National Institute for Health Research

CREAM Study
Summary for Healthcare Professionals

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Do antibiotics (oral or topical) help children with a "clinically infected" eczema flare?

Summary

Background

NICE currently recommends topical antibiotics for localised infections and oral antibiotics for widespread infection. However, systematic reviews have found limited and conflicting evidence about the clinical effectiveness of antibiotics in the treatment of infected (and non-infected) eczema.

New evidence from the CREAM study

CREAM randomised 113 children with clinically infected eczema in primary care to receive oral antibiotic, topical antibiotic, or placebo, in addition to topical corticosteroids (TCS) and emollients, in a blinded, double dummy (all participants received both an oral liquid and a topical treatment) RCT. We found evidence of no clinically important benefit in terms of subjective eczema severity between each antibiotic group and the placebo group at two weeks.

Implications

Children with mild-moderate flares of apparently infected eczema show marked improvement when treated with TCS and emollients, and may not benefit from the addition of oral or topical antibiotics. Consider prescribing TCS (or increasing potency if already using) and emollients, and using a 'wait and see' approach with regard to antibiotics, if the parent is in agreement.

Background

Children with eczema commonly experience flares or exacerbations, and these are associated with significant impairment in quality of life. *Staphylococcus aureus* is more prevalent on the skin of people with eczema and is found in greater concentrations in those experiencing more severe eczema. NICE guidance recommends that small areas of eczema with sings of infection are treated with topical antibiotics and widespread infection is treated with oral antibiotics, and this is common practice. However, Cochrane and other systematic reviews have found limited and conflicting evidence about the effectiveness of these interventions. Overuse of antibiotics contributes to increasing levels of antibiotic resistance and therefore it is important to only use antibiotics when there are clear benefits. Therefore, we set out to determine the effectiveness of oral and topical antibiotics in the treatment of clinically infected eczema in children in primary care.

What did we do?

CREAM was a randomised controlled trial comparing oral antibiotics and topical antibiotics with matched placebos in children with infected eczema in primary care. Children aged 3 months to 7 years consulting in primary care with clinically infected eczema were assessed within 72 hours. Eligible children were randomised to: oral antibiotic and topical placebo (oral antibiotic); topical antibiotic and oral placebo (topical antibiotic); or oral and topical placebos (control). The interventions under evaluation were flucloxacillin suspension or erythromycin suspension for those with penicillin allergy (dose per age per British National Formulary guidance), and fusidic acid cream (Fucidin®) applied three times a day, all for 1 week. In addition, all children were prescribed hydrocortisone 1% for use on the face and clobetastone butyrate 0.05% (or another moderate-strength topical corticosteroid)

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for use on other parts of the body. Outcomes were measured at 2 weeks, 4 weeks and 3 months. The primary outcome was a comparison of a validated subjective eczema severity scale – the Patient-Orientated Eczema Measure (POEM) – at 2 weeks between each active intervention group and the control (placebo/placebo) group.

What were the study findings?

We randomised 113 children (36 to oral antibiotic, 37 to topical antibiotic and 40 to placebo) from 32 general practices and 1 primary care dermatology clinic. 74.6% had a flare that had lasted for ≤ 14 days, 92.0% reported having one or more of weeping, crusting, pustules or painful skin as a symptom at baseline and 70% had *S aureus* cultured from the skin at baseline. We followed up 101 (89.4%), 98 (86.7%) and 74 (65.5%) participants at 2 weeks at 4 weeks and 3 months respectively. **Controlling for baseline POEM score, oral antibiotic and topical antibiotic resulted in non-significant increases (worse severity) in mean (95% confidence interval) POEM scores of 1·5 (-1·4 to 4·4) and 1·5 (-1·6 to 4·5) respectively.** Symptom scores improved rapidly over the first week, with no significant differences between groups. We found similar non-significant differences in secondary outcomes or adverse effects.

What are the implications for clinical practice?

We found no clinically important benefit from oral or topical antibiotics in children with clinically infected eczema flares who were treated with topical corticosteroids and emollients. However, we did not include children with severe eczema, and although most children in the study had one or more 'classical signs' (weeping, crusting, pustules or painful skin) of infection and 70% had *S aureus* cultured from the skin, most did not have signs of severe infection. Therefore, the results are not generalisable to children with severe eczema or more severe signs of infection.

We recruited less than our original planned sample size, and some have suggested that the study lacked sufficient power. The 95% confidence interval around the effect size estimates of the range of values that the true effect is likely to fall within. The lower band of the confidence interval in this study represents the maximum likely beneficial effect (reduction in POEM score) from each intervention, and both (-1.4 and -1.6) of these are smaller than the minimum difference in POEM score that is thought to be important (POEM scores range from 0 to 28 and the published minimal clinically important difference is around 3). Therefore, even though a larger study would provide a more precise estimate of effect, the results of this study tell us that we can be confident that oral and topical antibiotics do not produce a clinically important beneficial effect in this population.

All children that participated in the CREAM study were provided with topical corticosteroids, emollients, and advice about good eczema care. There is a good evidence base for topical corticosteroid use, and they are often underused because of fears about adverse effects that are not backed up by good scientific evidence.

Full study details available at: http://www.annfammed.org/content/15/2/124

See also: https://discover.dc.nihr.ac.uk/portal/article/4000444/antibiotics-for-eczema-that-looks-infected-may-be-unnecessary-in-some-cases

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