

Primary care



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Randomised controlled trial of short bursts of a potent topical corticosteroid versus prolonged use of a mild preparation for children with mild or moderate atopic eczema

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Abstract

Objective To determine whether a three day burst of a potent corticosteroid is more effective than a mild preparation used for seven days in children with mild or moderate atopic eczema.

Design Randomised, double blind, parallel group study of 18 weeks' duration.

Setting 13 general practices and a teaching hospital in the Nottingham area.

Participants 174 children with mild or moderate atopic eczema recruited from general practices and 33 from a hospital outpatient clinic.

Interventions 0.1% betamethasone valerate applied for three days followed by the base ointment for four days versus 1% hydrocortisone applied for seven days.

Main outcome measures Primary outcomes were total number of scratch-free days and number of relapses. Secondary outcomes were median duration of relapses, number of undisturbed nights, disease severity (six area, six sign atopic dermatitis severity scale), scores on two quality of life measures (children's life quality index and dermatitis family impact questionnaire), and number of patients in whom treatment failed in each arm.

Results No differences were found between the two groups. This was consistent for all outcomes. The median number of scratch-free days was 118.0 for the mild group and 117.5 for the potent group (difference 0.5, 95% confidence interval -2.0 to 4.0, $P = 0.53$). The median number of relapses for both groups was 1.0. Both groups showed clinically important improvements in disease severity and quality of life compared with baseline.

Conclusion A short burst of a potent topical corticosteroid is just as effective as prolonged use of a milder preparation for controlling mild or moderate atopic eczema in children.

Introduction

Atopic eczema, or atopic dermatitis, is an itchy inflammatory skin disorder that affects around 15% of British school children.¹ In most children the disease follows a chronic relapsing course, and most children are

managed in primary care.^{1,2} Although topical corticosteroids have been the mainstay of treatment for the past 40 years, few clinical trials have studied their optimum use.³ Side effects such as thinning of the skin can occur with these preparations. This causes anxiety for both patients and clinicians and is the main reason for patients' poor compliance with treatment.^{4,5}

A recent systematic review of treatments for atopic eczema identified 83 randomised controlled trials dealing primarily with topical corticosteroids.⁶ Most trials lasted less than six weeks. None were conducted in primary care, and most compared a new preparation with an established preparation, rather than addressing key issues such as duration of use, potency, and cotreatment.⁷

We aimed to determine whether a three day burst of a potent topical corticosteroid was more effective than a mild preparation used continuously for seven days, without causing an increase in thinning of the skin. We also determined the costs of these treatment regimens to the NHS.

Methods

Participants

We enrolled children aged 1 to 15 years with mild or moderate atopic eczema within the past month.^{8,9} Children with severe eczema were excluded. Other reasons for exclusion were known sensitivity to the study treatments, or eczema confined to the face or nappy area.

Participants were recruited from the eczema clinic at Queen's Medical Centre and from 13 general practices in the Nottingham area.

Interventions

We performed a pragmatic, double blind, randomised controlled trial of 18 weeks' duration, with follow up every six weeks. We randomised participants to one of two treatment groups. Children in the mild arm received 1% hydrocortisone ointment twice daily for seven days. Children in the potent arm used 0.1% betamethasone valerate (Betnovate; GlaxoWellcome) twice daily for three consecutive days, followed by a base emollient only (white soft paraffin) for four days. Both treatments were dispensed in white tubes labelled A

and B to maintain blinding of the treatment allocation. Treatment was given in seven day bursts when required.

Primary outcomes

Primary outcomes were based on reports of scratching recorded in a daily diary. Scratch scores were graded in response to "how much has your eczema made you scratch today?" from 1 (not at all) to 5 (all the time). Scores of 2 or less were categorised as a scratch-free period. Participants were assumed to be in relapse if they scored more than 2 for at least three consecutive days. The primary outcomes were the number of scratch-free days and the number of relapses during the study period.

Secondary outcomes

Secondary outcomes were the median duration of the first relapse, the median duration of the first remission, the number of undisturbed nights, disease severity,¹⁰ quality of life,^{11,12} the proportion of treatment failures in each group defined as the number of participants who used concurrent treatments or who were lost to follow up, and skin thickness measured with a 20 MHz B mode ultrasound scanner. Sites scanned were the elbow and knee creases, the lateral aspect of the forearm, and the back of the calf.

