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Change of Oral to Topical Corticosteroid Therapy Exacerbated Glucose Tolerance in a Patient with Plaque Psoriasis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Yui Hongo
ABCDEFG 2 Kenji Ashida
DEF 3 Kenji Ohe
DE 3 Munechika Enjoji
BCDEF 1 Miyuki Yamaguchi
BCDEF 2 Tsuyoshi Kurata
BCDEF 4 Akiko Emoto
BCDEF 1 Hiroko Yamanouchi
BCDE 1 Satoko Takagi
BDCEF 1 Hitoe Mori
BCDEF 1 Nozomi Kawata
CDEF 2 Yoshio Hisata
BE 2 Yuta Sakanishi
BCDEF 1 Kenichi Izumi
BCDEF 2 Takashi Sugioka
ADEFG 1 Keizo Anzai

1 Department of Internal Medicine, Saga University Hospital, Saga City, Saga, Japan
2 Community Medical Support Institute, Saga University Faculty of Medicine, Saga City, Saga, Japan
3 Health Care Center, Fukuoka University, Fukuoka City, Fukuoka, Japan
4 Japan Department of Pharmacy, Saga University Hospital Pharmacy, Saga University Hospital, Saga City, Saga, Japan

Corresponding Author: Kenji Ashida, e-mail: ashida@intmed3.med.kyushu-u.ac.jp
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Patient: Male, 80
Final Diagnosis: Plaque psoriasis• drug induced diabetes
Symptoms: Hyperglycemia• adrenocortical dysfunction
Medication: Oral steroid• Topical steroid• Insulin
Clinical Procedure: Changing route and strength of steroid administration
Specialty: Endocrinology• Dermatology

Objective: Rare disease

Background: Psoriasis is known as the most frequent disease treated by long-term topical steroids. It is also known that patients with thick, chronic plaques require the highest potency topical steroids. However, the treatment is limited to up to four weeks due to risk of systemic absorption.

Case Report: An 80-year-old man was diagnosed with type 2 diabetes 16 years before, and was being administered insulin combined with alpha glucosidase inhibitor. He was diagnosed with plaque psoriasis and his oral steroid treatment was switched to topical steroid treatment due to lack of improvement and poorly controlled blood glucose level. The hypoglycemic events improved after the psoriatic lesions improved.

Conclusions: Control of blood glucose level is difficult at the very beginning of topical steroid treatment for psoriasis especially if a patient is receiving insulin treatment. Intense monitoring of blood glucose level during initiation of topical steroid treatment is necessary to prevent unfavorable complications.

MeSH Keywords: Administration, Topical • Diabetes Mellitus, Type 2 • Psoriasis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/905470

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Background

Systemically administered steroids increase insulin resistance [1] along with impaired insulin excretion [2], and thus are well known for causing impaired glucose tolerance as well as attenuated control of blood glucose level in type 2 diabetes mellitus. In contrast, topical administration of strong steroids, at even high doses, are thought to rarely effect blood glucose level or cause side effects found in systemic administration of steroids [3]. Here, we report a case of severe plaque psoriasis of a diabetic patient treated by topical steroids resulting in difficult control of blood glucose level. With more severe psoriatic skin lesions, stronger and higher dose topical steroids are needed, which could result in increased absorption of the steroids with side effects comparable to systemically administered steroids. In this study, we proposed that intense monitoring of blood glucose levels should be performed during the initial period of topical steroid administration in diabetic cases with severe psoriasis.

