Use of Topical Corticosteroids in Dermatology: An Evidence-based Approach

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Abstract

Topical corticosteroids (TCs) are the pillars of dermatotherapeutics. These drugs are the “magic molecules,” provided they are used judiciously and appropriately, following a rational prescription. On exhaustive literature search in multiple databases, we found a significant evidence favoring the use of TCs in atopic eczema, localized vitiligo, psoriasis, chronic hand eczema, and localized bullous pemphigoid. However, contrary to conventional wisdom, we did not find any high-level scientific evidence in support of prescribing TCs in cutaneous lichen planus, sarcoidosis, and seborrhoeic dermatitis. Besides, evidence clearly advocates judicious use of mild-to-moderate corticosteroids (if required) in pregnancy and lactation and there is no risk of any fetal abnormality.

Key Words: Meta-analysis, randomized controlled trials, systematic reviews, topical corticosteroids

What was known?

- Topical corticosteroids are the most commonly prescribed drugs by dermatologists in an outpatient setting
- TCs are being used since ages, in eczema, vitiligo, psoriasis, lichen planus, hand eczema, etc
- Topical steroid addiction or red burning skin syndrome is increasingly being recognized, due to illegitimate prescriptions by physicians.

Introduction

Since the introduction in early 1950s, topical corticosteroids (TCs) have become the most commonly prescribed drugs by dermatologists in an outpatient setting. These agents form the mainstay of treatment for many skin conditions. If used appropriately, they are safe and effective, and side effects are rare. Not only dermatologists but also steroids have been rampantly prescribed by quacks, general physicians, pediatricians, gynecologists, and specialists of innumerable disciplines.

Unfortunately, TCs are increasingly being abused by doctors and patients. Topical steroid addiction and red burning skin syndrome are legitimate clinical entities which are well recognized these days. Sometimes, these terms are used synonymously. As a result, the problem of steroid phobia is being increasingly recognized by physicians worldwide which, sometimes, is associated with simple fear, due to ignorance of the patient. In addition, current advice to patients to apply TC preparations “sparingly” or “thinly” contributes to steroid phobia, increasing the risk of poor clinical response, and treatment failure. Such cautionary advice also overlooks the fact that the vast majority of patients are prescribed TCs of mild potency for which the evidence suggests that the risk of harm is minimal. In the patient’s mind, the current advice groups all steroids together regardless of their potential for adverse effects. The advice also tends to reinforce an erroneous concern that the risks from TCs may be similar to those from systemic corticosteroids.

In this article, we have reviewed the various indications of TCs in dermatology with an overview of the evidence available in support of using these drugs in various dermatoses. Wherever possible, we have tried our best to corroborate the evidence, and analyze them in such a manner that both the opposing concerns may be addressed, and we may come up with a balanced view on TC use in clinical dermatology. At the outset, we would like to summarise the levels of evidence. Level I suggests evidence from a systematic review of randomized controlled trials. Level II corroborates with evidence obtained from at least one well-designed Randomized Controlled Trial. Level III takes into consideration, evidences obtained from well-designed case-control and cohort studies. Level IV relates to well-designed case-control and cohort studies and Level V considers evidence from systematic reviews.

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How to cite this article: Das A, Panda S. Use of topical corticosteroids in dermatology: An evidence-based approach. Indian J Dermatol 2017;62:237-50.

Received: March, 2017. Accepted: April, 2017.
Discussion and Evidence

Ecema

Ecema is a noninfective, chronic, inflammatory dermatological entity manifesting as inflamed, pruritic, erythematous, and/or astematotic skin. Numerous therapeutic modalities are available to combat this notorious dermatosis, TCs being the most commonly prescribed ones. However, most of the patients show excellent response to emollients. According to the traditional school of thought, it is advisable to use TCs during acute episode and withdraw them, once the symptoms have been controlled. However, recent authors are of the opinion that proactive approach is better than the more commonly followed reactive approach. As per recent guidelines, it is favorable to use high-dose corticosteroids during the acute flares and continue with low-dose corticosteroids when the episode is under control. Besides, step-up and step-down approach can be followed which refers to increasing the potency of the steroid in acute flares and lowering the potency in the periods of remission. Overall, a systematic review of the best strategies for using TCs in the treatment of established ecema is, therefore, required.

Here is a brief overview of some of the major randomized controlled trials (RCTs) comparing the use of different TCs in ecema [Table 1].

These studies showed significant improvement in 13%–100% of patients after 1–12 weeks of treatment. Most of the studies found significant improvement with TC in comparison with placebo. However, three studies could not demonstrate a significant difference between placebo and TC. Few RCTs showed that intermittent treatment with a potent TC could reduce the number of flare-ups. Three RCTs and two small randomized within-patient comparison studies have examined the use of wet-wrap bandaging applied over TC. To summarize, we are not in a position to recommend the “best” TC, as till now, not a single RCT has compared all the available preparations of TC of similar potency. Besides, there is no clear RCT evidence supporting the use of twice-daily over once-daily TC administration. However, it is now clear that application of twice-weekly potent TC to stable ecema can reduce the number of flare-ups in adults as well as children although the long-term safety profile of such intermittent or pulse therapy in infants, is absent.

