

Efficacy and safety of fluticasone propionate 0.005% ointment in the long-term maintenance treatment of children with atopic dermatitis: Differences between boys and girls?

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Treatment of atopic dermatitis (AD) in children tends to stabilize the condition in the short term. 'Maintenance' treatment options in children are limited. To assess the efficacy and safety of twice daily treatment with fluticasone propionate 0.005% (FP) ointment during 4 wk and the efficacy and safety of twice weekly maintenance treatment with FP in preventing exacerbations or remissions of AD during a 16 wk follow-up period. Ninety children (aged 4–10 yr) with moderate to severe AD were included in a randomized, multi-centre study and received FP ointment twice daily during the acute phase. Children whose AD was in remission after 4 wk of treatment, entered the maintenance phase. In addition to twice daily emollient, children were randomly allocated to receive FP or placebo ointment twice weekly on consecutive days. Efficacy was assessed by the objective SCORAD. Eighty-seven (97%) completed the 4-wk acute study period. Extensive remission was achieved in 78 (87%) children, and 75 children entered the maintenance phase. Intermittent treatment with FP resulted in less severe AD and significantly reduced risk of further relapse as compared with placebo. The risk of an exacerbation of AD was more than twice as high in the placebo group as in the FP group (hazard ratio 2.182, 95% CI). AD in girls was better controlled than in boys. This long-term study shows that the addition of twice weekly FP to standard maintenance therapy significantly reduces the risk of relapse in children with moderate severe AD.

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Atopic dermatitis (AD) affects 8.9–20.4% of those born after 1970 (1). Despite the introduction of topical immune modulators, topical corticosteroids and emollients are still the mainstay of drug therapy in AD. Although the history of topical corticosteroids in dermatology covers half a century and many trials, available clinical studies do not reflect the common clinical

practice and the need for long-term treatment. As a consequence, there is no consensus as to the best treatment regimen. While mild AD can be managed with emollients and mild to moderately potent topical corticosteroids, treatment of moderate severe and severe AD requires more potent corticosteroids. However, bringing an acute episode of AD under control is only one aspect of

this disease. Perhaps even more important is to keep patients in remission because a notorious characteristic of AD is its chronic recurrent character with persisting pruritus.

Specific studies in children are highly needed, not only because of the increasing prevalence of AD in this category of the population, but also because of the specific problems involved in treatment.

Having a high ratio of body surface area to body weight, children are more at risk of systemic side effects. Concerns over systemic absorption of topical corticosteroids in children have led to restrictions on duration of use and potency of steroid.

Topical FP is a potent corticosteroid with a low rate of percutaneous absorption and consequently a low potential for systemic toxicity (2, 3). In an earlier study, it was found that FP cream once daily applied was safe and effective in children with an exacerbation of AD (4). However, in this study, after withdrawal of FP, all of the children experienced a relapse of AD within 2 wk, indicating the need for maintenance treatment (4).

The current study design was chosen to assess a treatment regimen that would reflect both clinical need and common clinical practice. The main objective of the study was to assess the efficacy and safety of long-term intermittent treatment with FP 0.005% ointment in preventing exacerbations once AD is in remission.

Methods

Patients and design

We performed a randomized, multi-centre study with two distinct phases, involving 12 clinical centres in the Netherlands and 1 clinical centre in Belgium. Non-hospitalized children (aged 4–10 yr) with a documented history of moderate to severe recurring AD of whom AD exacerbated (5), were eligible for the study. Randomization was achieved by a computer-generated scheme and performed by the statistician (P.M.). The inclusion criteria were based on standard criteria for patients with AD as defined originally by Hanifin and Rajka and modified by Williams et al. Children should have at least four or more of the following basic features: history of flexural dermatitis, presence of an itchy rash, onset under the age of 2 yr, personal history of asthma, history of dry skin and/or visual flexural dermatitis.

At inclusion, children should have a representative index lesion with a target three-item severity (TIS) score (for an explanation see

clinical scoring systems) ≥ 3 and < 6 (as screening method). Children could not enter the study if they had received systemic treatment for AD in the month preceding the study. In the last week before study starts, only restricted medication (emollient, hydrocortisone acetate 1% and/or antihistamines when needed) was allowed. Local Medical Ethical Committees of all centres involved approved the study. Written informed consent was obtained from parents or legal guardians of all participating children. The study was explained to the children and if possible, children also gave their (written) consent.