Case Report

An 80-year-old man was admitted to the dermatology department in our hospital for itchy systemic erythema. He received daily oral administration of two tablets of betamethasone d-chlorophenylamine maleic acid (0.5 mg betamethasone per tablet) from a nearby dermatologist with no improvement of his erythema. He was treated for type 2 diabetes mellitus starting at 64 years of age and his mother and two brothers were also diabetic. Recently, he was treated with lispro-insulin at 42 units per day and voglibose at 0.9 mg per day, but his

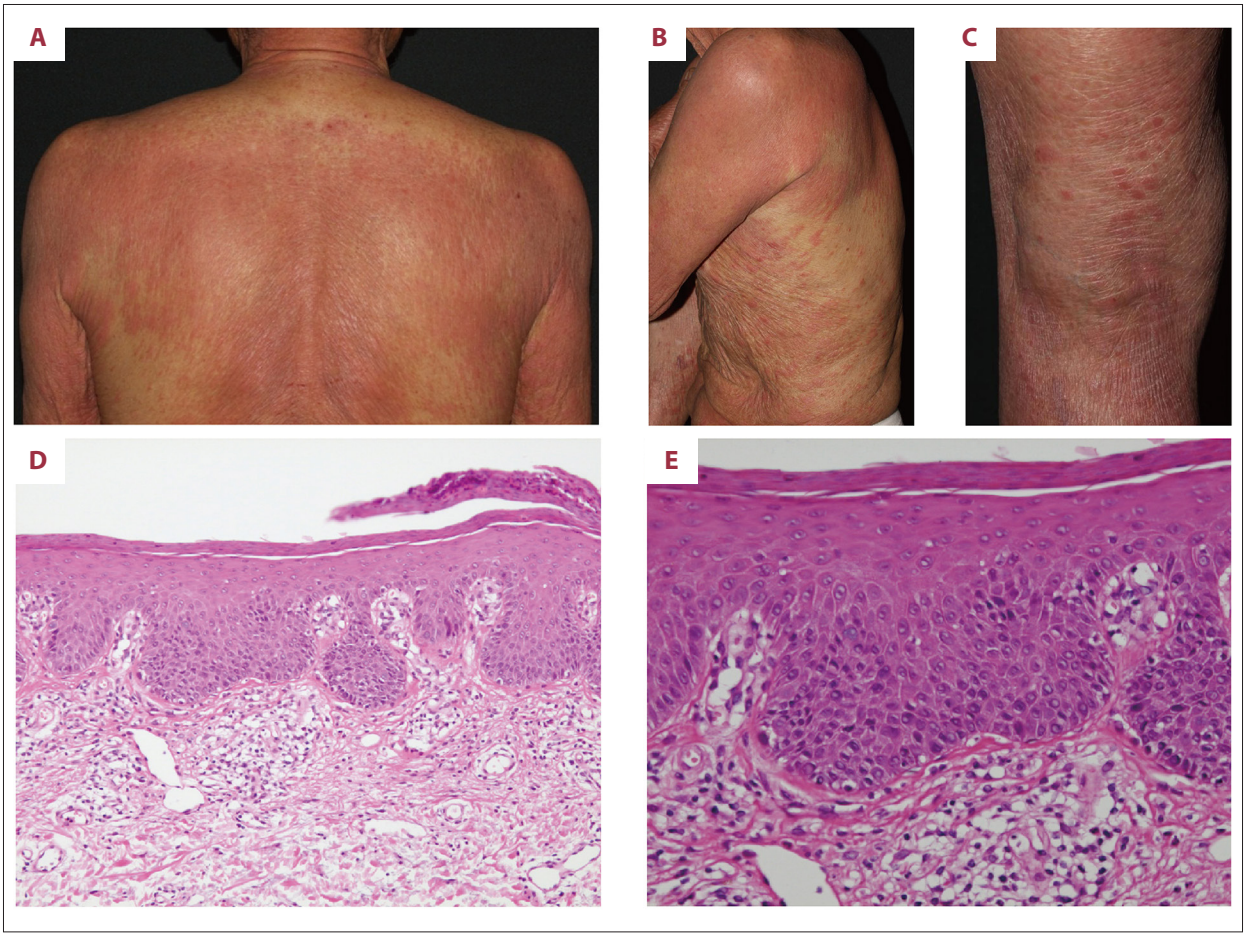

Figure 1. Skin lesions at first admission. (**A**) Back. (**B**) Left side of the chest. (**C**) Appearance of the right knee. Cobblestone-like fused erythematous macules with scales were found on the trunk and extremities. Moreover, scattered purple spots were also seen on the extremities. (**D**, **E**) Biopsy specimens from sites of skin rash on the trunk: (**D**) low-power field, (**E**) high- power field. The stratified squamous epithelial cell layer showed mild parakeratosis and enlarged epidermal projection. The liquefaction degeneration of the epithelial basal cells was very mild, and the upper dermis showed edema and infiltration of lymphocytes and neutrophils around the dilated capillaries. The erythematous macules had nonspecific findings, with no obvious atypical cells.

