Adding emollient bath additives to standard eczema management for children with eczema: the BATHE RCT

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Scientific summary

The BATHE RCT

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Scientific summary

Background

Childhood eczema is a common condition that can have a substantial impact on quality of life for both the child and their family. Guidelines state that the regular application of emollients should form the mainstay of eczema treatment, with other treatments, such as topical corticosteroids (TCSs), used in addition for flare-ups. Emollients are thought to help by providing a barrier over the skin, decreasing moisture loss and protecting against skin irritants.

There are three methods of application of emollients: (1) leave-on emollients, in which emollients are applied to the skin and left to soak in; (2) soap substitutes, in which emollients are used instead of soap or other washing products; and (3) bath additives, which are oil and/or emulsifiers designed to be added to bath water. All three emollient types can be used together ('complete emollient therapy') and some emollient products can be used for more than one method of application. In this report the term 'bath additives' rather than 'bath emollients' is used in order to emphasise the differences between the three methods of application (i.e. these three methods differ in their proposed actions, and evidence relating to their effectiveness should also be considered separately).

Although there is widespread clinical consensus on, and some evidence for, the value of leave-on emollients and soap substitutes, there is less agreement regarding the potential additional benefits of bath additives and there is a dearth of evidence of their clinical effectiveness and cost-effectiveness. Systematic reviews have found no evidence of their effectiveness and one small study has suggested that they may indeed worsen eczema outcomes. However, despite the absence of evidence for their benefit, bath additives are widely prescribed for childhood eczema and cost the NHS > £23M annually.

Objective

We aimed to determine the clinical effectiveness and cost-effectiveness of bath additives in addition to standard management of atopic eczema in children.

Methods

Trial design

A pragmatic, randomised, open-label, multicentre superiority trial with two parallel arms.

Setting and recruitment

Ninety-six general practices in Wales, the west of England and southern England. Invitation was by personal letter or opportunistically by usual clinical team.

Eligibility criteria

Children were eligible to participate if aged between 12 months and 12 years and if they had eczema according to the UK Diagnostic Criteria for Atopic Eczema. Children with inactive or very mild eczema over the past 12 months, defined as a score of ≤ 5 on the Nottingham Eczema Severity Scale, were excluded, as were children who usually had a bath less than once per week or whose carers were not prepared for the child to be randomised. Only one child per family was enrolled.

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Interventions

The intervention group members were prescribed bath additives by their usual clinical team and were asked to use them regularly for 12 months. We encouraged practices to issue Oilatum® (Stiefel Skin Science Solutions, a GlaxoSmithKline company, Middlesex, UK), Balneum® (Almirall Ltd, Middlesex, UK) or Aveeno® (Johnson & Johnson Ltd, Maidenhead, UK), which are the most frequently prescribed bath additives in the UK. Other bath additives could be issued on the basis of parent or prescriber preference, except for those products that contain antimicrobials or antipruritics as these can have an irritant effect greater than other bath additives. The control group were asked not to use any bath additives for 12 months. Both groups were advised to continue with standard eczema management, which includes the regular application of leave-on emollients and TCSs when required.

Outcomes

Primary outcome

Eczema severity was assessed by repeated measures of the Patient Oriented Eczema Measure (POEM), reported weekly, by parent/carer over 16 weeks. The POEM score range is from 0 (clear) to 28 (severe).

Secondary outcomes

- Eczema severity measured by POEM every 4 weeks from weeks 16 to 52.
- Disease-specific quality of life (QoL) at 16 weeks and at 1 year, measured by the Dermatitis Family Impact Questionnaire.
- Generic QoL at 16 weeks and at 1 year, measured by the Child Health Utility-9 Dimensions (CHU-9D).
- Number of eczema exacerbations resulting in a primary health-care consultation over 1 year [general practitioner (GP) notes review].
- Type (strength) and quantity of topical steroid/calcineurin inhibitors prescribed over 1 year (GP notes review).

Other outcomes

- Adherence to treatment allocation (parent/carer report).
- Adverse effects, such as slipping in the bath or stinging (parent/carer report).

Sample size

The sample size was calculated for repeated measures analysis of variance in weekly POEM scores over 16 weeks. We aimed to detect a mean difference of 2.0 [standard deviation (SD) 7.0] between the intervention and control groups. An alpha of 0.05 and power of 90% with a correlation between repeated measures of 0.70 gave a sample size of 338 participants. Allowing for a 20% loss to follow-up, this gave a total sample size of 423 participants.

