.[16]

1.3.18 OCULAR SIDE EFFECTS

There are few reports of such ocular complications due to TS.[7,11] Use of TS around eyes can rarely lead to glaucoma as penetration of TS is 300 times greater through the eyelid as compared to other body sites. Blindness due to glaucoma following extended TS use on the face is reported.[9]

1.3.19 EFFECT ON WOUND HEALING

Topical steroids have demonstrated to impair wound healing and re-epithelialization in animal and human models.[7] The effects are on keratinocytes (epidermal atrophy, delayed reepithelialization), fibroblasts (reduced collagen and ground substance), vascular connective tissue support and angiogenesis (delayed granulation tissue formation).[9]

1.3.20 ALTERATIONS IN SKIN ELASTICITY AND MECHANICAL PROPERTIES

Topical steroids are known to decrease skin elasticity. This can be assessed by pulling the skin and observing incomplete retraction on mechanical stress cessation.[9]

1.3.21 INFLUENCE OF SUN AND AGING

Skin aging pathophysiology is similar to the one that follows TS application. Marked skin thickness decrease, especially in light-exposed areas and delayed skin recovery are reported.[9]

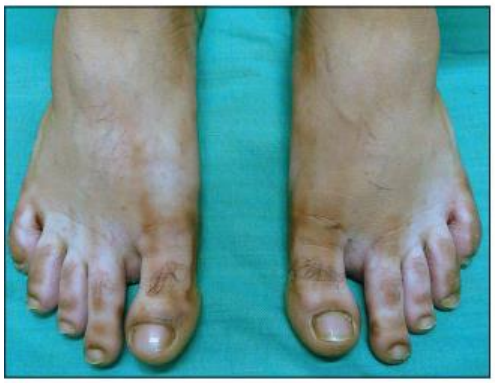
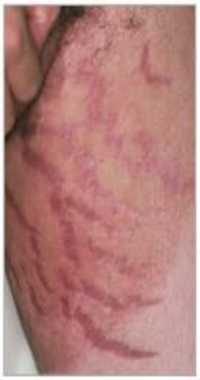
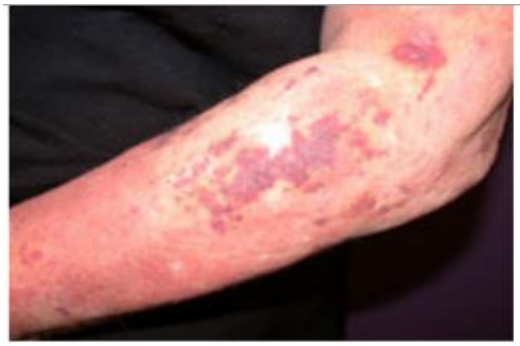


