Paediatrics

Emollients do not prevent eczema in infancy

Daily emollient use for the first 12 months of life did not protect against the development of eczema in high-risk children, a UK study has found.

Infants born at full term were recruited to a randomised controlled trial carried out at 12 hospitals and four primary care sites across the UK between 2014 and 2016. All the infants were deemed at high risk of developing eczema because of a family history of atopic disease i.e. at least one first-degree relative with parent reported eczema, allergic rhinitis, or asthma diagnosed by a doctor.

A total of 1,394 infants, 54% boys, were randomly assigned to receive either emollient (693) and best practice skin care advice or skin care advice only (701). Parents in the emollient group were offered the choice of two common emollients and advised to apply the emollient at least once daily to the whole body (apart from the scalp) until the child reached one year of age. They were also advised to apply emollient after every bath, even if they had already applied it earlier that day. Both groups received guidance on using mild cleansers and shampoos formulated for infants, and to avoid the use of soap, bubble bath and baby wipes.

The children were followed up at 2 weeks, by telephone, and at 3, 6, 12 and 18 months online or by postal questionnaire. At the two-year follow-up visit the skin was examined, saliva collected and skin prick testing performed. If testing or history indicated a possible food allergy diagnostic food challenges were carried out.

The primary outcome was eczema at the age of two, one year after emollient treatment had stopped, to determine if there had been a lasting effect from the intervention.

Adherence in the emollient group was 88% (466 of 532) at 3 months, 82% (427 of 519) at 6 months, and 74% (375 of 506) at 12 months in those with complete data available.

Washing and bathing practices were similar in both groups. In the intervention group the emollient was usually applied once a day after the bath. At age two years, there was no significant difference in the prevalence of eczema, between the two groups. Eczema was found in 139 (23%) of 598 infants with outcome data collected in the emollient group and 150 (25%) of 612 infants in the control group; adjusted relative risk (RR) 0·95 (95% CI: 0·78-1·16, P = 0·61).

There were higher numbers of skin infections per child in the emollient group in year 1, 0·23 compared with 0.15 in the control group; adjusted incidence rate ratio 1·55 (95% CI: 1·15-2·09).

Food allergies to milk, egg or peanut were confirmed in 41 (7%) of 547 infants in the emollient group and 29 (5%) of 568 in the control group; adjusted RR 1·47 (95% CI: 0·93–2·33). The proportion of infants with allergic rhinitis, wheezing, and sensitisation to cat dander, grass pollen, and dust mite were similar in both groups.

The investigators conclude: 'Our study does not support the use of emollients for preventing eczema in high-risk infants, a finding supported by PreventADALL, another large trial using a skin barrier enhancing intervention.[1]

'Our data relate only to prevention of eczema and do not directly challenge the practice of using emollients as first-line treatment for eczema.'

This study found no evidence to support the early use of emollients to prevent eczema and other atopic disease including food allergy. The data also suggest that their use may result in increased skin infections. There are practical issues too as using emollients can be burdensome to parents and waste NHS resources.

DR PETER SAUL

Chalmers JR, Haines RH, Bradshaw LE et al. Daily emollient use during infancy for prevention of eczema: the BEEP randomised controlled trial. *Lancet* 2020;395:962-72

Diabetes

SGLT2 inhibitors reduce risk of serious renal events

A Scandinavian observational study has shown that sodium-glucose co-transporter 2 (SGLT2) inhibitors are associated with a significant reduction in serious renal events compared with dipeptidyl peptidase-4 (DPP-4) inhibitors.

The study used Scandinavian disease registry data to compare population outcomes in the general diabetic population rather than selected groups of high-risk patients.

Data on a cohort of patients were drawn from disease registers in Sweden, Denmark and Norway. Potentially eligible patients were included from the Swedish and Norwegian registers between April 2013 and December 2016 and from Danish registers up to December 2018. These registers provide data on diagnoses, prescribing, investigations and cause of death.

Patients aged 35-84 years who had filled their first prescription for an SGLT2 inhibitor or a DPP-4 inhibitor were eligible for the study. Initially the registers yielded 38,273 new users of SGLT2 inhibitors and 107,854 of DPP-4 inhibitors.

Patients with prior exposure to the other drug, pre-existing serious renal disease, drug misuse, severe pancreatic disease or hospital admission in the past 30 days were excluded.

The remaining patients were carefully matched one to one as closely as possible, using multiple parameters, resulting in 29,887 pairs of matched patients who were eligible for admission to the study.

The mean age of participants was 61 years, and 39% were women. Around 19% had a history of major

REFERENCE

1 Skjerven HO, Rehbinder EM, Vettukattil R et al. Skin emollient and early complementary feeding to prevent infant atopic dermatitis (PreventADALL): a factorial, multicentre, cluster-randomised trial. *Lancet* Published online 19 Feb 2020. doi.org/10.1016/S0140-6736(19)32983-6

cardiovascular disease (CVD), but only 3% had a history of chronic kidney disease (CKD). Total follow-up for the SGLT2 inhibitors was 42,632 years (mean 1.4 years) and for DPP-4 inhibitors 58,473 years (mean 1.7 years).

