

VIEWS ON UNWANTED EFFECTS OF LEAVE-ON EMOLLIENTS AND EXPERIENCES SURROUNDING THEIR INCIDENCE

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Abstract

Background: The mainstay treatment for eczema is leave-on emollients. The aim of this study was to find out more about unwanted effects that have been reported with their use, as little is known due to a lack of formal reporting. **Aims:** To gain a greater understanding of eczema patients' experiences of unwanted effects such as stinging, what influence unwanted effects had on their therapy, why subsequent variations in leave-on emollient adherence followed and what patients desire in their emollients.

Methods: An anonymous online survey was conducted among eczema patients and their carers in March 2016 (using SurveyMonkey™). **Results:** 210 respondents, including adults and young people with eczema plus carers of children with eczema, which included family and friends. 68% (n=126/185) reported a wide range of 38 unwanted effects. Accounts highlighted the impact on quality of life of these unwanted effects and variations to eczema management that followed. 71% (90/126) of respondents stopped a leave-on emollient due to unwanted effects. Desired characteristics in emollients related to the absence of unwanted effects and product improvements. **Conclusion:** Eczema patients and their carers all reported high levels of unwanted effects from leave-on emollient use. Experiences of unwanted effects were multifactorial but common themes arose as did the desire for emollient improvements. Unwanted effects need to be considered when optimising therapy.

Citation: Oakley R, Lawton S. Views on unwanted effects of leave-on emollients and experiences surrounding their incidence. *Dermatological Nursing* 2016 15(4): 38-43

KEY WORDS

- ▶ Emollients
- ▶ Moisturisers
- ▶ Patient experiences
- ▶ Qualitative
- ▶ Eczema
- ▶ Adverse events
- ▶ Treatment preferences

Introduction

Atopic eczema is a common disease that affects around 1 in 5 children and is indiscriminate of gender or ethnicity¹. The

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incidence of the disease has increased in recent years and generally has a 10-year clearance rate in around 60% of children¹. However, relapse can occur in later life, and for some it is a lifelong condition¹. Leave-on emollients are emollients that are applied and left on the skin to alleviate symptoms such as dryness. These emollients are the mainstay of treatment for eczema, but adherence can be poor and is one of the main reasons for treatment failure². Studies suggest that eczema patients report unwanted effects from leave-on emollients, which may contribute to adherence issues². Reasons for this are multifactorial^{2,3,4} and are not fully understood.

This paper will present the results of a study which focused on the unwanted effects of leave on-emollients, specifically looking at key aspects including: what unwanted effects patients may have

experienced, issues that arose between the interaction of emollients and eczema treatment and what advice patients were given by healthcare professionals, what the reasoning was behind the actions patients took as a result and what they felt makes a good leave-on emollient. There is a breadth of information and data resulting from this study and this is why the emphasis of this paper will focus specifically on patient and carer experiences.

Ethical considerations

The questionnaire that generated the data for this study was reviewed by the University of Nottingham's School of Pharmacy Research Ethics Committee and given a favourable opinion (Ethics Reference No. 010-2016) before use.

Literature review

There are few formal reports on the

unwanted effects of leave-on emollients, how these may influence adherence and what wider implications this may have for total therapy. Despite patient reports^{2,3}, unwanted events are poorly reported both in clinical practice⁵ and in trials of leave-on emollients⁶. This suggests healthcare professionals are unaware of the range and impact of unwanted effects that eczema patients experience.

The Medicines and Healthcare Products Regulatory Agency Drug Analysis Prints of all adverse event reports for common ingredients included within emollient medicinal products in the UK since 1963 suggest that very few reports of adverse events (such as skin reactions), following leave-on emollient application, have ever been made⁶. In addition, clinical trials involving leave-on emollients or moisturisers post year 2000 showed that 27 (66%) did not mention any adverse events, either because the trials were not designed to report them or any adverse reactions encountered were not considered to have any significance⁶. These findings suggest that any adverse incident with leave-on emollients is generally disregarded by healthcare professionals.