In a systematic review of treatments for atopic ecema, RCTs of TCs collected data on thinning of the skin and suppression of pituitary – adrenal axis. These RCTs could not show any evidence of harm although the studies were short-term. There is no RCT evidence that skin thinning is a problem with the correct use of TC although the fact that most RCTs are of short duration is a limitation in basing the conclusions solely on RCT-generated evidence in this regard, and other non-RCT evidence should be used to issue firm recommendations.

Vitiligo

Vitiligo is an acquired pigmentary disorder, attributed to the destruction of melanocytes. Therapeutic modalities which are present include topical and systemic corticosteroids, topical calcineurin inhibitors, photo (chemo) therapy, vitiligo surgery, and depigmentation of normally pigmented skin. Immunosuppressive therapy with highly potent TCs (clobetasol) gives excellent results in cases of localized stable vitiligo.

Herein, we have tabulated the evidence available in favor of using TCs in vitiligo [Table 2].

A meta-analysis, an additional systematic review, and several RCTs showed that Class III TCs are effective in comparison with placebo, either alone or in combination with narrowband – ultraviolet B (UVB), or psoralen plus UVA light (using sunlight or artificial light sources), in treating generalized and localized vitiligo. There is some RCT evidence that topical clobetasol propionate is of equivalent effectiveness with tacrolimus in treating this condition. All studies examining the effect of TCs reported adverse effects, with the more frequent being atrophy, telangiectasia, hypertrichosis, and acneiform papules.

Psoriasis

Topical steroids have been used since ages to manage mild-to-moderate plaque psoriasis (scalp and nonscalp). These are available in different potencies and formulations, but their use relies mostly on the basis of individual experience. Here is a brief summary of evidence in favor of using topical steroids in psoriasis [Table 3].

To summarize, both Class III and Class IV TCs are effective in inducing remission in psoriasis; however, Class IV appears superior. It remains unclear whether once- or twice-daily dosing should be recommended, but frequency, as well as duration, should be tapered down in a maintenance phase because of concerns with cutaneous and systemic adverse effects of TCs. Skin atrophy is the most common complication, but it is less of an issue in psoriatics than atopics. However, the continuous use of very potent or ultrapotent TCs may cause irreversible skin atrophy and striae, may cause psoriasis to become unstable, and may have systemic effects when used over a large surface area. The ointment formulations appear
### Table 1: Evidence in favor of using topical corticosteroids in eczema

| Name and year of study | Type of study | Drugs | Result |
|------------------------|---------------|-------|--------|
| Almeyda and Burt 1974[40] | Randomized, double-blind, paired comparison trial | Desonide hydrogel 0.05% versus vehicle | 1% HC is as effective as 0.1% betamethasone 17-valerate cream |
| Yasuda 1976[54] | Randomized, double-blind study | HC 17-butyrate 0.1% ointment versus triamcinolone acetonide 0.1% ointment or HC acetate 1% ointment | HC 17-butyrate was superior to triamcinolone and comparable to HC acetate 1% ointment |
| Fisher and Kelly 1979[51] | Randomized, double-blind, left-right comparison trial | Fluocinonide 0.05% versus betamethasone valerate 0.1% tds | Mean clinical response better in fluocinonide than betamethasone |
| Lassus 1983[52] | Randomized double-blind, parallel-group trial | Alclometasone dipropionate 0.05% versus HCB 0.1% b.d | 76%–100% marked improvement in 40% alclometasone patients and 35% HC patients |
| Andersen et al. 1988[53] | Randomized, double-blind, left-right multicenter study | Mildison lipocream 1% HC ointment Twice daily versus uniderm cream 1% HC ointment b.d | Little efficacy difference between treatments yet patients preferred the mildison lipocream 1% HC ointment |
| Vernone et al. 1991[54] | Randomized, double-blind, parallel group trial | Mometasone furoate 0.1% cream versus HC 1.0% cream o.d | Mometasone group showed better response |
| Rafanelli et al. 1993[55] | Randomized, third party blind parallel group trial | 0.1% mometasone furoate o.d versus 0.05% clobetasone b.d | Mometasone was better |
| Marchesi et al. 1994[56] | Randomized, third-party blind evaluator, parallel group-controlled trial | Mometasone furoate ointment 0.1% o.d versus betamethasone dipropionate ointment 0.05% b.d | 100% patients in both groups had experienced good improvement by week 3 |
| Koopmans et al. 1995[57] | Randomized, double-blind, controlled trial | 0.1% HC 17-butyrate cream b.d versus o.d plus vehicle o.d | “BD” group noticed considerable improvement |
| Jorizzo et al. 1995[58] | Randomized, investigator-masked, parallel-group design trial | Desonide 0.05% ointment versus HC 1% ointment b.d | 68% desonide group and 40% HC group had marked improvement |
| Bleeohen et al. 1995[59] | Randomized, double-blind, parallel group controlled trial | FP 0.05% cream OD versus BD | Improvement within first week in “BD” group was higher |
| Wolkerstorfer et al. 1998[60] | Randomized, double/single-blind/open/cluster, controlled trial | FP 0.05% cream o.d versus clobetasone butyrate 0.05% cream b.d | Fluticasone group showed better response |
| Lebowohl et al. 1999[61] | Randomized, evaluator-blind, parallel-group trial | 0.1% mometasone furoate cream o.d versus 0.2% HC valerate cream b.d | Improvement in severity in 87% of mometasone and 79% of HC group |
| Prado de Oliveira et al. 2002[62] | Randomized, double-blind, comparative trial | Mometasone furoate 0.1% b.d versus desonide 0.5% o.d | Better outcome in mometasone group |
| Hanifin et al. 2002[63] | Randomized, double-blind, parallel trial | Intermittent FP or vehicle, once daily 4 days per week for 4 weeks followed by once daily 2 days/week | Once stabilized with fluticasone, risk of relapse significantly reduced by extended intermittent dosing with fluticasone cream in addition to emollient therapy |
| Torok et al. 2003[64] | Investigator-blinded, parallel, randomized study | Clocortolone pivalate 0.1% (cloderm 0.1%) and tacrolimus 0.1% (protopic 0.1%) versus clocortolone pivalate 0.1% versus tacrolimus 0.1% (all b.d) | Concomitant therapy minimized the adverse effects of both treatments taken alone and improved global response |
| Kirkup et al. 2003[65] | Multicenter, randomized, double-blind, parallel-group trials | One study compared FP with HC 1% cream and the other with HCB 0.1% cream | FP demonstrated a high level of efficacy and maintenance of disease control with a tolerability similar to HC 1% |
| Beattie and Lewis-Jones 2004[66] | Randomized, single-observer trial | HC 1% o.d versus b.d. Both groups were instructed to apply emollient as and when required | Therapy with HC and emollients alone is as effective as wet wrap therapy in severe, widespread AD |
| Hebert et al. 2007[67] | Multicenter, randomized, blinded, vehicle-controlled studies | Desonide hydrogel 0.05% versus vehicle b.d | Desonide hydrogel 0.05% was extremely well-tolerated and provided statistically significant improvements |