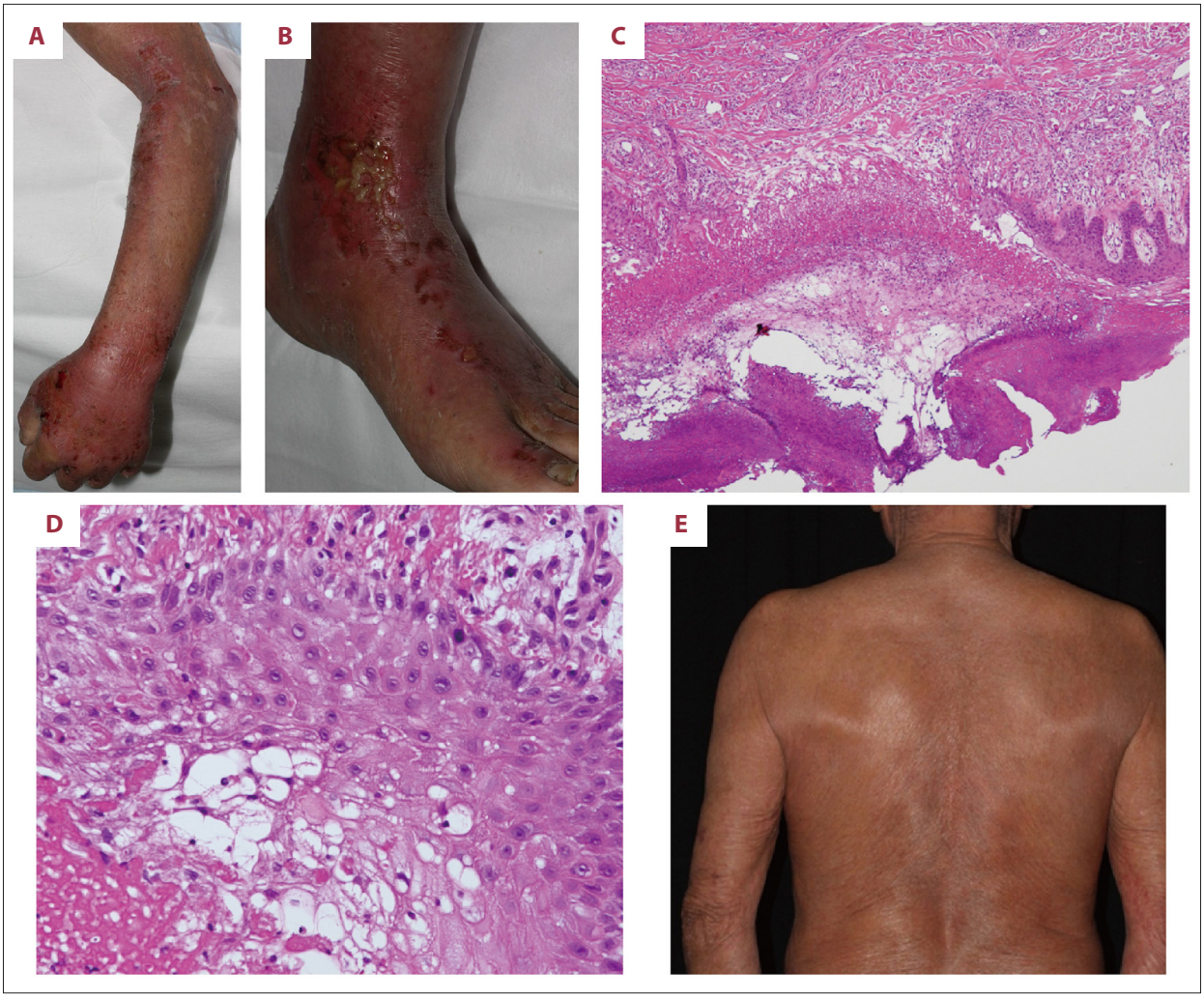

Figure 2. Skin lesions at the time of readmission and at second discharge. (**A**) Left forearm. (**B**) Left foot. Scattered erosive lesions and pus were observed on the extremities and buttocks. (**C, D**) Biopsy specimens from the erosive erythematous macules with pustule crusts on the extremities were compatible with impetigo: (**C**) low-power field, (**D**) high-power field. Cystic lesions were noted between the stratified squamous intraepithelial and subepithelial layers. The surface of the cyst showed collapse and necrosis, and fibrin formation and neutrophil infiltration were observed in the cyst. Moreover, spongiosis was seen in the surrounding stratified squamous epithelial cell layer. No club-like enlargement of the epidermal projection was seen but dilated capillaries were present in the upper layer of the dermis, which may indicate pustular psoriasis. (**E**) Back. An obvious improvement of the redness and erosion was observed.

hemoglobin (Hb)A1c was poorly controlled (8–9%). Insulin excretion was normal with blood C-peptide level of 1.98 mg/dL (C-peptide index 0.98) when fasting blood glucose level was 202 mg/dL. The skin lesions (Figure 1A–1C) showed erythema accumulated in a cobble-stone manner with psoriatic lesions from abdomen to extremities covering 80% of his body. Many scratches due to itchiness were also observed. Purpura was also seen on his extremities. There was no systemic inflammation. The oral steroid treatment was switched to 10 g/day of an "upper mid-strength, class 3" topical steroid, mometasone furoate [4], combined with psoralen-ultraviolet A therapy (PUVA) on the psoriatic lesions. The patient's blood glucose level was poorly controlled and it was necessary to increase his insulin administration to a final level of 36 units of neutral protamine hagedorn (NPH) and 38 units of lispro-insulin per day. We checked the systematic effect of the topical steroid by evaluating the patient's adrenocortical function. His early morning ACTH level was less than 2.0 pg/mL with blood cortisol level less than 1.0 µg/dL, which showed secondary central suppression of adrenocortical function by the exogenous topical steroids. The skin lesions and blood glucose control improved and the patient was discharged from the hospital with follow-up as an outpatient. However, on the second day after discharge, he found painful erosions and pus lavers on his extremities and buttocks (Figure 2A, 2B). Antibiotic treatment by oral and skin administration route did not improve the lesions

