

Q&A 416.1

Why is aqueous cream no longer recommended as a leave on moisturiser?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
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Background

Eczema is a persistent skin condition characterised by symptoms such as dry, itchy, red and swollen areas of skin. These symptoms can flare up at different times, sometimes in response to allergic or irritant triggers. Emollients soothe, smooth and hydrate the skin and are indicated for all dry or scaling disorders. Their effects are short-lived and they should be applied frequently even after improvement occurs. They are useful in dry and eczematous disorders and are designed to be left on the skin (1).

Aqueous cream has been used as an emollient or moisturiser and as a wash off soap substitute to relieve the symptoms of dry skin conditions such as atopic eczema since the 1950's in adults, children and babies. It is still widely used today and is available over the counter in supermarkets and retail pharmacies and may also be prescribed by healthcare professionals; however it is now only recommended as a wash off soap substitute (2).

Answer

Aqueous cream, also known as simple cream or hydrous emulsifying ointment contains emulsifying ointment, purified water and a preservative such as phenoxyethanol or chlorocresol (1,3). Emulsifying ointment consists of an anionic emulsifying wax consisting of cetostearyl alcohol and the anionic surfactant sodium lauryl sulphate (SLS). SLS is used in medicated shampoos, as a skin cleanser and also as a tablet lubricant. In skin research, SLS is a known enhancer of drug permeation across the skin, has induced damage to the skin barrier to mimic effects of skin disease, and has been used to elicit skin irritation in experimental models of irritant contact dermatitis. Since SLS is not directly added to aqueous cream formulations but is a component of emulsifying wax its inclusion has not always been listed in the product labelling or prescribing information until recently (4,5). Other possible ingredients of aqueous cream, including chlorocresol, cetostearyl alcohol and parabens have also been associated with skin irritation (2,6).

The NICE clinical guideline on atopic eczema in children, and the National Eczema Society have reported that aqueous cream may be associated with skin reactions, such as burning, stinging, itching and redness, when used as a leave-on emollient but not when used as a wash product (7,8). This is also stated in the current British National Formulary (1). The reactions, which are not generally serious, often occur within 20 minutes of application but can occur later (6). The difference in the irritation potential in some patients may be related to the contact time with the skin, as soap substitutes are largely removed in the washing process. The National Eczema Society advise to never use aqueous cream as a leave-on emollient as it is likely to exacerbate rather than improve the eczema (8).

There have been several studies which have assessed the effect of aqueous cream on skin structure.

A retrospective audit of the notes of 100 children aged 1-16 years, who attended an outpatient dermatology clinic at Sheffield's children's hospital for the management of atopic eczema was published in 2003. The audit assessed the occurrence of immediate cutaneous reactions to emollient creams and ointments. The percentage of episodes of exposure to aqueous cream associated with an immediate cutaneous reaction (within 20 minutes of application), including burning, stinging, itching and redness were compared to all other emollients. Of the 100 children audited, 71 used aqueous cream and 40 (56.3%) developed an immediate cutaneous reaction. Fourteen other emollient creams or ointments were used and 17.8% of exposures resulted in an immediate cutaneous reaction. The difference between the two percentages was statistically significant ($p < 0.001$). The authors considered that the adverse skin reactions could be due to the chlorocresol and phenoxyethanol

preservatives contained in the cream but suggested that the most likely cause of the reactions was the SLS included in the formulation (9).

In 2009 10 adult volunteers with a previous history of atopic eczema applied aqueous cream twice daily to one forearm for 4 weeks with the other untreated forearm acting as control. The structural and functional integrity of the stratum corneum was measured using the tape-strip/transepidermal water loss (TEWL) technique, which detects damage to the skin barrier. The higher the TEWL score, the more damage there is to the stratum corneum. The maximum difference between the TEWLs for aqueous cream and untreated sites was $60\text{g m}^{-2}\text{ h}^{-1}$. The mean difference was $40\text{g m}^{-2}\text{ h}^{-1}$ ($p=0.03$). The study authors concluded that aqueous cream caused severe damage to the skin barrier and should not be used as a leave on emollient in children with atopic eczema (10).