Contd....
Table 1: Evidence in favor of using topical corticosteroids in vitiligo

| Name and year of study | Type of study | Drugs | Result |
|------------------------|---------------|-------|--------|
| Kandil et al. 1974[39]  | Randomized controlled trial | Corticosteroids with or without a new emollient cream | More lesions showed complete repigmentation with active product. |
| Clayton 1977[40]        | Randomized double-blind controlled trial | Emollient with or without MPA 0.1% cream twice weekly | Active product was significantly better than base alone. |
| Khalid et al. 1995[41]  | Randomized parallel group study | PUVA vs CP (0.05%) b.d | Clobetasol showed favorable response. |
| Westerhof et al. 1999[42] | Randomized, parallel group, left/right comparison study | FP 0.5% alone on one side of body and FP + UVA on other versus UVA alone on one side, and FP+UVA on the other side | Combination treatment with FP and UV-A is much more effective. |
| Lepe et al. 2003[43]    | Randomized double-blind trial | 0.1% tacrolimus versus 0.05% clobetasol | Tacrolimus and CP, both were equally effective. |
| Agarwal et al. 2005[44] | Randomized, placebo-controlled, double-blind, parallel study | Levamisole (150 mg adults and 100 mg children) on 2 consecutive days in a week plus mometasone 0.1% o.d versus oral placebo plus mometasone 0.1% 0.d | Levamisole was not much effective. Cessation of spread of disease was similar in both groups. |
| Lim-Ong et al. 2005[45] | Randomized, double-blind, placebo-controlled, left/right comparison study | CP and NB-UVB versus placebo and NB-UVB | Clobetasol group showed better response. |
| Kumaran et al. 2006[46] | Randomized trial | Betamethasone dipropionate (0.05%) versus calcipotriol (0.005%) b.d versus betamethasone dipropionate (0.05%) morning and calcipotriol (0.005%) evening | Combined therapy showed faster and stable repigmentation with lesser side-effects. |

HCB: Hydrocortisone butyrate, FP: Fluticasone propionate, MPA: Methylprednisolone aceponate, HC: Hydrocortisone, AD: Atopic dermatitis, OD: Once daily, BD: Twice daily