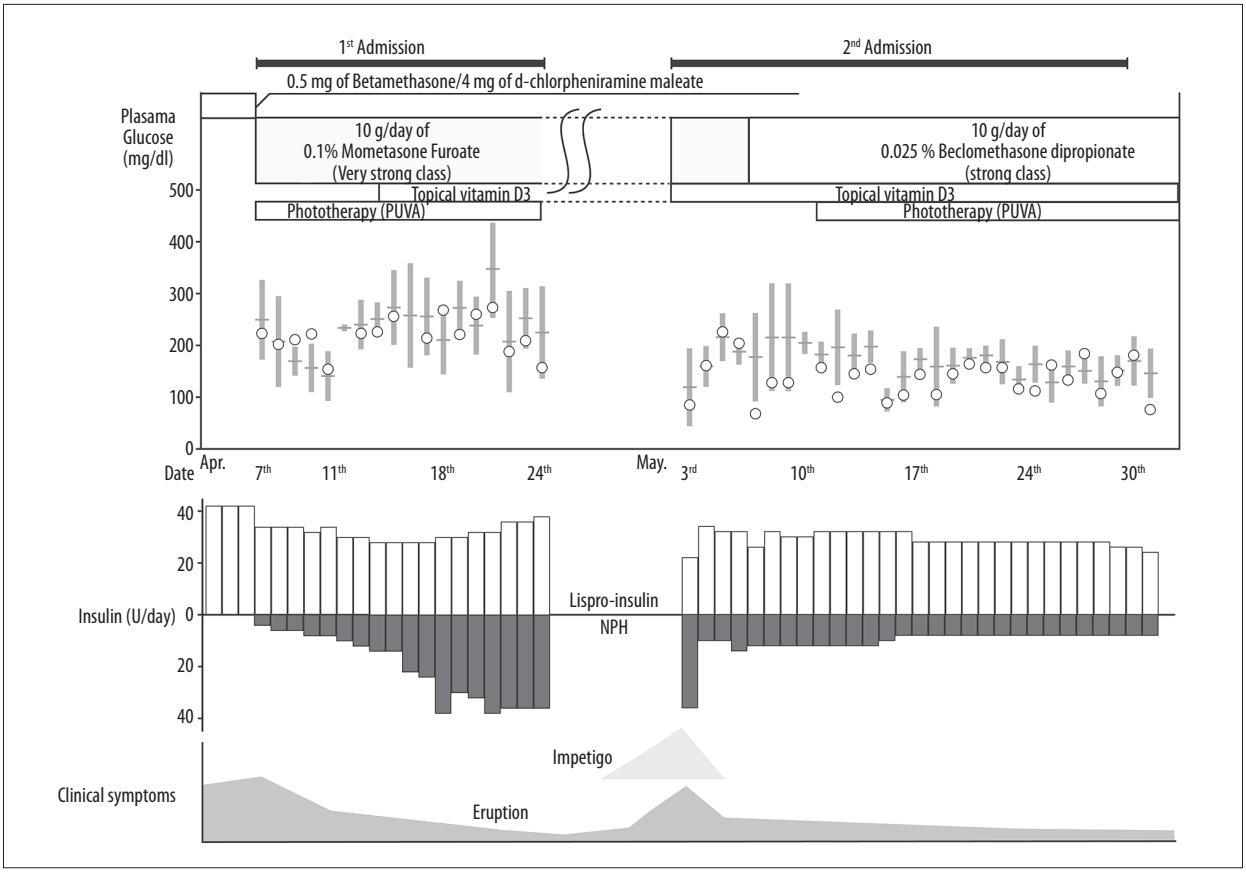

Figure 3. Clinical course. Upon switching from oral steroid treatment to external-use steroid preparation, blood glucose control worsened and the required insulin dose increased. The required insulin dose decreased with the improvement of inflammatory changes in the skin. Eventually, the patient continued the external steroid therapy but with the same insulin dose as before the start of treatment, which led to improved blood glucose control. Open circles indicate fasting blood glucose level in the morning, if available. Gray columns indicate standard deviations of the fasting blood glucose level before breakfast, before lunch, before dinner and at 21 o'clock with averages of them as a horizontal bar.

and thus he was readmitted to the hospital on the seventh day after discharge. His inflammation marker CRP was 7.85 mg/dL, and the skin biopsy (Figure 2C, 2D) of the pus lavers were diagnosed as impetigo. Methicillin-sensitive Staphylococcus aureus was identified from the pus, and the skin lesions were diagnosed as staphylococcus scalded skin syndrome. After he was discharged from the hospital, he stopped using the topical steroid on his own decision. On his second admission, his HbA1c was 7.6% and fasting blood glucose level was 130 mg/dL with lower doses of lispro-insulin than first admission, despite his infection. He experienced hypoglycemia and thus insulin administration needed to be further lowered. To our surprise, re-administration of topical steroids did not affect the blood glucose level, and the psoriatic skin lesions were improved. Since the skin lesions were improved, the topical steroid was substituted with mid-strength, class 4, beclomethasone dipropionate. Topical steroid treatment was continued, and skin lesions of redness and erosion almost completely improved (Figure 2E), and discharged from the hospital. The amount of insulin per day increased from 38 to 74 units during the first period of hospitalization, and lowered to 32 units at the day of discharge during the second period of hospitalization (Figure 3). The total amount of topical steroids until the second time he left the hospital was upper mid-strength, class 3: total 245 g (mometasone furoate), mid- strength, class 4: total 115 g (beclomethasone dipropionate), and lower mid-strength, class 5: total 15 g (hydrocortisone butyrate).