Figure 13: Diffuse Hypopigmentation

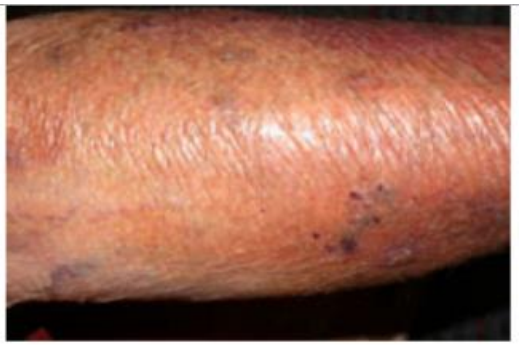
Skin Atrophy

Striae

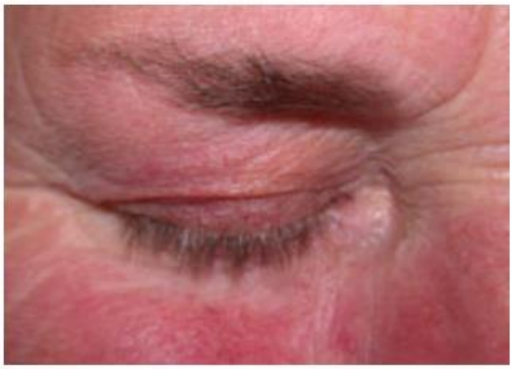




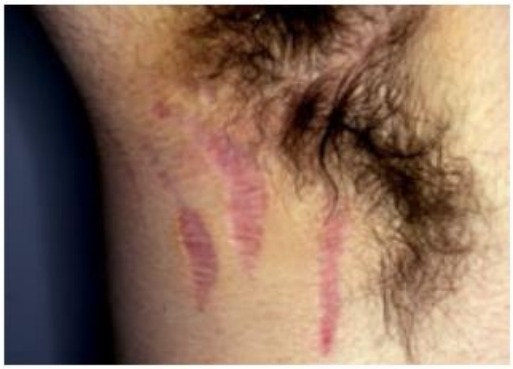
Bruising



Skin thinning



Prominent capillaries



Stretch marks

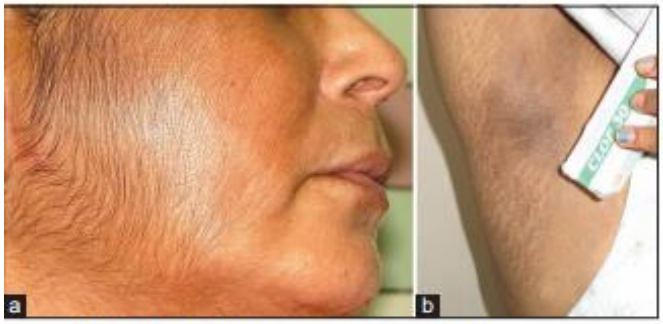


Figure 11: (a) Facial hypertrichosis (b) Striae alba

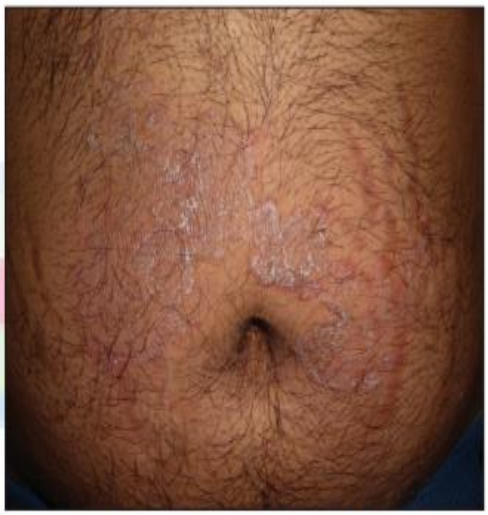
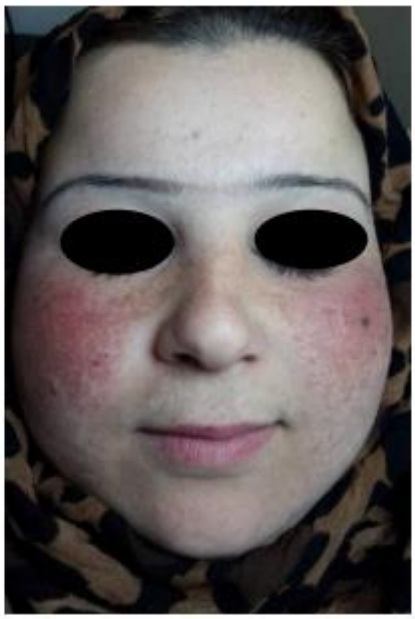
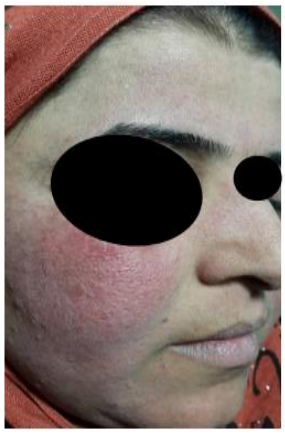


Figure 12: Striae secondary to steroid application for tinea corporis





'rominent facial erythema with telengactsia in patient presented with triggered by exposure to sun or heat after TCS misuse for 6 months.

: Young woman has obvious melasma overshadowed by the facial erythema due to improper use of potent TCS on the face for 1 year duration.