Table 2: Evidence in favor of using topical corticosteroids in vitiligo

| Name and year of study | Type of study | Drugs | Result |
|------------------------|---------------|-------|--------|
| Msika et al. 2008[38]  | Randomized controlled trial | Corticosteroids with or without a new emollient cream | Twice daily application of a new natural emollient proved to be a major steroid-sparing alternative and improved the quality of life. |
| Peserico et al. 2008[28] | Double-blind, placebo-controlled, randomized study | Emollient with or without MPA 0.1% cream twice weekly | MPA twice weekly plus an emollient provides an effective maintenance treatment regimen. |
| Glazenburg et al. 2009[29] | Randomized, double-blind controlled trial | Placebo versus FP 0.005% ointment b.d | Twice weekly FP reduces the risk of relapse in moderate-severe AD. |
| Trookman and Rizer 2011[31] | Single-center, randomized, evaluator-blinded, parallel-comparison, noninferiority study | Desonide gel 0.05% versus desonide ointment 0.05% b.d | Hydrogel was preferred by patients. |
| Rubio et al. 2013[32]    | Randomized controlled, double-blind trial | FP cream 0.05% versus vehicle cream b.d | Excellent improvement with fluticasone. |
| Ruzicka et al. 2012[33]  | Randomized, double-blind controlled trial | Mometasone furoate with a water content of 33% (Monovo® Cream) and with a smooth consistency versus the commercially available fatty cream of mometasone furoate (Erusal® Fetttcreme) | New formulation was preferred by the patients. |

Contd....
Table 2: Contd...

| Name and year of study          | Type of study                      | Drugs                                                                 | Result                                                                 |
|---------------------------------|------------------------------------|----------------------------------------------------------------------|------------------------------------------------------------------------|
| Sanclemente et al. 2008[47]     | Randomized, matched-paired, double-blind trial | 0.05% betamethasone versus topical catalase/dismutase superoxide  | Both showed good results                                               |
| Sassi et al. 2008[48]           | Randomized parallel group study    | 308 nm laser phototherapy twice weekly plus HC 17-butyrate cream b.d versus 308 nm laser phototherapy twice weekly alone | Recalcitrant vitiligo of face and neck showed good results with combination of excimer laser phototherapy with topical HC 17-butyrate |
| Wazir et al. 2010[45]           | Randomized parallel-group study    | Mometasone 0.01% versus tacrolimus 0.03% mometasone 0.01%            | Combination therapy showed good results                                |
| Köse et al. 2010[50]            | Randomized parallel group study    | 0.1% mometasone (M-Furo) o.d versus 1% pimecrolimus (Elidel) b.d     | Mometasone was found to be effective in vitiligo on any part of the body, but pimecrolimus was effective on face only |
| Yaghoobi et al. 2011[51]        | Randomized parallel group study    | 0.05% CP in isopropyl alcohol for body and 0.1% triamcinolone acetonide for the face and flexures, used twice daily for both groups. Oral zinc was add-on for one group | Combination therapy showed excellent results in vitiligo              |
| Xing and Xu 2012[52]            | Open, uncontrolled trial           | Calcipotriol 0.005% versus betamethasone dipropionate 0.05% b.d      | Both were effective                                                    |
| Kathuria et al. 2012[53]        | Randomized parallel group study    | 0.1% tacrolimus b.d versus 0.05% FP o.d                              | Both produced variable results in segmental vitiligo                   |
| Akdeniz et al. 2014[54]         | Randomized parallel group study    | Calcipotriol, NB-UVB, and betamethasone versus NB-UVB and calcipotriol versus NB-UVB | Group receiving calcipotriol, NB-UVB and betamethasone showed excellent results |

PUVAsol: Psoralen and solar ultraviolet A, UVA: Ultraviolet A, NB-UVB: Narrowband-ultraviolet B, CP: Clobetasol propionate, HC: Hydrocortisone

Table 3: Evidence in favor of using topical corticosteroids in psoriasis (nonscalp)

| Name and year of study         | Type of study                      | Drugs                                                                 | Result                                                                 |
|--------------------------------|------------------------------------|----------------------------------------------------------------------|------------------------------------------------------------------------|
| Kuokkanen 1976[56]             | Randomized double-blind comparative trial | 0.25% desoxymethasone versus 0.05% fluocinonide                      | Desoxymethasone-treated side showed a significantly better improvement |
| Fabry and Yawalkar 1983[59]    | Multicenter, between-patient, comparative trial | 0.05% halometasone versus 0.25% fluorocortolone+0.25% fluorocortolone caproate | Halometasone-yielded higher success rate                                |
| Jegasothy et al. 1985[40]      | Randomized double-blind, parallel comparison study | 0.05% CP versus 0.05% fluocinonide                                   | Clobetasol was statistically significantly superior to fluocinonide    |
| Jacobson et al. 1986[41]       | Randomized double-blind, parallel-group, comparative trial | CP 0.05% versus betamethasone dipropionate 0.05%                     | Clobetasol was better                                                  |
| Blum and Yawalkar 1991[42]     | Double-blind, parallel-group, multicenter comparative trial | 0.05% halobetasol propionate versus 0.1% betamethasone valerate     | 0.05% halobetasol propionate ointment was superior                     |
| Goldberg et al. 1991[43]       | Randomized double-blind, parallel-group, multicenter trial | 0.05% halobetasol propionate versus 0.05% CP                      | Halobetasol was superior to clobetasol                                  |

Contd....
Table 3: Contd...