Acute treatment phase

Children presenting with an acute exacerbation of AD entered an open acute treatment phase during which they received FP 0.005% ointment (brand Cutivate[®], Glaxo Wellcome b.v., the Netherlands and Glaxo Wellcome GmbH & Co, Bad Oldesloe, Germany) applied twice daily for 4 wk on all originally affected sites, even if no visible signs of AD were detectable, and on all newly occurring lesions. If necessary, lesions on the face were treated with emollients or/and with hydrocortisone acetate 1% cream. A control group was considered inappropriate in this acute treatment phase, firstly because it would have been unethical to treat children experiencing an acute exacerbation of moderate to severe AD with placebo, and secondly the intention of treatment was to stabilize an acute exacerbation of AD prior to entry into the maintenance phase.

Throughout the acute treatment phase, standard emollient was supplied for use as required. Study visits were at study entry (day 0) and after 2 and 4 wk. Children whose AD was in remission after this period (according to stringent defined criteria, index lesion target TIS ≤ 1) then entered the maintenance phase. Compliance was monitored by weighing the tubes of the used fluticasone propionate 0.005% ointment.

Long-term maintenance treatment phase

In the randomized, double-blind, maintenance phase, in addition to twice daily emollient (standard maintenance therapy, SMT), children were randomly allocated to receive FP ointment twice weekly (intermittent FP; IFP) or placebo ointment twice weekly (intermittent placebo; IPL) on two consecutive evenings for up to 16 wk. Study treatment started on the third day after the acute treatment ended. The days on which intermittent treatment was applied remained the same throughout the maintenance

phase. On days when study medication was applied, emollient was applied only in the morning. This maintenance phase lasted 16 wk or until the child suffered an exacerbation or relapse of AD. Study visits in the maintenance phase were at 4, 6, 8, 12, 16 and 20 wk from the start of the study.

Efficacy

Clinical scoring systems objective SCORAD and target TIS. The severity of disease activity was scored using the SCORing Atopic Dermatitis (objective SCORAD) system (6, 7), which is a composite index including the assessment of two items in a standardized manner: (i) extent (applying the rule of nine) and (ii) intensity on a scale from 0 to 3 (erythema, oedema/papulation, oozing/crusts, excoriation, lichenification and dryness). Total objective SCORAD is $0.2 \times \text{extent} + 3.5 \times \text{intensity}$. This scoring system reflects the modified consensus of the European Task Force on Atopic Dermatitis. Unlike the initial version of the SCORAD index (8), subjective symptoms were not included for the scoring of AD (6). Maximum value of objective SCORAD is 83, mild AD is characterized by $\text{SCORAD} < 15$, $15 \leq \text{SCORAD} < 40$ is moderate AD, and $\text{SCORAD} \geq 40$ is severe (to very severe) AD.

While the inclusion of a well-validated objective scoring system is undoubtedly important, particularly with regard to multi-centre clinical studies, if the treatment strategy is to be recommended for wider use by physicians whose primary area of expertise is not dermatology (e.g. general practitioners), then the results from these objective scoring systems must be reflected in simpler assessments with easier methodology. A number of simpler assessments exist often involving an 'index' or 'target' lesion. For example, the TIS score (TIS score), i.e. total sum score of three AD key symptoms: erythema, oedema/papulations and excoriation with a maximum of 9, shows good correlation with objective SCORAD (9, 10).

In this study, objective SCORAD was used to assess overall disease severity at any given time point. The target TIS score, being a simple scoring system that is most appropriate for the common clinical practice, was used to define exacerbation and remission.

All objective measurements for any particular child were made by the same experienced investigator.

Clinical endpoints. The primary objective of the study was to assess the efficacy of twice weekly

maintenance treatment with FP ointment in preventing exacerbations of AD compared with placebo ointment. Therefore, the primary endpoint of the study was objective SCORAD at the end of the study (week 20), or, if the child discontinued prematurely, at time of withdrawal.