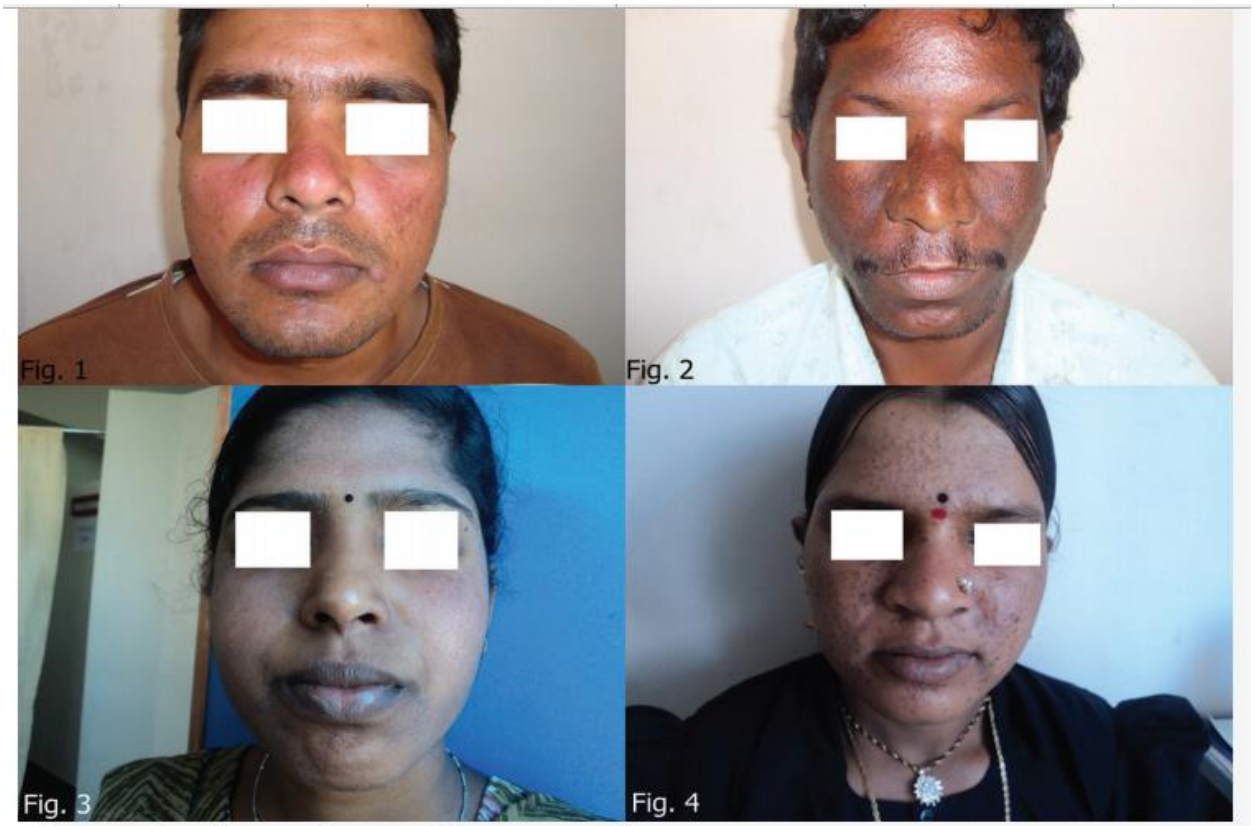


Figure 1. Erythema of central face - steroid rosacea.
Figure 2. Acneform eruption following steroid application for pigmentation of face.
Figure 3. Steroid dependent face (SDF) showing diffuse erythema and scaling.
Figure 4. Steroid induced pigmented monomorphic acne.

1.4 Study done on topical corticosteroids misuse :

110 Iraqi patients with steroid rosacea or perioral dermatitis with history of topical steroid use on their faces for at least 1 -3 months at Department of Dermatology - Baghdad Teaching Hospital between January 2011 to December 2013.

The results : Majority of patients were young, poorly-educated women who used a combinations of potent and very potent topical steroid for average period of 0.25-12 years. Facial erythema (92.7%) and hotness (89%), dryness (62.7%), telangiectasia (53.6%) and rebound phenomenon (86.3%) with or without papulopustular eruption were the main clinical complaints. Searching for beauty and facial fairness in 51(46%) of patients, hyperpigmentory problems like melisma in 40(36%) patients were the main indications for steroid misuse on the face mostly accomplished through recommendations from non medical personnel.

Chapter Two

Methodology

2.1 Methodology :

We made a campaign to increase awareness about topical steroid and its side effects this campaign included :

1-posters that put in pharmacies as much possible as we can cover , in doctor's clinic , these posters inform people about topical steroids side effects and not to use these medications unless the doctor or pharmacist say so

2-making a page on facebook about the campaign that increase awareness

https://www.facebook.com/Topical-steroid-Misuse-154493708352123/

3- making a small posters and giving them to people in public and beauty centers and herbal shops as well as in the mosque .