Discussion

Psoriasis is a chronic inflammatory skin disease found in 2–3% of the population in western countries [5], but around 0.1% in Japan with a tendency for males. The red scalp-like erythema can occur in local regions or occur systemically, and is known for the inflammation it causes; it has also been associated with increasing the rate of diabetes as well as evoking diabetic complications [6]. Psoriasis is frequently encountered

in clinic settings when treating patients with diabetes and is often requires long-term treatment with topical steroids [7]. Topical steroids are known to be effective for treating psoriasis; its application to skin lesions that are less than 10% of the whole skin area, is up to 30 g per week, with re-evaluation of the treatment every four weeks, has been suggested to prevent desultory treatment [8]. Topical steroids are categorized by their strength of effectiveness: super potent (class 1); potent (class 2); upper mid-strength (class 3); mid-strength (class 4); low mid-strength (class 5); mild (class 6); and least potent (class 7) [9]. Different absorption efficacies of topical steroids between skin regions must also be considered during treatment [10]. While steroids are very effective, they also have associated risks of local side effects, such as irreversible striae cutis. Skin atrophy is the most frequent and important of these side effects [11]. The strength and amount of topical steroid is also related to systemic side effects. The amount of topical steroid that may trigger suppression of adrenocortical function (shown as equivalent to betamethasone amount) is as follows: 10 g of 0.05% clobetasol propionate (class 1) is equivalent to 0.5 mg of betamethasone; and 40 g of it is equivalent to 1 mg of betamethasone [12]. It is known that 2 g per day of this cream can decrease morning cortisol level in a few days [13,14]. Thus, it has been suggested that less than 50 g per week of potent steroids should be used to prevent these systemic adverse effects [15]. However, many cases show a transient suppression of adrenocortical function at the start of topical steroid treatment and rarely show clinical problems [7]. Thus, the systemic adverse effects of topical steroids need more study, especially for patients receiving insulin therapy. For the case reported here, we used a two-rank lower topical steroid for the face, and 10 g per day of an "upper mid-strength, class 3" topical steroid. This cleared the alert level of "strength and amount" of topical steroid usage, but induced suppression of adrenocortical function and exacerbation of blood glucose level. This was interesting. Despite, 10 g of 0.05% clobetasol propionate being the equivalent to 0.5 mg of betamethasone [12], the systemic adverse effect of steroid exacerbated upon switching from oral betamethasone at 0.5 mg per day to 0.05% clobetasol propionate at 10 g per day. We speculated that the barrier function of the skin was destroyed by psoriasis and peeled off by scratching due to the itchiness, leading to higher absorption rate of the topical steroid. Generally, though there are differences between regions of the skin in abortion, simple applications to the skin have uptakes of 3%–5% of steroids, with a peak in blood cortisol concentration at 12–24 hours after administration. This peak slowly declines after five additional days [10]. However, if the skin is peeled off its stratum corneum, it is known that a tremendous rate (78–90%) of steroid uptake peeks at 4–6 hours after administration [12]. The skin barrier function at psoriatic lesions in our patient's case was possibly abrogated, inducing an increase in topical steroid absorption, evoking higher blood cortisol concentration from external steroid administration to a wider portion of the skin, resulting in exacerbated blood glucose levels as well as suppressed adrenocortical function. This was confirmed when the amount of topical steroid was lowered due to impetigo. Improvement of the skin surface by topical steroid can restore skin barrier function as well as lower the absorption rate of the topical steroid. In most cases, the suppression of adrenocortical function is restored after the effect of the topical steroid has been attenuated [7,15]. The case presented here showed rapid improvement of blood glucose control after the skin surface was improved by topical steroid on readmission to our hospital, despite the presence of infection. In such situations, one must be careful that adrenocortical function is transiently suppressed; that improvement of inflammation improves insulin resistance; that improvement of blood glucose to normal levels relieves glucose toxicity, and necessary insulin doses are rapidly reduced with increased risks of hypoglycemia and for prolonged hypoglycemia. The rapid change in psoriatic skin condition by topical steroid treatment changes steroid uptake dramatically, and thus, delicate handling is required in severe cases of psoriasis.