Sample size

To detect a difference of at least 15% in the mean number of scratch-free days between the two groups, with an 0.05 two sided significance level and 90% power and an attrition rate of 10%, we needed 100 participants in each group.

Randomisation and blinding

Randomisation was computer generated in blocks of four. Participants and assessors were blinded to group assignment during collection of the data.

Economic evaluation

We evaluated the costs of the two treatments to the NHS. We included direct costs (ointments and rescue treatment), consultations with health professionals (with general practitioners and visits as outpatients and inpatients), and the use of prescribed drugs or treatments during the trial. We calculated the quantity of ointments used by weighing the returned tubes. Rescue treatment was deemed to be required if participants dropped out of the study because their eczema was uncontrolled. For these participants standard care was assumed to consist of Eumovate (GlaxoWellcome) used twice daily for three days, at a cost of 18p.

Costs were taken from the September 2000 edition of the *British National Formulary* and the Personal Social Services Research Unit for the same year.¹³

Statistical methods

We analysed severity scores by using a repeated measures analysis of variance. The proportions of participants achieving >20% improvement in scores at 18 weeks and of those in whom treatment failed were compared by using χ^2 tests with continuity correction. We compared changes in quality of life between the groups by using Student's *t* test. Clinically important thinning of the skin was defined as >25% reduction in skin thickness compared with baseline at any of the predefined sites.

Most of the children (84%) were recruited from the community. As these participants were more likely to reflect patients treated in primary care, we concentrated our analysis mainly on them.

We conducted our analysis on an intention to treat basis, and we imputed missing data by carrying forward the last known value. For the economic data if an activity was not recorded it was assumed that it had not occurred, and we recorded a zero cost.

Results

We recruited participants from October 1999 to October 2000 and completed follow up assessments by March 2001. Major differences in severity were observed between community and hospital patients at baseline; 60% and 36%, respectively, had mild disease (table 1). Community patients also had less severe eczema, less impairment of quality of life, and were less likely to use potent topical steroids, oral antibiotics, and wet wraps than hospital patients.

Primary outcomes

The median number of scratch-free days was 118.0 for the mild group and 117.5 for the potent group (difference 0.5, 95% confidence interval -2.0 to 4.0; $P=0.53$). The number of relapses per patient ranged from 0 to 9 and was also similar between the two groups.

Secondary outcomes

No differences were observed for any of the secondary outcomes between the groups (table 2). Both groups improved by 2.0-2.5 points compared with baseline values of 8 or 9. Improvements were achieved by six weeks and maintained throughout the study. Both groups had a similar proportion of participants who showed >20% improvement in severity (mild arm, 48 (55%); potent arm 49 (56%); $P=1.00$). The groups showed similar improvements in quality of life (table 2).

The proportion of participants who dropped out of the study or resorted to concurrent treatment was slightly higher in the mild than potent arm (31 (36%) *v* 22 (25%), respectively) (11% difference, -3 to 25; $P=0.19$). In the mild arm, six participants dropped out owing to uncontrolled eczema, 10 dropped out for other reasons, and 15 used concurrent treatments but remained in the study. In the potent arm, three participants dropped out owing to uncontrolled eczema, eight dropped out for other reasons, and 11 used concurrent treatments but remained in the study.

Adverse events

Eighteen participants reported adverse events: nine in the mild group and five in the potent group reported worse symptoms, and two in the potent group reported spots or rashes and one reported hair growth. One patient in the potent group was admitted to hospital with viral encephalitis. None of the patients developed any clinical evidence of skin thinning. Complete ultrasound data were available for 106 (51%) patients. Data were unavailable from 1 April to 31 July 2000 either because the machine was unavailable or because facilities prevented its use. The mean change in skin thickness was measured in millimetres at each site. Skin thickness of the elbow crease at baseline was 0.91 mm (mean change -0.04 (SD 0.11) mm) for the mild