Early data suggested that approximately 80% of participants in both groups were strictly adherent to treatment allocation. Therefore, to report a per-protocol analysis with 90% power, in addition to the primary intention-to-treat analysis, we submitted an ethics amendment requesting recruitment of an additional 68 participants, giving a revised target recruitment of 491 participants.

Randomisation and blinding

Children were randomised in a 1 : 1 ratio to either standard eczema care plus bath additives or standard eczema care only, using online software following simple randomisation stratified by recruiting centre. This was an open-label trial.

Statistical methods

The primary analysis for the total POEM score was performed using a mixed multilevel model (MMLM) framework, with observations over time from weeks 1 to 16 (level 1) nested within participants (level 2) nested within centres (level 3). The primary outcome was based on adjusted results, controlling for baseline POEM, recruiting centre and any significant confounders. Unadjusted results are also reported.

Health economics

The aim of the health economic component was an assessment of the economic impact of the intervention on both the NHS and parents at 16 weeks and 52 weeks post randomisation. The costs included in the analysis relate to the primary and secondary care consultations, including accident and emergency, hospitalisations and use of medications. Family-borne costs (FbCs) were those associated with increased household expenditure because of the child's eczema. Quality-adjusted life-years (QALYs) were estimated using the paediatric QoL measure CHU-9D. Results were presented in the form of cost–consequences analysis and a MMLM framework was used and presented adjusted results for baseline POEM and recruiting centre.

Results

Invitations were sent to the parents/carers of 12,504 children and responses were received from 1451. There were 920 replies expressing a willingness to be contacted and including a completed screening questionnaire. Of these, 662 children met eligibility criteria and were approached regarding participation, with 483 children entering the trial. One carer subsequently withdrew permission to use their data. Analysis was thus carried out on data from 482 participants (intervention group, $n = 264$; control group, $n = 218$).

Baseline characteristics

The questionnaire completion rate was high, with 76.7% of participants completing > 80% of the time points for the primary outcome (12 out of 16 weekly questionnaires from week 1 to 16).

In the bath additives group, 73.8% of participants reported that they used a bath additive every time the participant had a bath and a further 19% reported using bath additives more than half of the time. In the no bath additives group, 87.4% of participants reported that they had never used a bath additive in the bath, and an additional 4.7% reported using them less than half of the time.

Primary outcome

The baseline POEM score was 9.5 (SD 5.7) in the bath additives group and 10.1 (SD 5.8) in the no bath additives group. The average POEM score over the 16-week period was 7.5 (SD 6.0) in the bath additives group and 8.4 (SD 6.0) in the no bath additives group. There was no statistically significant difference in weekly POEM scores between the two groups over the 16-week period. After controlling for baseline severity and confounders (ethnic group, TCS use and soap substitute use) and allowing for the clustering of patients within centres and responses within patients over time, the POEM score in the no bath additive group was 0.41 points higher than in the bath additive group [95% confidence interval (CI) –0.27 to 1.10], which is substantially lower than the published minimal clinically important difference of 3 points [Schram ME, Spuls PI, Leeflang MM, Lindeboom R, Bos JD, Schmitt J. EASI, (objective) SCORAD and POEM for atopic eczema: responsiveness and minimal clinically important difference. *Allergy* 2012;**67**:99–106; Gaunt DM, Metcalfe C, Ridd M. The Patient-Oriented Eczema Measure in young children: responsiveness and minimal clinically important difference. *Allergy* 2016;**71**:1620–5].

There was no significant difference between groups in any of the secondary outcomes or in adverse effects such as redness, stinging or slipping.