| Name and year of study | Type of study | Drugs | Result |
|------------------------|---------------|-------|--------|
| Bernhard et al. 1991[64] | Randomized, double-blind, and vehicle-controlled | 0.05% halobetasol ointment versus vehicle b.d | Halobetasol ointment was better |
| Katz et al. 1991[65] | Randomized, double-blind comparative clinical trial | Fluocinonide 0.05% cream (Lidex) versus fluocinonide 0.05% cream (Vasoderm) | Lidex’ cream demonstrated better results |
| Olsen 1996[66] | Double-blind, randomized, vehicle-controlled parallel-group trial | FP 0.005% versus placebo b.d | Fluticasone ointment was superior |
| Roberts 1996[67] | Randomized, double-blind, parallel-group, multicenter study | FP 0.005% versus betamethasone dipropionate 0.05% | Both were equally good |
| Sears 1997[68] | Double-blind, randomized, placebo-controlled | HC 0.1% versus placebo | HC group showed good results |
| Peharda et al. 2000[69] | Randomized double-blind, parallel trial | Mometasone 0.1% versus betamethasone dipropionate 0.05% | Betamethasone group showed better |
| Stein et al. 2001[70] | Randomized, double-blind, placebo-controlled, split-body study | Betamethasone valerate foam versus placebo b.d | Betamethasone valerate foam was highly effective |
| Green and Sadoff 2002[71] | Multicenter, investigator-masked, randomized, parallel-group | Tazarotene 0.1% versus tazarotene plus high-potency topical corticosteroid (fluocinonide 0.05, mometasone 0.1%, or diflorsone 0.05%), versus tazarotene plus a mid-high-potency topical corticosteroid (betamethasone 0.05% or fluticasone 0.005%, or diflorsone 0.05%) all applied o.d | Betamethasone 0.05% was the best option followed by mometasone 0.1% and diflorsone diacetate 0.05% |
| Lebwohl et al. 2002[72] | Randomized, double-blind, placebo-controlled study | CP 0.05% foam b.d versus placebo | CP foam is more effective than placebo |
| Gottlieb et al. 2003[73] | Multicenter, randomized, double-blinded, placebo-controlled study | CP foam 0.05% b.d versus placebo | CP foam 0.05% is safe and effective |
| Decroix et al. 2004[74] | Randomized, controlled comparative, double-blind trial | CP lotion versus vehicle b.d | CP lotion was efficient, safe, and well tolerated |
| Lowe et al. 2005[75] | Multicenter, randomized, vehicle-controlled, parallel-group study | CP lotion versus CP emollient cream versus vehicle | CP lotion was significantly more effective than vehicle lotion and comparable to the emollient cream |
| Koo et al. 2006[76] | Randomized, multicenter sequential study | Clobetasol foam plus calcipotriene ointment or monotherapy | Combination therapy was better |
| Jarratt et al. 2006[77] | Randomized, double-blinded, vehicle-controlled, parallel-group, comparative study | CP spray 0.05% versus vehicle | CP spray 0.05% was effective and safe |
| Angelo et al. 2007[78] | Double-blind, randomized, right-left comparison study | Tazarotene 0.1% versus CP 0.05% | Clobetasol was better |
| Mraz et al. 2008[79] | Randomized parallel clinical study | CP 0.05% spray versus foam | Spray was better than foam |
| Tiplica et al. 2009[80] | Randomized, parallel multicenter trial | Mometasone 0.1% and salicylic acid 5% 7 days followed by mometasone 0.1% 14 days versus mometasone 0.1% 21 days | Sequential treatment was better |
| Fleming et al. 2010[81] | Randomized, parallel group, double-blind, exploratory study | Calcipotriol plus betamethasone dipropionate gel compared with its active components in the same vehicle and the vehicle alone | Two-compound gel was safe and more efficacious than its individual ingredients |

FP: Fluticasone propionate, CP: Clobetasol propionate, HC: Hydrocortisone
to be the most effective, but there are many alternative galenicals to increase feasibility and treatment adherence without losing too much effectiveness of the drugs.

Scalp psoriasis, though, responds to a wide array of topical therapies but TCs form the first line of management, and the response is excellent. The evidence in favor of steroids has been tabulated [Table 4].

The results in scalp psoriasis are similar to that seen in chronic plaque psoriasis elsewhere in the body.

**Lichen planus**

Lichen planus (LP) is a common chronic inflammatory dermatosis associated with disrupted cell-mediated immunity. Cutaneous lesions are often extremely pruritic and require rigorous intervention. Symptomatic oral LP is painful, and complete healing is uncommon, which necessitates active intervention. TCs are conventionally used as first-line therapy in cutaneous LP, but high-level scientific evidence is conspicuous by its absence. However, TCs show good results in oral LP, and the evidence has been summarized below [Table 5].

There is no evidence in favor of prescribing TCs in cutaneous LP although it is widely accepted as the first-line treatment for the same. This an indicator of the fact that, like several other more uncommon inflammatory dermatoses, in LP too, the use of TCs is fairly undocumented, but not necessarily unwarranted, as the advent of TC as a group of agents happened in the age of empiricism when the use of medicines was dictated by hypothetical reasoning rather than being guided by evidence generated from RCTs.