Secondary endpoint assessments of the effectiveness of an intermittent FP maintenance regimen included the proportion of children experiencing a relapse and the time to relapse. A relapse was defined as an index lesion with a target TIS score of ≥ 3 . A relapse could occur either at the site of the original index lesion (target lesion) or at any new lesion (new target lesion) appearing during the maintenance phase.

Safety. Safety was assessed by monitoring adverse events throughout the study. Local side effects were visually assessed by systematically recording evidence of skin atrophy, telangiectasia, striae and hypertrichosis at each visit.

To assess the systemic load, urinary overnight cortisol/creatinine ratio were measured at the beginning, after 4 wk of treatment and at the end of the study. This measurement is reported to have excellent sensitivity comparable to the ACTH stimulation test (11, 12).

Statistical analysis. Statistical analysis was performed with SAS (Statistical Analysis Software) version 6.12. The Wilcoxon matched pairs signed ranks test and the Friedman test were used to analyse the improvement of AD as measured by changes in Index lesion and objective SCORAD and whether there was a change in urinary cortisol/creatinine ratio. McNemar's test and Cochran's *Q*-test were used to analyse changes in AD prevalence, mild AD or AD under control being defined as objective SCORAD < 15 , and moderate AD and severe AD being defined as $15 \leq \text{objective SCORAD} < 40$ and objective SCORAD ≥ 40 , respectively.

The distribution of time to relapse was estimated using the Kaplan–Meier product-limit method, and differences between treatment groups were tested using Cox's proportional hazards regression model. The results were presented in terms of the hazard ratio, 95% confidence interval and associated p-value. Centres and the covariates of age and sex were included in the model. The effect of any treatment by covariate interaction was investigated. The assumption of proportional hazards was checked by plotting the log of the negative log of the survival distribution against time for each treatment group. Lines that remain essentially parallel over time support the assumption of

proportional hazards. Statistical significance was defined as $p < 0.05$.

Results

Acute treatment phase

Ninety children (38 males and 52 females, mean age 5.7 ± 2.2 yr) entered the study and received FP ointment twice daily. Of these, 87 (97%) children completed the 4-wk study period. Reasons for premature discontinuation were one serious adverse event (accidental craniocerebral injury, which was judged as not related to study drug), one consent withdrawn and one lost to follow-up. The duration of the current episode of AD was >3 wk in 83 (92%) and 1–3 wk in 7 (8%) children. Thirty-nine (43%) of the children had suffered from AD for more than 5 yr, 49 (54%) for 1–5 yr and 2 (2%) for less than 1 yr.

The most common concurrent medication started during the study period was topical hydrocortisone acetate 1% cream for facial eczema, followed by cetirizine for allergic rhinitis and salbutamol for asthma. Treatment compliance was reported to be good in 82 (93%) children. Compliance was monitored by weighing the returned tubes of fluticasone propionate ointment.

All children had at least four of the major features of AD. Each feature was present in the majority of children with the exception of 'personal history of asthma' (only present in 36% of children). History of flexural dermatitis, presence of an itchy rash, history of dry skin and visual flexural dermatitis were reported in 99%, 98%, 97% and 98% of children, respectively. Eighty-eight per cent of children had an onset of their AD when they were less than 2 yr of age.

As shown in Fig. 1, after 2 and 4 wk of treatment, the objective SCORAD had significantly decreased. At the beginning of the study, most of the children had moderate or severe AD ($n = 86$; 96%). However, after 2 and 4 weeks only 22 (25%) and 14 (16%) children, respectively had moderate or severe AD. The other efficacy criterion, the improvement of the index lesion, showed a similar improvement (mean TIS $\pm$ s.d. at baseline: 4.6 ± 1.1 ; at week 2: 1.4 ± 1.3 ; at week 4: 0.7 ± 0.9), allowing 78 (87%) children to enter the maintenance phase. The single items scored at the index lesion are shown in Fig. 2.