On the other hand, there is evidence that some emollients cause immediate cutaneous reactions⁷ and disturb important epidermal functions^{7,8,9}. Such incidences contributed to the release of an MHRA report in 2013⁹ which warned against the adverse events that had been reported with aqueous cream.

Aims and objectives

The aim of the study was to establish a deeper insight into the wider issues surrounding unwanted effects experienced with leave-on emollients. This was to be reported by, or on behalf of adults, young people and children with eczema. The study objectives were:

- ▶▶ To compare the reports of unwanted effects of leave-on emollients from eczema patients and their support network
- ▶▶ To establish the details of how unwanted effects may contribute to variations in emollient adherence
- ▶▶ To gain a greater understanding of patients' and carers' (family members

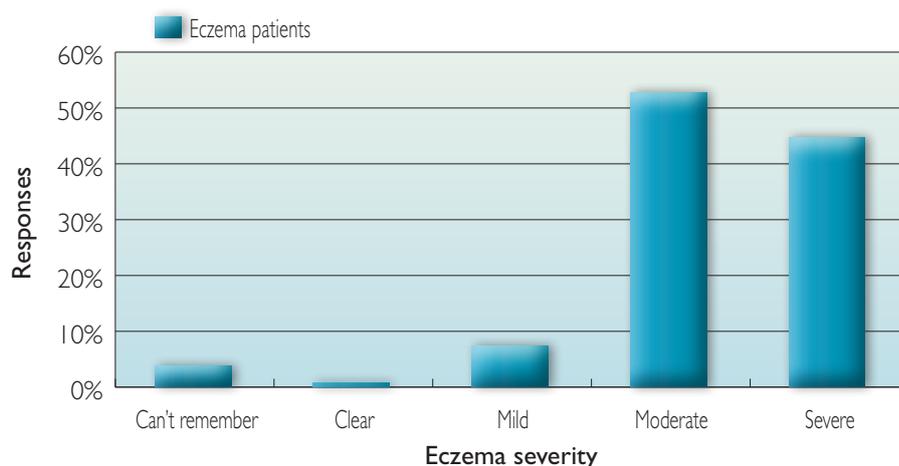


Figure 1

Results to the question: At the time you, or the person you are filling in this survey for, experienced the unwanted effect(s), how bad was the eczema? Severity scale adapted from reference 1.

and friends) experiences of leave-on emollients

- ▶▶ Understand what patients want from their leave-on emollients.

Methods

An anonymous online survey was conducted among eczema patients and their carers in March 2016 (using SurveyMonkey™). A questionnaire was developed by an expert group of 11 healthcare professionals and patients to capture leave-on emollient experiences. The 20-question questionnaire was tested for content validity with this expert group (3 dermatologists, 2 eczema researchers, 2 pharmacists, a general practitioner, a nurse, and 2 adult eczema patients). Categorical questions were organised into sections including demographics, previous history of treatments and experiences with leave-on emollients. Open questions were also asked for further clarification and opinions. Patients were contacted through online eczema support groups including the National Eczema Society and Nottingham Support Group for Carers of Children with Eczema via Twitter® and Facebook®. Analysis of the data collected in these questionnaires consisted of frequency counts and percentages. Open responses were thematically analysed and the patient and carer responses will be discussed within this paper.

Results

210 patients and their carers self-selectively enrolled into the survey. Not all respondents completed the

whole survey, therefore the number of respondents who responded to each question differs in reporting some results. The study is limited in its generalisability to the wider eczema community, as recruitment via support groups is likely to have resulted in responses relating to severe eczema patients.

Respondents all reported considerable levels of the same unwanted effects from the application of leave-on emollients. These unwanted effects were common, diverse in nature and stopped the use of some leave-on emollients, which further suggests that they have a role to play in adherence. 68% (n=126/185) of patients and/or carers responding on behalf of patients reported an unwanted effect due to a leave-on emollient¹⁰. Of these respondents, 71% (90/126) reported that they had stopped using a leave-on emollient due to unwanted effects and almost all (n=133/138, 96%) occurred when eczema was moderate to severe¹⁰ as can be seen in Figure 1. Reports included a wide range of unwanted effects, with stinging being the most common (n=72/104, 69%), followed by greasiness that interfered with everyday life (n=50/104, 48%) and lack of efficacy (n=51/104, 49%)¹⁰. There were 38 unwanted effects reported.