### Tables 4: Evidence in favor of using topical corticosteroids in psoriasis (scalp)

| Name and year of study | Type of study | Drugs | Result |
|------------------------|---------------|-------|--------|
| Willis et al. 1986[63]  | Randomized, double-blind, multicenter study | Desoximetasone 0.05% versus fluocinonide 0.05% b.d | Both were equally effective but desoximetasone was better tolerated |
| Olsen et al. 1991[64]   | Double-blind vehicle-controlled parallel group study | CP 0.05% versus placebo b.d | CP 0.05% is a safe and an effective treatment |
| Klaber et al. 1994[65]  | Multicenter, randomized, double-blind, parallel group study | Calcipotriol solution versus betamethasone 17-valerate solution b.d | Betamethasone group was significantly better |
| Katz et al. 1995[66]    | Randomized, multicenter, investigator-blinded, parallel-group study | Augmented betamethasone 0.05% lotion versus clobetasol 0.05% solution | Both were equally effective, but betamethasone dipropionate lotion was better |
| Franz et al. 1999[67]   | Randomized, multicenter, double-blind, placebo-controlled trial | Betamethasone valerate foam 0.12% versus placebo b.d | The novel foam formulation had greater efficacy without increased toxicity |
| Feldman et al. 2001[68] | Randomized, single-blind, open-label study | Betamethasone valerate in foam vehicle o.d versus b.d | BVM foam was effective with both once-a-day and twice-a-day use |
| Andreassi et al. 2003[69] | Open, investigator-blinded, multicenter, randomized, cross-over study | BVM versus standard therapies (steroid or calcipotriol) | BVM is more effective than lotion-based standard therapy |
| Pauporte et al. 2004[70] | Randomized, double-blind, vehicle-controlled multi-center study | Fluocinolone acetonide 0.01% in oil versus placebo | Fluocinolone group had significantly better response |
| Jarratt et al. 2004[71] | Randomized, vehicle-controlled, double-masked and parallel-group study | CP shampoo 0.05% versus placebo | The novel, short-contact shampoo formulation of CP was efficacious and safe |
| Reygagne et al. 2005[72] | Multicenter, randomized, investigator-masked, parallel group study | CP shampoo 0.05% versus calcipotriol solution 0.005% | CP was significantly superior |
| Jemec et al. 2008[73]   | Multicenter, randomized, double-blind study | Calcipotriene plus betamethasone versus calcipotriene versus betamethasone versus placebo b.d | Calcipotriene plus betamethasone dipropionate scalp formulation showed best results |
| Buckley et al. 2008[74] | Randomized, double-blind clinical study | Calcipotriol plus betamethasone dipropionate scalp formulation versus betamethasone o.d | Calcipotriol plus betamethasone dipropionate scalp formulation was superior |
| van de Kerkhof et al. 2009[75] | Randomized, multicenter, double-blind, parallel-group study | Calcipotriol plus betamethasone dipropionate versus calcipotriol versus betamethasone dipropionate b.d | Two-compound scalp formulation was well tolerated and more effective |

FP: Fluticasone propionate, BVM: Betamethasone valerate mousse, CP: Clobetasol propionate dipropionate b.d
Only limited evidence exists for the efficacy of TCs in oral LP. In addition, there is no evidence that topical calcineurin inhibitors are more effective than TCs in oral LP.\(^{[111]}\)

**Mycosis fungoides**

The most common form of cutaneous T-cell lymphoma is mycosis fungoides (MF), which accounts for approximately 60% of cases. Several reviews and guidelines on the management of MF have been published. TCs have been used in the treatment of mild, patch stage MF with good results,\(^{[112]}\) but unfortunately, evidence in favor of using them, is lacking.\(^{[113]}\) The current evidence-based recommendation is: TCs, especially Class I (potent) compounds, are effective at temporarily clearing patches and plaques in some patients with early-stage IA/IB MF.

**Bullous pemphigoid**

Bullous pemphigoid (BP) is an acquired common autoimmune blistering dermatosis characterized by the development of autoantibodies against the components of the basement membrane zone of the skin. Interestingly, superpotent topical steroids have emerged as a first-line therapy for limited disease.\(^{[114]}\) Two randomized clinical trials have been published in favor of topical steroids, and the summary has been tabulated as under [Table 6].

The two RCTs suggest the use of TCs as the first line for the treatment for both localized and mild disease. Relatively, few and mild side effects are associated with TC use in BP; however, their use in extensive disease may be limited by more side effects and practical factors.

**Cutaneous sarcoidosis**

Sarcoidosis is a granulomatous disease with multisystem involvement. Topical high potency fluorinated corticosteroids (with or without occlusive dressing) have been successfully used in localized cutaneous sarcoidosis, but high-level scientific evidence is lacking.\(^{[117,118]}\)