Two studies have assessed the effect of aqueous cream twice daily for 4 weeks (28 days) on healthy skin on the left and right forearms of 6 healthy female volunteers.

In the first study the forearms of the volunteers were separated into treated and control sides. The treated sides of the forearms were subjected to aqueous cream and the untreated sides were not exposed to any products containing SLS. After 4 weeks, cream application was discontinued 24 hours before skin barrier function was assessed by measuring TEWL and stratum corneum thickness. The result showed a 20% increase in baseline TEWL between treated and untreated areas ($p<0.0001$) and an increase in rate of TEWL during tape stripping as well as a 12% decrease in SC thickness ($p=0.0015$). The study authors concluded that repeated short duration application of aqueous cream on healthy skin causes a decrease in stratum corneum thickness and a concomitant increase in baseline transepidermal water loss. The study authors advised that the use of aqueous cream BP to treat eczematous skin should be reconsidered. Although this was a small laboratory study involving healthy volunteers, amplification of the responses are, it would seem, inevitable in patients with eczema (4).

In the second study changes in corneocyte size and maturity, protease activity, protein content and TEWL were investigated. Aqueous cream was applied to the left and right mid palm side (volar) forearm. After 28 days, the site was tape stripped and corneocyte size, maturity and selected protease activity of the desquamatory kallikrein proteases KLK5 and KLK7, and the inflammatory proteases; trypsin and plasmin were measured. Protein content and TEWL measurements were also recorded. The results showed that corneocyte maturity and size decreased and was significantly lower in the treated sites compared to the untreated sites ($p<0.05$). Protease activity and TEWL values were higher for the treated sites compared with untreated sites ($p<0.05$) (11).

In a study published in 2011, 13 volunteers with a previous history of atopic dermatitis, but no active symptoms for 6 months applied aqueous cream twice daily to the volar side of one forearm for 4 weeks. The other forearm was left untreated as control. Skin barrier function was measured before and after treatment by measuring TEWL in conjunction with tape stripping. Another 13 volunteers with current atopic dermatitis were recruited for assessment without treatment. The study authors reported that the topical application of aqueous cream BP resulted in significant elevation of baseline TEWL and concomitant decrease in stratum corneum integrity, suggesting that aqueous cream negatively affects the skin barrier. The study authors recommended that aqueous cream should not be used as a leave on emollient (12).

Another study in 2011 compared the effects of Oilatum Cream and aqueous cream in 50 patients with a previous history of atopic dermatitis. Results showed washing with aqueous cream resulted in a significantly reduced skin barrier integrity compared with washing with Oilatum. Furthermore, washing with aqueous cream was associated with a significant and persistent (18 hours after final wash) elevation of skin-surface pH. Immediately following washing, both treatments transiently increased skin-surface pH; however this increase did not persist on the sites washed with Oilatum. Protease activity was significantly elevated on the site washed with aqueous cream compared with Oilatum following washing. The authors concluded aqueous cream should not be used as a soap substitute or leave-on emollient because it damages, rather than repairs, the defective skin barrier in atopic dermatitis (13).

Although SLS, parabens and chlorocresol all have possible adverse effects on the skin, no definitive controlled studies using aqueous cream have been conducted to determine if any particular excipient is responsible for the skin reactions observed and no studies have been performed to assess if any one particular brand of aqueous cream is responsible for the observed skin reactions.

The MHRA Drug Safety Update in March 2013 advises that if a patient reports or shows signs of skin irritation with the use of aqueous cream, treatment should be discontinued and an alternative emollient that does not contain sodium lauryl sulfate should be tried (6).

Summary

The use of aqueous cream as a leave on emollient has the potential to damage skin with increasing evidence for sodium lauryl sulphate as the causative ingredient. However, the evidence for the damage caused when it is used as a soap substitute is less clear. Aqueous cream is not particularly effective as an emollient because of its low lipid content and ointments, although greasier, are preferable in patients with eczema. In terms of alternatives, emollients should be prescribed according to the dryness of the skin and individual preference.

Limitations

Larger studies are needed to provide further evidence of the harmful effects of aqueous cream on patients with dry skin conditions. Further studies are also needed to determine its safety for use as a soap substitute.

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