Table 1 Baseline characteristics of children recruited from hospital and the community with mild to moderate atopic eczema. Values are numbers (percentages) unless stated otherwise

	Hospital patients		Community patients	
	Mild arm (n=17)	Potent arm (n=16)	Mild arm (n=87)	Potent arm (n=87)
Male	8 (47)	10 (63)	49 (56)	36 (41)
White	14 (82)	15 (94)	77 (89)	79 (91)
Mean (SD) age	5 (3.2)	6 (3.0)	5 (3.8)	6 (4.0)
Family income:				
<£7999	2 (12)	2 (13)	10 (12)	8 (9)
>£34 000	3 (18)	4 (25)	16 (18)	17 (20)
Education of main care giver (basic)	9 (53)	5 (31)	35 (40)	34 (39)
Mild eczema	6 (35)	6 (38)	62 (71)	52 (60)
Mean (SD) disease severity*	13.6 (8.7)	16.2 (9.7)	8.2 (6.1)	9.0 (6.3)
Mean (SD) quality of life:				
Children's life quality index	7.6 (6.8)	7.8 (5.9)	5.1 (4.1)	5.6 (4.6)
Dermatitis family impact questionnaire	4.9 (6.1)	4.1 (5.3)	2.5 (3.2)	2.9 (3.9)
Mean (SD) skin thickness (mm):				
Elbow (n=141)	0.91 (0.2)	0.99 (0.3)	0.91 (0.2)	0.92 (0.1)
Forearm (n=142)	0.95 (0.2)	0.89 (0.1)	0.95 (0.2)	0.95 (0.1)
Knee (n=127)	1.01 (0.3)	0.98 (0.15)	0.99 (0.2)	1.04 (0.2)
Calf (n=123)	1.08 (0.2)	1.19 (0.2)	1.12 (0.1)	1.16 (0.2)
Mean (SD) areas of involved skin	8.0 (8.1)	7.6 (5.3)	2.5 (2.9)	2.8 (3.2)
Mean (SD) amount of steroid used in past month	15.7 (14.3)	12.8 (15.5)	13.8 (18.5)	14.9 (21.3)
Potent steroids prescribed	14 (88)	14 (88)	19 (23)	23 (27)
Wet wraps used	7 (41)	10 (63)	3 (3)	12 (4)
Antibiotics taken for skin in past year	7 (41)	8 (50)	20 (23)	20 (2)
Oral steroids used	3 (17)	2 (13)	3 (3)	9 (10)
Steroid inhaler used	6 (35)	8 (50)	23 (26)	29 (33)

*According to six area, six sign atopic dermatitis severity scale.

group and 0.99 mm (-0.05 (0.14) mm) for the potent group. Findings were similar at sites on the knee, calf, and forearm. Eleven participants had a reduction in skin thickness $>25\%$ at 12 sites. Four (8%) had been allocated to the mild group and 7 (12%) to the potent group ($P=0.7$).

Economic evaluation

Participants in the mild arm used an average of 68 g of hydrocortisone and those in the potent arm used 33 g of betamethasone valerate. Both groups used similar quantities of emollients (mean 400 g). Total costs were similar for the two groups. The slightly higher mean costs for the mild group reflected the participant admitted to hospital (mean £12.11 *v* £8.61 for the mild and potent groups, respectively). This difference was not significant (mean difference £3.51, $-\text{£}4.79$ to $\text{£}11.80$; $P=0.41$).

Discussion

Strengths and weaknesses of our study

The strengths of our study include its pragmatic design, long duration, and the use of patient specific outcomes alongside validated scales for severity and quality of life. The study population also reflects a wider group of patients with eczema than in previous hospital based studies and is thus better able to inform general practice, where most cases are treated. Nevertheless, some reservations exist. In particular, the median number of scratch-free days was high in both groups, which could make a further 15% reduction in symptoms difficult to achieve. Our definition of relapse may have failed to capture the true morbidity. Comparison of the number of 7 day treatment blocks initiated in each group showed that participants

Table 2 Intention to treat analysis of outcome measures of children with mild to moderate atopic eczema treated with short bursts of a potent topical corticosteroid (potent arm) or continuous use of a mild preparation (mild arm). Secondary outcomes presented for participants recruited in community only. Values are medians (interquartile ranges) unless stated otherwise

