Side to side comparison of topical treatment in atopic dermatitis

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Abstract

Objectives—To document and evaluate the outcome of side to side comparisons of different corticosteroids in determining the most effective topical treatment for individuals admitted to hospital for control of atopic dermatitis.

Methods—Retrospective case note study of 82 admissions (66 children) to a children’s hospital for treatment of atopic dermatitis between 1 June 1993 and 31 October 1995. Different topical corticosteroid ointments were applied to the two sides of the body. The outcome measure was a comparison between the two sides, to see whether one treatment was better than the other.

Results—More potent topical corticosteroid preparations appeared more effective than weaker preparations on 25 occasions, there was no difference on 20 occasions, and on seven occasions a weaker preparation appeared more effective. Incorporation of an antimicrobial agent did not appear to increase the efficacy of a preparation.

Conclusions—The management of atopic dermatitis is bedevilled by considerable spontaneous fluctuations in severity, leading to uncertainty as to whether a new treatment is beneficial; a coincidental flare up of the skin lesions may be wrongly attributed to a particular treatment, which is then discarded. Comparing different topical treatments simultaneously on opposite sides of the body is a feasible and rational way to determine the optimum treatment for an individual with atopic dermatitis.

Keywords: atopic dermatitis; corticosteroids; topical corticosteroids

Once relevant trigger factors have been identified and where possible eliminated, the main treatment of atopic dermatitis is the topical application of emollients and corticosteroids. Whereas chronic conditions such as hypertension, diabetes, hypothyroidism, asthma or short stature can be managed by reference to relatively simple, reliable, and objective clinical or laboratory measurements, there is no such marker in atopic dermatitis. The management of atopic dermatitis is further bedevilled by considerable day to day and even minute to minute variation. Skin lesions that are quiescent at 08:00 can become highly inflamed by 09:00 after a journey in a hot car, a confrontation with a parent, the ingestion of a trigger food or, most commonly of all, for no apparent reason. Thus, there is often uncertainty as to whether a change in treatment is beneficial. In particular, there is a risk that a coincidental flare up of the skin lesions may be wrongly attributed to a particular treatment, which is then discontinued.

Side to side comparisons have been used in clinical trials of various topical treatments, mainly in psoriasis.1–10 A fundamental principle of this approach is that it can only be used when skin lesions are relatively symmetrical, as is commonly the case in atopic dermatitis. We have used side to side comparison when introducing new topical treatments to inpatients with atopic dermatitis, and this study aimed to document and evaluate the outcome of these comparisons.

Subjects and methods

We admit two categories of patient with atopic dermatitis to hospital, those with severe acute flare ups that cannot be controlled at home, and those with poorly controlled severe and chronic skin lesions. The management of the latter group routinely comprises side to side comparisons of different topical preparations. The side to side treatment comparison method incorporates the following principles.

• An overall aim to find the most suitable topical corticosteroid for continuing use; we do not use the strategy of starting with a very potent corticosteroid and then switching to a weaker preparation

• To treat the face and neck separately from the rest of the body, dividing it into left and right portions, never applying a corticosteroid stronger than mild potency

• To divide the rest of the body into four quadrants, ensuring that one quadrant is treated as a control with emollient only but no corticosteroid, to detect changes in the overall condition

• To allow the free use of one emollient ointment or cream preparation (as preferred by the patient), with the exception that emollients are not applied to all areas of skin treated with topical corticosteroids up to two hours before or two hours after the application of corticosteroids

• To continue with the same frequency of bathing used before starting side to side comparisons

• To compare different topical corticosteroid preparations, usually from a different potency category (mildly potent, moderately potent, potent, and very potent, as defined in the British National Formulary)11
of 21 potent corticosteroids. A sedating antihista-
mamine had been prescribed for bedtime use in
53 of 82 cases. The agent used was trimepra-
zine in all but seven children, who were
prescribed other sedating antihistamines (hy-
droxylazine, promethazine, chlorpheniramine,
azatadine, methotrimeprazine).
In 28 of 82 admissions, children were using inhaled β2 agonists for asthma; 23 of these chil-
dren were also using inhaled corticosteroids.
Five patients were on long term oral cortico-
steroids: beclomethasone for atopic dermatitis (two cases)17 18 and prednisolone (for atopic
dermatitis in one case and for asthma in two
cases). Emollients were used in 81 of 82
admissions. The sedative H1 receptor antag-
nist trimeprazine was given at bedtime during
73 of 82 admissions.

CORTICOSTEROID ✈ EMOLLIENT
We compared a topical corticosteroid with an
emollient alone on 22 occasions in 20 children,
10 of whom were newly referred. We compared
a mildly potent corticosteroid (1% hydrocorti-
sone ointment) with emollient on 17 of 22
occasions. The corticosteroid appeared more
effective in 10 of the 17 cases, there was no dif-
fERENCE between the two preparations in five
cases, and the emollient appeared more
effective in two cases (χ² = 5.33, df 2,
p < 0.05). A moderately potent topical corti-
costeroid was compared with an emollient in
three of 22 cases. The corticosteroid appeared
more effective in one comparison, but in the
other two cases there was no difference. A
potent topical corticosteroid was compared
with emollient alone in two cases and in both
the corticosteroid appeared more effective.