### Table 5: Evidence in favor of using topical corticosteroids in lichen planus

| Name and year of study | Type of study | Drugs | Result |
|------------------------|---------------|-------|--------|
| Voûte et al. 1993\(^{[100]}\) | Randomized, placebo-controlled, parallel clinical trial | Fluocinonide in adhesive cream (0.025%) versus placebo 6 times a day | Fluocinonide group showed excellent results |
| Rodstrom et al. 1994\(^{[101]}\) | Randomized double-blind clinical trial | CP 0.05% in orabase versus triamcinolone acetonide 0.1% ointment | Clobetasol was more effective than triamcinolone acetonide with respect to clinical improvement at the end of 3 weeks, but at the end of study, no significant difference was found |
| Hegarty et al. 2002\(^{[102]}\) | Randomized, crossover study | Sequence FP and BSP versus sequence betamethasone and fluticasone | FP and BSP were both effective but FP was more acceptable |
| Campisi et al. 2004\(^{[103]}\) | Randomized controlled single-blind Phase IV clinical trial | CP in microphases 0.025% versus CP 0.025% in a dispersion of a lipophilic ointment in a hydrophilic phase | New topical drug delivery system increased symptom remission, compliance, and effectiveness of CP |
| Conrotto et al. 2006\(^{[104]}\) | Double-blind, randomized controlled trial | CP 0.025% versus topical ciclosporin 1.5% both in hydroxyethyl cellulose b.d | Clobetasol was more effective in inducing clinical improvement but associated with more side effects |
| Yoke et al. 2006\(^{[105]}\) | Double-blind, randomized controlled trial | Topical ciclosporin solution 0.1% versus triamcinolone acetonide 0.1% in Orabase tds | Triamcinolone group showed better results |
| Laejendecker et al. 2006\(^{[106]}\) | Randomized, double-blind, clinical trial | Tacrolimus 0.1% ointment versus triamcinolone acetonide 0.1% in hypromellose 20% | Topical tacrolimus 0.1% ointment induced a better initial therapeutic response but associated with frequent relapses |
| Gorouhi et al. 2007\(^{[107]}\) | Investigator-blinded parallel-group randomized clinical trial | Pimecrolimus 1% qid versus triamcinolone acetonide 0.1% paste qid | Both showed excellent results |
| Carbone et al. 2009\(^{[108]}\) | Randomized, double-blind, placebo-controlled trial | Topical clobetasol 0.025% versus topical clobetasol 0.05% both in hydroxyethyl cellulose b.d | Both showed excellent results, without any statistically significant difference |
| Ghabanchi et al. 2009\(^{[109]}\) | Randomized comparative study | Mucoadhesive prednisolone tablet (5 mg) b.d versus triamcinolone acetonide paste (0.1%) tds | Both were equally effective |

FP: Fluticasone propionate, CP: Clobetasol propionate, BSP: Betamethasone sodium phosphate
Hand eczema
Chronic hand eczema is an extremely common and notorious entity encountered by general physicians and dermatologists. Currently, evidence-based guidelines for the management of this condition is lacking. However, there a few randomized clinical trials favoring the use of TCs [Table 7].

There is insufficient data on which to base a choice between short bursts of potent TCs compared with continuous application of mild TCs. There is little evidence of steroid-sparing effect of emollients. There is an insufficient evidence of an additive effect of topical antibacterial agents. In addition, there is a lack of data supporting the superiority of topical calcineurin inhibitors to TCs.[122]

Infantile hemangiomas
Superficial infantile cutaneous hemangiomas are difficult to manage. Two small case series using ultrapotent TCs for periorificial hemangiomas have been reported. However, evidence in favor of using this therapy for other sites is lacking. Garzon et al. assessed the cessation of growth, shrinkage or flattening of the lesion, and lightening of the surface color. Seventy-four percent of the cases demonstrated either good or partial response to ultrapotent TCs. In another study by Pandey et al., mometasone was applied twice daily and compared with intralesional triamcinolone acetonide injections at monthly intervals

Miscellaneous Conditions
Alopecia areata
One RCT demonstrated that potent TCs are marginally more effective than placebo when used continuously for a minimum of 3 months. In observational case series, children between the ages of 3 and 10 years appear most likely to respond.[125]

Anogenital pruritus
In idiopathic cases, TCs may be helpful, but they may mask malignancy and other underlying disease.[126]

Cutaneous lupus erythematosus
All the controlled trials of TC were of short duration, but the evidence supports the use of potent TCs in DLE (Discoid lupus erythematosus). Although TC use may be associated with skin atrophy, it is probably not important in DLE, which produces severe scarring and atrophy in itself.[127]

Melasma
There have been one systematic review[128] and one trial of 17 participants followed for 3 months.[129] Although the study reports that betamethasone was effective as a depigmenting agent (P < 0.05), the numbers were very small, and seven of 16 women in the study found no therapeutic difference between treatment and placebo.

| Table 6: Evidence in favor of using topical corticosteroids in bullous pemphigoid |
|---------------------------------------------|-------------------------|---------------------------------------------------------------|
| Name and year of study | Type of study | Drugs | Result |
|-------------------------|-----------------|-------|--------|
| Joly et al. 2002[115]    | Randomized nonblind comparative trial | CP versus prednisone, 0.5 mg/kg (moderate disease) and 1 mg/kg (severe disease) | 100% disease control in both groups with moderate disease, but patients with extensive disease had better control with clobetasol |
| Joly et al. 2009[116]    | Randomized nonblind comparative trial | CP: Mild dose (10–30 g/day depending on disease severity and body weight) versus standard dose (40 g/day) | Disease control was excellent in both groups, along with 70% reduction in cumulative doses of cream used in mild regimen. Mortality was less in patients with treated with mild regimen |