The primary endpoint of serious renal events was a composite of renal replacement therapy i.e. dialysis or transplant, death from renal causes and hospital admission for renal events.

After adjusting for confounding variables such as BMI, blood pressure (BP) and smoking status, the use of SGLT2 inhibitors compared with DPP-4 inhibitors was associated with a 58% reduced risk of serious renal events (2.6 events per 1,000 person years vs 6.2 events per 1,000 person years); hazard ratio 0.42 (95% CI: 0.34-0.53). The difference was mainly driven by lower rates of renal replacement therapy and hospital admissions with use of SGLT2 inhibitors. No significant differences were seen in death rates from renal causes between the groups.

The SGLT2 inhibitors are the most recent class of hypoglycaemic drugs introduced for type 2 diabetes. They work by reducing glucose/sodium exchange in the proximal tubule and increasing urinary loss of glucose. From first licensing, they have been subject to outcome studies. Not only have they been shown to result in weight reduction, BP lowering and improved HbA_{1c} levels, but outcome studies suggest a real reduction in cardiovascular deaths on these drugs.

The study authors conclude: 'Complementing data from clinical trials, this study provides further support for the use of SGLT2 inhibitors in a broad range of patients with type 2 diabetes.'

An accompanying editorial in the *BMJ* states that although there is no evidence of a protective effect against renal disease by DPP-4 inhibitors, they do not worsen renal outcomes.[1] The author of the editorial concludes that SGLT2 inhibitors seem preferable to DPP-4 inhibitors in diabetes patients who may be more at risk of renal disease.

In the UK, SGLT2 inhibitors are not recommended to be initiated in patients with an eGFR below 60 ml/min/1.73m^2, or continued in patients with an eGFR below 45 ml/min/1.73m^2.

The findings of this study are encouraging. The realisation of the role of lifestyle in preventing and treating type 2 diabetes, combined with new classes of drugs that assist weight loss and improve outcomes give grounds for cautious optimism about the future for diabetes management.

DR MATTHEW LOCKYER

Pasternak B, Wintzell V, Melbye M et al. Use of sodium-glucose co-transporter 2 inhibitors and risk of serious renal events: Scandinavian cohort study. *BMJ* 2020;369:m1186

REFERENCE

1 Smith SM. (Editorial) SGLT2 inhibitors and kidney outcomes in the real world. *BMJ* 2020;369:m1584

Addiction

Increased risk of fatal overdose or suicide associated with stopping opioids

Ceasing treatment with opioids is associated with an increased risk of death from overdose and suicide, an observational study from the United States has found.

A total of 1,394,102 patients, mean age 60 years, in the Veterans Health Administration system who had received outpatient prescriptions for an opioid medication during the 2013 fiscal year were included in the study. Data on death rates up to the end of the fiscal year 2014 were analysed. The vast majority of participants were men (92%). Just over half the patients had three or more medical diagnoses. Alcohol use disorders were diagnosed in about 10% of patients and the most common mental health conditions were depressive disorders and post-traumatic stress disorder.

There were 2,887 deaths from overdose or suicide (1,851 overdoses and 1,249 suicides, these figures were not mutually exclusive). Just over half of patients (57.4%) stopped opioid treatment during the study period.

Patients had been prescribed opioids for variable periods, and the longest period identified, longer than 400 days, accounted for 37% of patients. Around a third (32%) of patients were prescribed opioids for up to 30 days, 9% for 31-90 days and 23% for 91-400 days.

The hazard ratios (HR) for death by overdose or suicide for patients who stopped opioid treatment were:

- HR 1.67 for ≤ 30 days' opioid treatment
- HR 2.80 for 31-90 days' opioid treatment
- HR 3.95 for 91-400 days' opioid treatment
- HR 6.77 for > 400 days' opioid treatment

Other factors that were independently associated with a greater risk of death from overdose or suicide were: prescriptions for long- or short-acting opioids as opposed to tramadol; log maximum daily morphine mg equivalents; the number of medical diagnoses; and having a mental health or substance use disorder. Older age, female gender, and being married were independently associated with a lower risk of death from overdose or suicide.

Concerns about recent rapid increases in the prescribing of opioid medication, particularly for chronic non-cancer pain, and associated risks such as overdose and dependence, has led to a range of initiatives to support clinicians in reducing and stopping prescribing opioids when appropriate.

The authors conclude that: 'Patient-centred efforts to mitigate the risk of death from overdose or suicide in patients prescribed opioids need to look at a broad array of risk factors for patients rather than focus solely on long-term prescription management. Our findings suggest close monitoring for at least three months for any patient stopping treatment with opioids but especially in those on long-term treatment or those with other risk factors (e.g. mental health and substance use disorders)'.

DR JEZ THOMPSON

Oliva EM, Bowe T, Manhapra A et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *BMJ* 2020;368:m283

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