Results of patient/carer questions relating to leave-on emollients

Unwanted effects question

Within the last 3 years, have you or the person you are filling in this survey for ever

Table 1.

Frequency of skin reactions reported by eczema patients and their carers

Number of reports	%	Skin reaction
72	69%	stinging
64	62%	itching
58	56%	burning
39	38%	worsened eczema
33	32%	worsened a rash
29	28%	reddening or darkening of the skin
25	24%	tingling
22	21%	swelling or inflammation
19	18%	got a new rash
19	18%	dryness
19	18%	pain
9	9%	peeling
3	3%	none of these
1	1%	patient reported allergic reaction
1	1%	hives
1	1%	red bumps (infected hair follicle)

experienced an unwanted effect (such as those listed below) when applying a leave-on emollient or moisturiser to treat symptoms of eczema? Unpleasant sensation (eg, itching, stinging, burning, tingling, feeling of hotness), a rash (reddening or darkening of skin), worsened eczema, cosmetic issues, odd smell or other problems?

68% (n=126/185) had experienced an unwanted effect from leave-on emollients, 24% (n=45/185) had no experience and 8% (n=14/185) were unsure¹⁰. As seen in Table 1, the top 3 reactions experienced were the sensations felt on the skin: stinging, itching and burning. Other reactions related to a deterioration of the eczema and skin appearance following the application of the leave-on emollient. Patients, carers and relatives of all ages reported that if application of a product causes discomfort or does not improve the condition, then the default position is often to stop the product. Usually, alternatives may then be sought from a healthcare professional or retail outlets.

NICE guidance (which is applicable to children under 12 years but could be generalised to young people and adults) could explain such behaviours as 'not all types of emollients suit all people' and 'children may have adverse reactions to some products, or may not like the way they feel on their skin'. However, there appears to be a misconception with the extent that unwanted effects are being experienced by patients in the literature. For example, best practice guidance highlights that 'emollients are generally thought to be safe, with limited adverse effects'¹¹.

Licensed leave-on emollients for eczema are rigorously tested for quality, safety & efficacy¹². However, toxicology studies exist for common ingredients within some emollients which mimic a selection of reported unwanted skin reactions^{10,13,14,15,16}. Although such reactions are not dangerous, their nature suggests that some emollients could irritate or damage the skin^{7,8,9}, which may exacerbate the eczema. However, interplay between ingredients in emollient formulations is also complex with potentially irritant properties of ingredients able to be mitigated by formulation design¹⁷. Therefore, such observations could be due to formulation approaches of specific products. Although, such stipulation requires further evidence and research for clarity.

The most commonly reported adverse reaction was stinging or discomfort on application and could be related to one or more of the constituents of the emollient and the severity of eczema^{10,13,14,15,16}. Clinical experience suggests that such reactions are usually transient and could often be considered a normal response to an application of emollient. Whether such reactions are truly adverse or a reflection of other factors, such as eczema severity, requires further investigation. It is acknowledged that the relationship between the skin and an emollient is complex so the effects of emollients may not always be predictable¹¹. However, the consensus is that regulator-approved emollients do not harm the skin barrier.

Child described (proprietary licensed

emollient) and similar cream as "burning cream".

"Child gets very upset at the idea of cream, hates on hands (hands have really bad eczema), hates getting it on bed sheets, hates the feel of wearing cream next to clothes. Fear it will hurt going on due to bad experiences."

"(Proprietary licensed) ointment was applied in a trial on my legs only. Within 10 minutes they were burning hot and had turned red. (Proprietary licensed) cream can only be applied just before bed in the knowledge it will be washed off in a shower the next day. If not washed off causes mild itching."