لا يجور استعمال الكريمات او المراهم الحاوية على الستيرويد الا باستشارة الطبيب او الصيدلاني لما فيها من اثار جانبية شديدة :-

اشهر المراهم والكريمات الحاوية على الستيرويد	الاثار الجانبية للستيرويد : ١-ضمور البشرة ٢- ضهور الشعر على وجه النساء عند استخدامه ٣- يسبب التهابات فطرية او بكتيرية او فيروسية لانه يقلل مناعة الجسم ٤- احمرار البشرة ٥- ظهور حب الشباب ٦- اذا وضعت على جرح توخر التئام الجرح ٧- استعمالها لفترة طويلة يسبب ادمان البشرة عليها
درمودين	
هيدروكورتزون	
بتنوسام	
اليكا- ام	
ميلاكير	
كينالوغ	

طلاب كلية الصيدلة جامعة القادسية

حسين عبد الامير .. علي حيدر عبد زيد باشراف الصيدلاني : حسين علي صاحب

Chapter Three

Conclusion, Discussion and Recommendation

3.1 conclusion :

Topical steroids may be suggested by the doctors , pharmacists ,other health practitioners , the patient himself , friends or relatives . Many people was unaware of topical steroids side effects and respond positively to us ,other were aware that they are bad for them as general concept and un aware of the side effects or know little about it , we covered some pharmacies ,clinics ,herbal shops , beauty shops and we handled some posters to people , but a lot of people still don't know about topical steroids misuse side effects . the campaign must grow bigger and cover all over Iraq as a national campaign ,we did the first step and we'll try to continue in our campaign hoping other specialist and government will do the same.

3.2 discussion :

as many doctors consider steroids as a magical medications , steroids may also be misused by doctors ,pharmacists and other medical practitioners , although in many cases steroids misused by the patient himself or recommended by their families or friends ,so all included in raising awareness of topical steroids misuse , although studies on topical steroids misuse and researches are done in Iraq but steroids still being misused . a campaign must be done to raise awareness about the side effects of steroids and decrease this misuse .while in Iraq this kind of subjects still ignored till these days but with time and repetition of the message may improve the proper use and avoid misuse .

3.3 Recommendations :

1- Dermatologists have responsibility to make studies and statics on topical steroids misuse

2-Based on studies the dermatologist have done , the government should take the action and build campaigns that raise awareness about side effects and to educate people .

References :

1- - *Nussey, S.; Whitehead, S. (2001). Endocrinology: An Integrated Approach. Oxford: BIOS Scientific Publishers.*
2- Nussey, Stephen; Whitehead, Saffron (2001). *The adrenal gland*. BIOS Scientific Publishers.
3- Sulzberger MB, Witten VH (1952). effect of topically applied compound F in selected dermatoses
4- Saraswat A, Lahiri K, Chatterjee M, Barua S, et al.(2011). Topical corticosteroid abuse on the face . J Dermatol Venereol Leprol multicenter study of dermatology outpatients .
5- Coondoo A, Chattopadhyay C . (2014). Use and abuse of topical corticosteroids in children . Indian J Paediatr Dermatol
6- T, Breathnach S, Cox N, Griffiths C(2010). Berth-Jones J.(2010). Topical therapy . Rooks Textbook of Dermatology .8th ed. Blackwell Science Ltd
7- Valia RG, Valia AR .(2008). IADVL Textbook of Dermatology. Srinivas CR, Lakshmi C. Principles of topical therapy in dermatology . 3rd ed. Mumbai, India: Bhalani Publishing House .
8- Habif, Thomas P. (1990). Clinical dermatology. St. Louis. a color guide to diagnosis and therapy (2nd ed.)
9- Hengge UR, Ruzicka T, Schwartz RA, Cork MJ.(2006). Adverse effects of topical glucocorticosteroid
10-Dermatology. [Last accessed on 2014 May 27]. Available from: http://www.about.com/cs/medications/a/steroideffects.htm
11- Saunders Elsevier; 2007. Topical Corticosteroids. Wolverton SE. Comprehensive Dermatologic Drug Therapy. 2nd ed . Philadelphia USA: Saunders Elsevier . 595–624.
12- Verma SB, Hay R. (2014) Topical steroid induced tinea pseudoimbricata . A striking form of tinea incognito. Int J Dermatol.
13-Fisher DA.(1995). Adverse effects of topical corticosteroid use .
14-Kuflik JH, Schwartz RA.(2000) Acneiform eruptions.
15-Momin S, Peterson A, Del Rosso JQ.(2009). Drug-induced acneform eruptions. Cosmet Dermatol . Definitions and causes.

16-Saraswat A, Lahiri K, Chatterjee M, et al.(2011). Topical corticosteroid abuse on the face. Indian J Dermatol Venereol Leprol. multicenter study of dermatology outpatients