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Health economics

The individual costs were estimated alongside individual QALYS and presented in the form of mean (SD) values per study group. The 95% CIs around differences were also reported. The mean annual costs were estimated at £180.50 (SD £237) for the bath additives group and £166.12 (SD £293) for the no bath additives group. Similarly, the annual results for QALYs were 0.91 (SD 0.1) and 0.90 (SD 0.1) for the bath additives and the no bath additives group, respectively. The difference in mean cost was £14.38 (95% CI –£33.45 to £62.21) and in mean QALYs was 0.00 (95% CI –0.01 to 0.02). Across all the measures considered within the economic evaluation, there is only one statistically significant cost difference between the trial groups, relating to the 16-week result for which the cost difference was £20.89 (95% CI –£39.13 to –£2.65) in favour of the intervention group; this difference was not sustained in the 52-week results. The FbCs showed an annual increase in spending within the no bath additives group of £51.37 (95% CI –£118.49 to £15.74), which was not statistically significant. The economic analysis considered a comprehensive health profile to assess the cost-effectiveness of bath additives when used for childhood eczema. The analysis found no benefits that could be used to consider the intervention cost-effective. In fact, there were no significant differences observed in any economic outcome between the trial groups to alter this conclusion.

Discussion

This is the first large pragmatic trial on the role of bath additives. Published case series and case reports have not been strongly suggestive of beneficial effect. This trial provides the strongest evidence to date that emollient bath additives provide little additional benefit beyond standard eczema care in the management of childhood eczema.

The Bath Additives for the Treatment of Eczema in cHildren (BATHE) trial was an adequately powered randomised controlled trial, with high follow-up/questionnaire completion rates and good adherence to trial intervention allocations. The study has strong external validity as it was pragmatic in design to reflect normal practice, and participants were broadly reflective of children with eczema seen in primary care.

This was an open trial, as it is not possible to create a convincing placebo for bath additives, with a primary outcome measure that was participant reported, as our main concern was with the impact of symptoms. An unblinded trial with a participant-reported outcome could be biased in favour of finding a treatment effect because of a perception of positive benefits of treatment. However, the negative result of the trial suggests that this was not the case.

These findings are timely for clinicians and prescribing advisers in England, as many Clinical Commissioning Groups are currently reviewing emollient prescribing guidelines in order to reduce costs. However, there is currently very little research evidence to guide these discussions and there is concern from patient advocacy groups that decisions are being made solely based on cost in the absence of considerations around impact on quality of eczema care. There are also concerns that decisions concerning emollient bath additives could be erroneously extended to leave-on emollients. Data presented here suggest that adding bath emollients to bath water should be a low priority for prescribing, although we did not examine the use of these products as soap substitutes. It is important to note that, although more research is needed in this area, there is evidence that the regular use of leave-on emollients prevents flare-ups in eczema, and there is widespread clinical consensus around the role of emollients as soap substitutes. Promoting choice and adequate prescribing of these products is likely to improve QoL and reduce consulting and prescribing for flare-ups.

Conclusions

Implications for health care

This trial found no evidence of any clinical benefit of including emollient bath additives in the standard management of atopic eczema in children aged between 12 months and 12 years. These findings suggest that parents/carers can be advised that using emollient bath additives by pouring them into bath water is unlikely to provide any reduction in eczema symptoms, but that they should continue to use leave-on emollients regularly and to use emollients as a soap substitute as recommended by the National Institute for Health and Care Excellence (NICE) [National Institute for Health and Care Excellence. *Atopic Eczemain Under 12s: Diagnosis and Management*. Clinical guideline (CG57). London: NICE; 2007].

These trial results provide prescribing advisers and clinicians with good evidence on which to base decisions about bath additives for childhood eczema. The findings also provide parents/carers with useful information regarding those treatments that are unlikely to work as, anecdotally, bath additives may cause extra cleaning as well as rotting of rubber bath mats and toys.

Implications for research

Several questions around emollients and washing in eczema that were highlighted in the James Lind Alliance Priority Setting Partnership (Batchelor JM, Ridd MJ, Clarke T, Ahmed A, Cox M, Crowe S, *et al.* The Eczema Priority Setting Partnership: a collaboration between patients, carers, clinicians and researchers to identify and prioritize important research questions for the treatment of eczema. *Br J Dermatol* 2013;**168**:577–82) remain outstanding, including which emollient is the most effective and safe in treating eczema? Which should be applied first when treating eczema: emollients or topical steroids? Which is the best way for people with eczema to wash (frequency of washing, water temperature, bath vs. shower)?

We have not explored the role of leave-on emollients, and previous evidence suggests that these are of central importance to eczema management. However, there is little evidence regarding the leave-on emollients that are most effective and commissioners are increasingly restricting prescribing on the basis of cost alone. Further research would be needed to explore optimal emollient and bathing regimens.

Trial registration

This trial is registered as ISRCTN84102309.

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