Thirty-four adverse events were reported by 28 (31%) children. The most common adverse events were related to ear, nose and throat

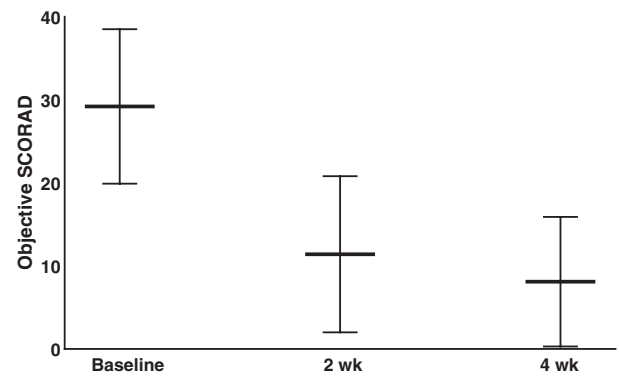


Fig. 1. The objective SCORAD (mean $\pm$ standard deviation) at the beginning of the study and after 2 and 4 wk of treatment with fluticasone propionate 0.005% ointment. An objective SCORAD below 15 indicates mild AD, between 15 and 40 indicates moderate AD and above 40 indicates severe AD.

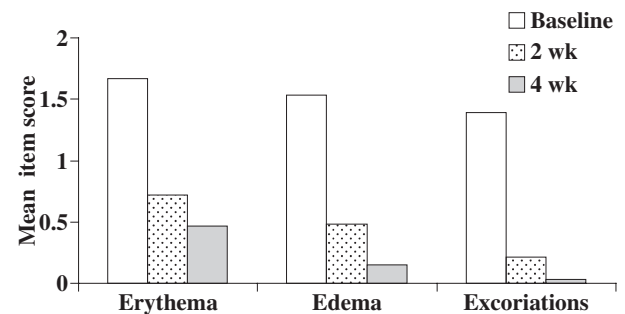


Fig. 2. The three items of the TIS score at the beginning of the study and after 2 and 4 wk of treatment with fluticasone propionate 0.005% ointment.

(ENT) or to the lower respiratory tract. Of these events asthma (5%) was the most common. None of these events were related to the study medication. Drug-related side effects were reported in 3 (3%) children, all pertained to the skin: flexural hyperpigmentation occurred in a dark-skinned child, folliculitis in a Caucasian child and transient telangiectasia in another Caucasian child. All of these side effects disappeared during follow-up.

Skin atrophy or striae were not observed. Hypertrichosis in two children and telangiectasia in one child already existed at the beginning of the study and remained unchanged.

To evaluate possible systemic adverse events, urinary overnight cortisol/creatinine ratio was assessed. No evidence of any treatment effect was found after 4 wk of treatment ($p = 0.2$).

Maintenance treatment phase

Of the 87 children completing the acute treatment phase of the study, 75 entered the maintenance

nance phase. Twelve children discontinued after the acute phase because of the following reasons: target TIS >1 (nine children), consent withdrawn (one child), target TIS ≤ 1 at the original lesion but target TIS >1 at another lesion (one child) and one exacerbation of AD between the end of the acute phase and the start of the maintenance phase (one child).

Of the 75 children who entered the maintenance phase, 36 received intermittent placebo (IPL group) and 39 received intermittent FP (IFP group). With the exception of a difference between numbers of females and males, there was no apparent difference between groups in terms of demographic characteristics. In the IPL group, there was an even distribution of females to males [20 (56%) : 16 (44%)] whereas, in the IFP group there were more females to males [26 (67%) : 13 (33%)].

Mean age was 5.8 and 5.9 yrs for IPL and IFP groups, respectively and the majority of children in both groups were Caucasian (69% and 76% for IPL and IFP groups, respectively).

At the start of the maintenance phase (week 4), the median target TIS score for the index lesion had improved following treatment with FP during the acute phase, with a 4 wk score of 0.0 (range 0–1) for both the IPL and IFP groups. Median objective SCORAD had also improved, falling to 7.0 (range 0–24) and 3.6 (range 0–26) for IPL and IFP groups, respectively. These results indicate that for the majority of children who entered the maintenance phase AD had been 'controlled' (i.e. TIS score ≤ 1) as required by the study protocol.