Outcome measure	Mild arm	Potent arm	Difference (95% CI)	P value
Primary outcomes				
No of scratch-free days:				
All participants (n=198)	118.0 (99.8-124.0)	117.5 (99.3-125.0)	0.5 (-3.0 to 2.0)	0.68
Community only (n=165)	118.0 (105.5-124.5)	117.5 (92.3-124.8)	0.5 (-2.0 to 4.0)	0.53
No of relapses:				
Community only (n=165)	1.0 (0.0-3.0)	1.0 (0.0-3.0)	0	0.66
Secondary outcomes				
Duration of first relapse (n=92)*	4.0 (3.0-7.5)	4.0 (3.0-9.0)	0.0 (-1.0 to 0.0)	0.33
Duration of first remission (n=89)†	6.0 (4.0-20.5)	7.0 (3.0-15.0)	-1.0 (-2.0 to 3.0)	0.95
Undisturbed nights (n=165)	123.0 (109.5-126)	121.0 (101.3-126)	2.0 (0.0 to 2.0)	0.53
Mean (SD) change from baseline:				
Children's life quality index (n=168)	-2.4 (4.0)	-1.9 (3.0)	-0.5 (-1.52 to 0.62)	0.41
Dermatitis family impact questionnaire (n=169)	-0.5 (2.4)	-0.6 (2.2)	-0.1 (-0.60 to 0.80)	0.78

*Participants who had relapse.

†Participants who had relapse followed by remission.

What is already known on this topic

Topical corticosteroids have been used to control atopic eczema for 40 years

No studies have compared short bursts of a potent preparation with prolonged use of a weak preparation for controlling mild or moderate disease

What this study adds

A short burst of a potent topical steroid is as effective and safe as prolonged use of a weak preparation for mild or moderate atopic eczema

The type of preparation is immaterial provided that the dosage is adequate

resorted to treatment in the absence of self reported itch (median 7 treatment blocks initiated in mild group, 8 in potent group). This contrasts with a median of one relapse defined by the scratch scores in both groups.

Impact on skin thinning

Interpretation of the ultrasound data was difficult as methodological problems exist when this technology is used within a pragmatic randomised controlled trial. Location of the scan, time of day, temperature, and humidity affect skin thickness.^{14 15} Eczematous skin is also abnormally thick (lichenified) and much of the reduction in thickness may be due to a return to normal levels. We found that eight of the 12 sites with large reductions in skin thickness had active eczema at baseline, and in all but two instances baseline skin thickness was 20-50% higher than the mean for the site. The skin thickness after 18 weeks was within the normal range at baseline for all the participants. Therefore both mild and potent steroids seem to be safe when used appropriately over four months.

Patients' choice of treatment

Following feedback on the results, 50% of the participants who responded to the questionnaire said they would choose 1% hydrocortisone; largely because they preferred to use a mild steroid if it controlled the eczema successfully. By contrast, 50% chose to use betamethasone in short bursts as it reduced treatment time and controlled the eczema quickly. The final choice of treatment could be left to patients.

Care has to be taken when generalising our findings to clinical practice. Prescribing the preparations without full instructions may not result in the

clinical improvement we achieved.¹⁶ Practice nurses or nurses specialised in dermatology can help promote appropriate use.¹⁷ Greater care has to be taken when generalising our findings to secondary care, where children with severe disease predominate.

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One hundred years ago Quacks in Germany

Statistics recently published show that there are in Berlin 476 quacks, male and female, the number of legally-qualified practitioners being about 2,000. Of the male "healers" 20 per cent. have been servants or workmen, 40 per cent. artisans, and 16 per cent. tradesmen. Among 125 "lady healers" only one has had more than the most elementary education, while 58 per cent. are of the servant class, 24 per cent. shopgirls, 10 per cent. factory

hands, and 4 per cent. sick nurses. The number of illegal practitioners in Saxony in 1900 was 1,578. This does not include a number of quacks who ply their trade without the knowledge of the police authorities. The number of legally-qualified practitioners of medicine in Saxony in the same year was 2,029.

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