Leave-on emollients are the mainstay of managing eczema¹. National guidance advocates their use¹ and other sources¹¹ also advise prescribing a small amount of emollient prescription to gauge the suitability for the patient. Upon looking at the skin reactions patients experienced, most could have potentially been avoided if guidance had been followed. By providing a selection of emollients to try, unsuccessful emollients could have been identified. Irritant and cosmetic acceptability considerations could then be investigated before prescribing and patients could be involved in the choice of product¹⁸. Further resources with open access available to healthcare professionals in relation to emollient prescribing include: Emollients, Potential Skin Sensitisers as Ingredients¹⁹ and The Electronic Medicines Compendium (eMC), where summaries of product characteristics for individual medicines can be searched.

Patients' experiences with leave-on emollients

"A nurse practitioner at the dermatology department I was referred to noted that my experiences mirrored that of several of their patients and suggested that I might benefit from periodic rotation through a roster of products."

Cosmetic issues and product choice are also important considerations for patients and will affect adherence. Within this study the main aspects highlighted in Table 2 were: greasiness that interfered with everyday life, feeling hot, tacky and sticky sensations, stained clothing and

Table 2.

Frequency of cosmetic issues reported by eczema patients and their carers

Number of reports	%	Cosmetic issue
50	48%	greasiness that interfered with everyday life
38	37%	feeling of hotness
29	28%	tacky feeling on the skin
27	26%	stickiness
26	25%	stained clothes
24	23%	shininess
23	22%	none of these
12	12%	blocked pores
8	8%	feeling cold or clammy
1	1%	failure of product to remove when washing

shiny skin. Such reports appeared to be attributed to, not just one product, but: most available UK proprietary leave-on emollients licensed for eczema, unlicensed UK emollients which may be registered as a medical device, an approved UK Advisory Committee on Borderline Substances (ACBS) substance or a cosmetic.

"Hot behind knees, which closed pores, sweating then severe itching."

"It shouldn't leave any residue. Sometimes after I get a bit warm, the area the emollient was applied to feels really wet — I don't like this."

As can be seen in Table 3, other issues highlighted within the study related to the clinical effect and the refusal by children to have the products applied to the skin, which may confirm that unwanted effects from leave-on emollients do contribute to poor adherence as suggested in previous papers^{2,3}. This may be related to a behavioural component in children, but as previous papers have confirmed² this is usually due to stinging sensations. Similar to the findings of this study, families within previous studies^{2,3} reported employing a range of strategies, which included involving the child in treatment,

distracting the child during treatment, or making a game of it, using rewards, applying treatment to a sleeping child or, in a few cases, physically restraining the child. However, carers in this study also reduced the frequency of treatment applications², which could result in suboptimal therapy.

Poor treatment adherence, leads to 'cream wars' with battles between the patient, family and medical team over the consistent use of prescribed creams. Stories about eczema can help and a recent study developed personalised stories as a technique to improve treatment adherence, reduce stigma and facilitate effective adult-child communication²⁰. To facilitate better communication with children about their eczema, Nottingham University has produced story books. These stories can be used by parents and healthcare professionals and can be personalised for a child. Two stories introduce ideas to help break the itch-scratch cycle and two are targeted at improving treatment adherence. They are available from The Centre of Evidence Based Dermatology, Nottingham University. Visit www.nottingham.ac.uk/research/groups/cebd/resources/psychology-and-eczema.aspx to read and learn from these different experiences.

"We currently use (a proprietary licensed emollient) as the main emollient on our 1 6-month old son, but it's very slippery! We can't put it on when he's on the changing unit, has to be done sat on the floor because if he slips/tries to get away (usually!!) then we wouldn't be able to grip him to catch him!"

Stopping the leave-on emollient question

Was the unwanted effect(s) for you or the person you are filling in this survey for, bad enough for you, or them, to stop using the leave-on emollient or moisturiser that caused the unwanted effect(s)?