CORTICOSTEROID ✈ CORTICOSTEROID COMBINED
WITH ANTIBACTERIAL AGENT
Forty two comparisons involved topical corti-
coeroids of the same potency, with or without
an antibacterial agent. We found no difference
between the two types of preparation in 23
comparisons; the corticosteroid with an anti-
bacterial agent appeared more effective in 11
cases; and corticosteroid alone appeared more
effective in eight cases (χ² = 0.47, df 1,
p > 0.05).

MILDLY ✈ MODERATELY POTENT CORTICOSTEROIDS
There were 31 comparisons of mildly versus
moderately potent corticosteroids. The mildly potent
corticosteroid appeared more effective in five
cases; there appeared to be no difference in 10
cases; and the moderately potent cortico-
steroid appeared more effective in 16 compar-
isons. A moderately potent topical corticoster-
oid was significantly more effective than a
mildly potent corticosteroid (χ² = 5.76, df 2,
p < 0.05).

MILDLY POTENT ✈ POTENT CORTICOSTEROIDS
There were nine comparisons of mildly potent
vs potent corticosteroids. In six we could detect
no difference, and in three the potent cortico-
steroid appeared to be more effective.
MODERATELY POTENT v POTENT TOPICAL CORTICOSTEROIDS
There were 12 comparisons of moderately potent v potent topical corticosteroids. We could detect no difference in four cases. In six the potent corticosteroid appeared more effective, and in two we considered the moderately potent corticosteroid more effective. A potent topical corticosteroid was not more effective than a moderately potent corticosteroid (χ² = 2.0, df 1, p > 0.05).

COMPARISONS OF DIFFERENT BUT EQUIPOTENT CORTICOSTEROIDS
There were 10 comparisons of different, equipotent corticosteroids. We detected no difference in four cases, but in six one preparation appeared more effective than the other.

Discussion
There are a number of methodological drawbacks to this study. It was retrospective, and therefore dependent on the amount of information recorded routinely. The need to include the patient's original medication prevented complete standardisation, so that several different combinations of topical treatments were compared, leading to small numbers in some comparisons. The lack of an objective measure of local disease severity is a difficulty that applies to any clinical study of atopic dermatitis. The fact that the patients were referred and admitted implies they were a highly selected and a severe subset of the general population of patients with atopic dermatitis. An advantage of such a group is that compliance is more likely to be achieved during the study period. Admission to hospital is itself a confounding variable, because atopic dermatitis sometimes improves when patients are admitted, even without any change of treatment. One reason for maintaining one quadrant without corticosteroid treatment was to detect overall improvement, either as a non-specific result of admission or as a result of treatment with an oral antibiotic. However, factors leading to overall improvement would not account for differences between two sides of the body.

To compare treatments on opposite sides of the body successfully, it is important to prevent mixing of the different preparations and cross contamination. Nurses applied topical agents. They wore disposable gloves, and changed gloves and excipients or by causing contact dermatitis. A potent topical corticosteroid appeared more effective in two cases. A similar difference, and the emollient seemed more effective in two cases. A similar phenomenon has been made before in adults with chronic hand dermatitis in whom an emollient containing no active ingredients was as effective as 0.025% betamethasone valerate (a potent corticosteroid) over a one month period. It is possible that apparently bland emollients have pharmacological properties—for example, studies in mice have demonstrated that the "placebo" effect of topical applications such as white soft paraffin or cetomacrogol cream, corticosteroids, and anti-inflammatory activity. In addition, some bland preparations have an anticyclop-ogenase effect on the microsomal fraction of skin homogenates and this could account for many of the anti-inflammatory effects of these materials. Certain emollients, such as white soft paraffin, have been shown to have vasoconstrictor activity in the skin (to a lesser degree than topical corticosteroids) as well as a skin thinning effect (also to a lesser degree than topical corticosteroids).

It is known that the stratum corneum layer of the skin can act as a reservoir for topically applied corticosteroids. In healthy skin, this reservoir may last for a few days, but in eczematous skin the effect may only last for one or two days. Either systemic absorption or a reservoir effect might help to explain some of the cases where corticosteroid and emollient were equally effective, because the patients had been using topical corticosteroids on their skin before admission in six of the nine cases. However, a reservoir effect cannot explain the apparent equal efficacy of corticosteroid and emollient in the three children who had not been using topical corticosteroids before admission to hospital. Lastly, in cases where there was no apparent advantage of corticosteroid over emollient, it is theoretically possible that the topical corticosteroid caused worsening of the skin condition, either by irritation from the excipients or by causing contact dermatitis. However, we found no evidence of these types of worsening in these cases.

Comparing different topical agents simultaneously on opposite sides of the body is a feasible and rational way to determine the best topical treatment for an individual patient. However, the hypothesis that demonstrating efficacy to patients and parents leads to improved adherence to treatment or to a better outcome is as yet untested.

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9 Wendt H, Muggleston CJ, Wiseman RA. A study of the comparative efficacy of diflucortolone valerate 0.3% ointment and clobetasol propionate 0.05% ointment. Br J Dermatol 1978;99:411–16.