The primary endpoint of the study was objective SCORAD at the end of the study (week 20) or, if the child discontinued prematurely, at time of withdrawal. A summary of the objective SCORAD values at the start of the maintenance phase and the last measured values is given in Tables 1 and 2. The last measured value summarizes objective SCORAD values from both those patients who relapsed during this phase

and those who were controlled and continued in the study for the full 16 wk.

These results indicate that for the majority of children who entered the maintenance phase, AD had been brought under control following acute treatment with FP as illustrated by lower median objective SCORAD values. Median objective SCORAD at the beginning of the maintenance phase was higher for the IPL group than the IFP group (7.0 and 3.6, respectively), although such as difference in this lower category of objective SCORAD would not be expected to be of any clinical relevance.

Children in the IFP group had a lower median objective SCORAD value at their last visit assessment than children in the IPL group (10.7 and 19.2, respectively).

Throughout the maintenance phase, no subjects remaining in the study had an objective SCORAD value indicative of severe AD.

Because of non-normality of the data, the last measured objective SCORAD was categorized and analysed using logistic regression including terms for baseline (week 4) objective SCORAD, sex, age and centre/investigator. The interactions between treatment and covariates were assessed. The interaction between treatment and sex was showing a strong tendency at the 10% level ($p = 0.054$). The treatment effect is therefore presented overall and separately for males and females. A highly statistically significant treatment effect ($p = 0.007$) was observed for the female patients. The probability of a female patient having more severe AD was more than six times higher in the IPL group than in the IFP group [odds ratio = 6.164, 95% CI (1.642, 23.137)]. However, for the male patients no significant difference was observed between the IPL and the IFP group [$p = 0.694$, odds ratio = 0.705, 95% CI (0.124, 4.008)].

Baseline (week 4) objective SCORAD was found to be significantly lower in the IFP group in both analyses (adjusting for treatment by sex interaction $p = 0.006$ and not adjusting $p = 0.008$). The chance of being in a lower category of objective SCORAD (i.e. less severe disease) increased if the objective SCORAD at entry was lower. No evidence of a treatment by baseline interaction was found. Age and centre and each of their interactions with treatment were not found to be significant in either analysis.

Overall, a statistically significant treatment effect ($p = 0.043$) was observed. The probability of more severe AD was almost three times higher in the IPL group than in the IFP group (odds ratio = 2.827, 95% CI [1.033, 7.737]).

Table 1. Summary of objective SCORAD data at start of the maintenance phase and at last visit attended

	IPL + SMT		IFP + SMT	
	Start of maintenance phase	Last measured value	Start of maintenance phase	Last measured value
n	36	36	39	38
Median	7.0	19.2	3.6	10.7
Range	0–24	0–38	0–26	0–39

SMT, standard maintenance therapy (emollient); IPL, intermittent placebo; IFP, intermittent fluticasone propionate ointment.

Table 2. Summary of objective SCORAD data at last measured value by sex

	Male IPL + SMT	IFP + SMT	Female IPL + SMT	IFP + SMT	TOTAL IPL + SMT	IFP + SMT
n	16	13	20	25	36	38
None (SCORAD = 0)	1 (6)	1 (8)	3 (15)	7 (28)	4 (11)	8 (21)
Mild ($0 < \text{SCORAD} \leq 15$)	4 (25)	3 (23)	3 (15)	14 (56)	7 (19)	17 (45)
Moderate ($15 < \text{SCORAD} \leq 40$)	11 (69)	9 (69)	14 (70)	4 (16)	25 (69)	13 (34)
Severe (SCORAD > 40)	0	0	0	0	0	0

Values show the number and percentage of children with objective SCORAD results in the various categories at the last measured value, split by gender. SMT, standard maintenance therapy (emollient); IPL, intermittent placebo; IFP, intermittent fluticasone propionate ointment.