71% (90/126) of patients stopped leave-on emollients due to unwanted effects¹⁰. Leave-on emollients are stopped by patients and carers for several reasons. Commonly it is because of the adverse effect or because the eczema has cleared and they have not understood the importance of continuing the use. Some

Table 3.

The frequency of other unwanted effects reported by patients

Number of reports	%	Other unwanted effects
51	49%	it didn't work
31	30%	child refused application
22	21%	none of these
20	19%	off-putting smell
19	18%	slipping when gripping objects
12	12%	infection
3	3%	phobia of leave-on emollient
1	1%	upset child
1	1%	sweating, leading to itching

patients made the decision independently while others sought healthcare professional advice.

"She wants to but I keep having her use it"

"I have had these episodes before and was told by the doctor to persevere with the moisturisers."

"Baby was in pain but doctors said we had to do it."

"I stopped using it for a little bit but realised this happened when I first started using a cream. After getting used to the cream it would happen less often."

Use with other products

Within the last 3 years, have you or the person you are filling in this survey for ever applied a leave-on emollient or moisturiser to the same bit of eczematous skin immediately following or followed by another product and ever applied leave-on emollients or moisturisers under: bandages, gloves, wet/dry wraps, or other therapeutic material?

Patients and carers were also asked about the use of leave-on emollients with other products. National guidance advises that when emollients (excluding bath emollients) and other topical products are used at the same time of day, the different products should

ideally be applied one at a time with several minutes between applications where practical¹. The preferences of the child and parents or carers should determine which product should be applied first, leaving a gap (of several minutes) between emollient products and topical corticosteroids (TCS)¹. The evidence for emollient or TCS applied first is inconclusive, but according to a recent study the order of application of emollient and TCS does not matter in the treatment of atopic eczema in children²¹. Parents can also apply topical medications in whichever order they prefer²¹, which may contribute to patient adherence. However, 60% (82/136) had used emollients with TCS and some had mixed TCS or TCS and antibiotic combinations. For some topical calcineurin inhibitors (TCI) such as Protopic® ointment, patients are advised to leave a 2-hour gap between the two applications^{22,23}. Despite this guidance, 19% (26/136) had used TCIs with emollients and of these respondents 77% (17/22) experienced burning sensations compared with 56% (58/104) of all other respondents. TCIs are known to have burning sensations as listed side effects^{22,23}, which suggests that such reports could be attributed to either the emollient or mixing with the TCI^{19,22,23,24}.

"I have used different moisturisers such as (proprietary licensed emollient) and cocoa butter and (proprietary licensed emollient) and if skin is breaking I use (proprietary unlicensed antiseptic) on top covered too or steroid cream."

"(Proprietary licensed calcineurin inhibitor) then basic aqueous cream or (proprietary unlicensed emollient)."

49% (93/188) had also applied emollients under bandages, gloves, wet/dry wraps, or other therapeutic material. Interestingly, these respondents reported experiencing a greater proportion of all the reported types of unwanted effects; with 80% (74/93) describing unwanted effects with leave-on emollient use compared to 68% (126/185) of all other respondents.

Homemade emollients

"We use shea butter or a homemade mixture of shea butter + coconut oil +

cocoa butter."

"Oil-based cream with olive sunflower and rapeseed oils mixed with aqueous."

The mixing and creation of therapeutic products plus the use of therapeutic material with emollients could suggest that patients find it difficult to manage their condition with current treatments. However, this behaviour may be unsafe because such formulations may be liable to microbial contamination¹² and may exacerbate eczema¹⁷ due to a lack of formulator knowledge and ingredients that haven't undergone stringent quality control measures^{8,12,17}.

Natural emollients

"Natural moisturisers and oils such as raw coconut, shea butter, olive oil, cocoa butter, mango butter, Vaseline®."

It was observed that 5% (10/193) of respondents used natural oils and moisturisers as a form of emollient therapy. This trend may emerge from personal beliefs that may have arisen from negative experiences with preparations or marketing strategies.

However, research has highlighted that some natural oils, such as olive oil, significantly damage the skin barrier and may exacerbate eczema²⁵. Therefore healthcare professionals should be vigilant of such practices and recommendations should be made on the best available evidence.