Conclusions

We report here a case of psoriasis where blood glucose control was exacerbated when switching steroid treatment from oral treatment to topical treatment. Topical steroids are thought to have less systemic adverse effects than oral steroids, but it must be fully recognized that each treatment type has different strengths with different absorption rates depending on the region of the skin where it is administered; the amount and range of the administered area; and the condition of the skin surface. Unlike oral steroids where absorption rates do not change, topical steroids have differential absorption rates during different phases of skin disease where the skin condition changes dramatically with concurrent dramatic changes in blood glucose levels. Thus, topical steroids need delicate handling depending on the penetration of psoriasis (condition of the skin surface) and existence of impaired control of blood glucose levels.

Conflict of interest

None.

References:

1. Andrews RC, Walker BR: Glucocorticoids and insulin resistance: Old hormones, new targets. Clin Sci (Lond), 1999; 96: 513–23
2. Delaunay F, Khan A, Cintra A et al: Pancreatic beta cells are important targets for the diabetogenic effects of glucocorticoids. J Clin Invest, 1997; 100: 2094–98
3. Bewley A: Expert consensus: time for a change in the way we advise our patients to use topical corticosteroids. Br J Dermatol, 2008; 158: 917–20
4. WHO collaborating centre for Drug Statistics methodology. ATC/DDD Index (updated Dec 19, 2016)
5. Chen J, Kuai D, Zhang L et al: Psoriasis increased the risk of diabetes: A meta-analysis. Arch Dermatol Res, 2012; 304: 119–25
6. Azfar RS, Seminara NM, Shin DB et al: Increased risk of diabetes mellitus and likelihood of receiving diabetes mellitus treatment in patients with psoriasis. Arch Dermatol, 2012; 148: 995–1000
7. Castela E, Archier E, Devaux S et al: Topical corticosteroids in plaque psoriasis: A systematic review of risk of adrenal axis suppression and skin atrophy. J Eur Acad Dermatol Venereol, 2012; 26(Suppl. 3): 47–51
8. Paul C, Gallini A, Archier E et al: Evidence-based recommendations on topical treatment and phototherapy of psoriasis: Systematic review and expert opinion of a panel of dermatologists. J Eur Acad Dermatol Venereol, 2012; 26(Suppl. 3): 1–10
9. Tadicherla S, Ross K, Shenefelt PD, Fenske NA: Topical corticosteroids in dermatology. J Drugs Dermatol, 2009; 8: 1093–105
10. Feldmann RJ, Maibach HI: Regional variation in percutaneous penetration of 14C cortisol in man. J Invest Dermatol, 1967; 48: 181–83
11. Furue M, Terao H, Rikihisa W et al: Clinical dose and adverse effects of topical steroids in daily management of atopic dermatitis. Br J Dermatol, 2003; 148: 128–33
12. Takeda K, Harada T, Asato T et al: Review on systemic effects of topical corticosteroids – with special reference to adrenocortical suppression following percutaneous absorption. Igaku No Ayumi, 1977; 101: 817–29
13. Olsen EA, Cornell RC: Topical clobetasol-17-propionate: Review of its clinical efficacy and safety. J Am Acad Dermatol, 1986; 15: 246–55
14. Ohman EM, Rogers S, Meenan FO, McKenna TJ: Adrenal suppression following low- dose topical clobetasol propionate. J R Soc Med, 1987; 80: 422–24
15. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ: Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol, 2006; 54: 1–15; quiz 16–18