During the maintenance phase, median objective SCORAD increased slightly. This increase was greater for the IPL group than for the IFP group. The last measured median change from the start of the maintenance phase objective SCORAD was an increase of 12.2 for the IPL group and an increase of 3.8 for the IFP group. Overall a statistically significant difference was observed between treatment groups ($p = 0.021$). This supports the primary analysis and shows that the IPL group had a greater increase in objective SCORAD (i.e. a worsening of the disease) during the maintenance phase than the IFP treated group. A relapse (also known as an exacerbation) of AD was defined as an index lesion with a TIS score of 3 or more. The effect of any treatment by covariate interactions was tested and again a significant treatment by sex interaction was found ($p = 0.007$). No other interactions (objective SCORAD at baseline, age and centre/investigator) were found to be significant. Table 3 shows the number and percentage of children with an exacerbation during the maintenance phase of the study, in total and split by gender.

A highly statistically significant treatment effect was observed in the female patients ($p < 0.001$). The risk of an exacerbation of AD for female patients was more than five times higher in the IPL group than in the IFP group [hazard ratio = 5.124, 95% CI (2.017, 13.017)]. No statistically significant difference was observed for male patients [$p = 0.725$, hazard ratio = 0.850, 95% CI (0.343, 2.105)]. Overall, a statistically significant treatment effect was

observed ($p = 0.017$). The risk of an exacerbation of AD was more than twice as high in the IPL group than in the IFP group [hazard ratio = 2.182, 95% CI (1.153, 4.130)]. Seventy-five children were included in this analysis (36 IPL, 39 IFP). By week 20, at the end of the maintenance phase, 29 (81%) of the children in the IPL group had suffered an exacerbation compared with 17 (44%) of the children in the IFP group. The medium time to relapse was 2.6 wk in the IPL group and inestimable in the IFP group. Inestimable means that more than 50% of the children had not experienced an exacerbation during the maintenance phase. In the IFP group, medium time to relapse was greater than 16 wk.

Over the 16 wk of the maintenance phase, IFP plus standard maintenance therapy (emollient and bath oil), was well tolerated without any significant adverse events. During this phase, five (14%) patients receiving IPL and 18 (45%) patients receiving IFP reported adverse events.

Viral infection (0% IPL, 18% IFP), ENT infections (3% IPL, 10% IFP) and viral respiratory infections (0% IPL, 8% IFP) were the only events reported by 4% or more patients. However, patients in the IFP group remained in the study much longer and consequently received medication and reported data for a much longer period than those in the IPL group. No serious adverse events were reported and only one subject in the IPL group and two patients in the IFP group reported an adverse event that thought to be drug-related, none of which led to withdrawal. Two adverse events reported during

Table 3. Summary of time to relapse

	Male IPL + SMT	IFP + SMT	Female IPL + SMT	IFP + SMT	TOTAL IPL + SMT	IFP + SMT
n	16	13	20	26	36	39
Number (%) exacerbating	13 (81)	9 (69)	16 (80)	8 (31)	29 (81)	17 (44)
Median time to exacerbation (weeks)	4.5	2.4	2.3	*	2.6	*
Time (weeks) until 25% of patients had exacerbated	2.1	2.0	2.1	7.0	2.1	2.4

*Median time could not be estimated, but exceeded 16 wk. See details of abbreviations in Table 2.

the maintenance phase did lead to withdrawal and both were related to viral infections. Very few patients reported any skin-related adverse events and local skin atrophy was not observed in this study; only two patients reported any evidence of skin changes which could be indicative of local pre-atrophy (telangiectasia), one patient on IPL and one on IFP.

There was no evidence of any treatment effects on cortisol/creatinine ratios.

Discussion

The aim of this present study was to investigate the efficacy and safety of intermittent FP ointment when added to standard maintenance regime of emollients in the long-term management of AD in children once an acute episode of AD had been controlled. Subjects entered the study during an active flare of chronic recurrent AD and initially received daily treatment (bd) with FP ointment for 4 wk to control their AD.

Strict objective criteria were applied to define control. All subjects, whose AD was completely under control then received the standard maintenance regimen of daily emollients and bath oil as required with the addition of either FP or placebo on an intermittent ($\times 2$ days per week, in the evening) basis for 16 wk.

For both the primary and secondary efficacy measures, a statistically significant treatment by gender interaction was detected, a result which has not been evident in the other intermittent FP dosing studies (13, 14). Whilst intermittent dosing with IFP ointment was very effective in females, the benefit of IFP ointment in the management of chronic AD in boys was not evident in this study. However, both the total number of subjects who entered the maintenance phase ($n = 75$) and the number of males ($n = 29$) was small. In addition, there was an imbalance in ratio of males/females between treatment groups.