CP: Clobetasol propionate

| Table 7: Evidence in favor of using topical corticosteroids in hand eczema |
|---------------------------------------------|-------------------------|---------------------------------------------------------------|
| Name and year of study | Type of study | Drugs | Result |
|-------------------------|-----------------|-------|--------|
| Faghihi et al. 2008[119] | Randomized, double-blind, right-left, clinical trial | 0.05% clobetasol+2.5% zinc sulfate cream versus 0.05% clobetasol cream | 0.05% clobetasol+2.5% zinc sulfate‘ cream was more effective than “0.05% clobetasol alone” cream |
| Agarwal et al. 2013[120] | Observer-blinded randomized comparative trial | Clobetasol 0.05% b.d versus oral azathioprine 50 mg plus clobetasol 0.05% b.d | Both the groups showed good results, but low-dose oral azathioprine therapy was an effective adjunctive therapy |
| Gola et al. 2015[121]   | Randomized double-blind comparative trial | FP 0.05% versus clobetasol ointment 0.05% | Clobetasol group showed better response |

FP: Fluticasone propionate
There is controversy over the balance between benefits and harms of using TCs in the treatment of melasma, especially since long-term use on the face can cause skin thinning and telangiectasia.

**Perioral dermatitis**

There is insufficient evidence (level of evidence: D) on the effects of nonfluorinated steroids in patients with perioral dermatitis. A split-face RCT of hydrocortisone butyrate versus 1% hydrocortisone alcohol cream is available.[130] Two patients with perioral dermatitis showed a moderate rebound of the eruption after withdrawal of topical treatment, in each case on the hydroxybutyrate-treated side of the face. In view of the study design and the small number of patients, it is difficult to draw conclusions.

**Seborrheic dermatitis**

Even though, TCs are considered to be the first line therapy for the management of seborrheic dermatitis, but, there is absence of high-level evidence supporting the use of TCs. Studies have shown that steroids are superior to placebo in the treatment of mild to moderate seborrheic dermatitis. Besides, there were no statistically significant differences between steroids and calcineurin inhibitors in terms of the assessed outcomes in a few studies. In addition, no statistically significant differences were found between steroids and azoles in their effectiveness in producing total clearance of lesions of seborrheic dermatitis.[131]

**Pregnancy and Lactation**

Women with skin conditions often need TCs during pregnancy. However, the knowledge about the effects of TCs on the fetus is scarce. The current best evidence supports the use of mild-to-moderate TCs in comparison to potent/superpotent alternatives in pregnancy because of the associated risk of fetal growth restriction with the latter. There is no significantly increased risk of orofacial clefts, preterm delivery, growth retardation, and fetal death when mild-to-moderate TCs are used in pregnancy. However, it must be noted that potent or superpotent TCs should be used as second-line therapy only for the shortest possible duration. Whenever high potency corticosteroids are used, meticulous obstetric care is mandatory because they increase the likelihood of low birth weight baby. Depending on the severity of the dermatoses, women should use TCs of the least potency required, and the duration and amount of application of the drug must be monitored judiciously. The risk of adverse events is increased when areas with high absorption (genitals, eyelids, skin folds, armpits, and vulva) are treated with topical steroids. There is lack of evidence regarding the safety profile of newer lipophilic TCs (mometasone furoate, fluicasone propionate, and methylprednisolone acetonate) with a good therapeutic index. On theoretical grounds, these should be associated a lesser risk of low birth weight, but high-level scientific evidence is lacking, and it is not possible to comment on the adverse effect profile of these newer congeners.[132-135]

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**What is new?**

- Twice-weekly application of potent topical corticosteroids (TCs) in stable eczema significantly reduces the number of flares. Moreover, skin thinning and suppression of the pituitary – adrenal axis are not seen if TCs are used judiciously and appropriately.
- Class III TCs are highly effective in inducing remission in psoriasis (both scalp and non-scalp).
- TCs are widely used as first-line therapy in cutaneous lichen planus (LP), but high-level scientific evidence is categorically absent. There is not a single-randomized controlled trial (RCT) supporting the use of TCs in cutaneous LP. However, there is evidence in favor of prescribing TCs in oral LP.
- Interestingly, TCs have emerged as the first-line treatment for both localized and mild bullous pemphigoid.
- In chronic hand eczema, TCs have been found to be beneficial, but the choice between short bursts of potent TCs versus continuous application of mild TCs, is difficult, due to lack of evidence.
- Evidence in favor of using TCs in mycosis fungoides, cutaneous sarcoidosis, infantile hemangiomas, seborrheic dermatitis is lacking.
- In pregnancy and lactation, mild-to-moderate TCs can be safely prescribed, without the fear of associated risk of preterm labor and fetal growth restriction, provided TCs are not applied for a long duration and over areas with high absorption rates. Potent or superpotent TCs should be used only as second-line therapy because of risk of developing low birth weight baby.

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