What makes a good leave-on emollient?

The Eczema Priority Setting Partnership found that identifying the most effective and safe emollients was a top priority shared by patients and healthcare professionals²⁶. It was addressed within this study by asking what makes a good leave-on emollient or moisturiser. This answer elicited a wealth of suggestions, which at times were contradictory. The main themes from the open responses focused on:

►► Consistency

- *Non-greasy, easily absorbed, thick moisturiser. Lotions are often thin and have to be reapplied to be effective*
- *A well-balanced moisturiser with grease*

and cream

- *Something that isn't too oily*
- *I also much prefer a more 'natural' emollient wherever possible (just natural oils, etc, rather than petroleum derived). The reality is that the natural ones available over the counter aren't as good as the prescribed ones.*

►► Frequency of application

- *One product lasts a long time*
- *During the day I want something that absorbs quickly so I don't have to feel self conscious walking around — I hate it when it stays on your skin and sticks to clothes. For overnight treatments I think the thicker the better so it absorbs slowly and you can feel it working*
- *Not sticky, dries quickly, portable, easy to apply, gives long lasting relief.*

►► Minimising adverse effects

- *A moisturiser that removes the stinging sensation from my eczema*
- *Thick and oily as less painful*
- *Seems hit and miss as to whether she will react to the cream*
- *One that doesn't make it worse. SLS appears to increase itching..*
- *One that doesn't make me itch more*

►► Cosmetically acceptable

- *No odour, non-greasy, one that sticks but doesn't grease up and stain clothing/ bedding*
- *One that is deeply moisturising and soaks into the skin easy without leaving greasy residue on the skin surface.*

►► Adherence

- *Something which the person is comfortable to have applied and leave on, eg, my child was using creams but hated to be touched so was switched to spray*
- *How well it 'sticks'. Small children roll about, scratch, wipe and wriggle and some of the thinner emollients just don't stay put (especially if, for example, you're battling to get pyjamas on).*

►► Other comments

- *Its effectiveness. They are all different, it depends on the part of cycle you are in or what time of day/night and season.*

Implications for practice

This study and the patient-focused

questions discussed in this paper have highlighted that unwanted effects from leave-on emollients are commonly reported by patients, are diverse in nature, have an impact on adherence, and may be associated with the severity of eczema and the type of leave-on emollients used¹⁰. Unwanted effects need to be considered when optimising therapy for patients. Education and support for eczema patients in all care settings should be consistent; with a focus on the types of emollient product being used (either prescribed or purchased), how they are being applied, their use or mixing with other topical therapies and asking about any unwanted effects. If unwanted effects are an issue, providing a choice of products will help patients find a product that is right for them, which will improve adherence and quality of life for patients.

Conclusion

Eczema patients and their carers all reported high levels of unwanted effects from leave-on emollient use. Experiences of unwanted effects were multifactorial but common themes arose, as did the desire for emollient improvements. The reason why unwanted effects occur is still unclear, requiring further investigation and more robust adverse event reporting.

Declaration of interest

No declarations. This study was self-funded as part of a Master's degree.

Acknowledgements

Special thanks must be given to: Dr Natasha Rogers for assisting with the construction the questionnaires for the study in SurveyMonkeyTM and Dr Esther Burden-Teh for her feedback on survey questions and advice on disseminating the results. Dr Rosalind Simpson, Dr Jonathan Batchelor, Dr Miriam Santer, Dr Christine Clarke, Dr Margaret Cox, Mrs Amanda Roberts and Nurse Consultant Sandra Lawton OBE for their feedback on the suitability of survey questions during the survey design and guiding the content of the survey. Dr Sonia Ratib for kindly sharing the results of her unpublished scoping review on qualitative atopic eczema studies. Professor Hywel Williams and Professor Kim Thomas from the Centre of Evidence Based Dermatology plus Professor Phil Williams and Dr David

Scurr from the University of Nottingham Pharmacy Department for their guidance and supervision. **DN**

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