While there was an even distribution of females to males (56%: 44%) in the IPL group, there were more females to males (67%: 33%) in the IFP group. The cause of this difference do we not clearly understand and is not known. These factors together with possible issues of compliance and treatment preferences (i.e. perhaps boys do not like ointment-based formulations) may have influenced the overall results. The fact that IFP in ointment formulation was effective in female children leads us to speculate that compliance with the formulation may indeed be a key factor in the results in males.

Overall, combining the data from both females and males, the results from this study support previous findings in both children (8) and adults (9) and indicate that FP ointment is significantly more effective than placebo when used in addition to emollients and bath oil, in reducing the risk of relapse of AD. Children receiving additional FP were 2.18 times less likely to experience a relapse of AD than children receiving additional placebo (Cox's proportional hazards regression analysis, 95% CI 1.15, 4.13, $p < 0.02$). Also interesting is that children experiencing a relapse during the maintenance phase had a lower objective SCORAD than at the start of the acute phase, indicating that there was no rebound effect of FP.

Median time to relapse for those receiving intermittent FP ointment was in excess of 16 wk compared with 2.6 wk for those receiving intermittent placebo. The probability of more severe AD was almost three times higher in the group receiving intermittent placebo than the group receiving intermittent FP [odds ratio = 2.827, 95% CI (1.033, 7.737)].

Data from the acute phase (objective SCORAD, target TIS score, intensity and extent of AD) were in agreement with previously reported findings and showed that twice daily, regular FP ointment for 4 wk is an effective treatment for treating moderate to severe AD in children (3).

Subjects in the IFP group remained in the study longer than those in the IPL group and consequently received medication and reported data for a much longer period. Therefore, the likelihood of adverse events occurring was greater in the IFP group than in the IPL group. Nevertheless, intermittent FP applied twice weekly through the 16-wk maintenance phase was well tolerated. Two skin-related adverse events were recorded in the acute phase of the study (acne and folliculitis and pigmentary skin disorder).

However, in terms of potential pre-atrophy or skin atrophy, during regular visual assessments there was only one report of mild telangiectasia at the end of the acute treatment phase and one report of mild telangiectasia with intermittent FP at the end of 8 wk treatment in the maintenance phase. In addition, there were no significant differences between treatments (IFP and IPL) in urinary cortisol/creatinine ratios.

While only a few well-controlled clinical studies exist to support this approach, intermittent dosing with topical corticosteroids during periods of remission is proposed as an effective treatment strategy for AD in children and adults (1). The results from this study indicate that

intermittent dosing with FP twice weekly plus standard maintenance therapy (emollient plus bath oil) offers an effective long-term treatment strategy for use in children, with no evidence of any safety issues when used in this way.

This successful approach is earlier published for adults and children. Berth-Jones et al. studied the efficacy of intermittent application of FP cream and ointment (twice weekly vs. emollients) in AD in a randomized, double-blind, parallel group of adults aged 12–65 yr. Patients who applied FP cream twice weekly were 5.8 times less likely and patients using FP ointment 1.9 times less likely to have a relapse than patients applying emollient alone (13).

Hanifin compared the efficacy of intermittent application of FP cream 0.05% (twice weekly) with emollient in reducing the risk of relapse when added to regular daily emollient in adults and children (age range 3 months to 65 yr) with stabilized AD. Children were 8.1 times less likely to have an AD relapse and adults were 7.0 times less likely to have an AD relapse. For those receiving intermittent emollient, the median time to relapse was 5.1 for children and 4.1 wk for adults, respectively (14).

Our study is the first showing this approach in children only. In clinical practice, this approach could represent a 'steroid-sparing' alternative for those patients who frequently require repeat prescriptions of TCS for daily chronic use to treat their recurring AD flares. Not only does this intermittent treatment regimen potentially reduce the total exposure to TCS in such a patient, but also, by delaying the recurrence and hence reducing the frequency of exacerbations of AD, such a regime should significantly improve the quality of life and reduce the burden of the condition for both the patient and their family.

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