INVESTIGATIVE REPORT

Olive Oil, Sunflower Oil or no Oil for Baby Dry Skin or Massage: A Pilot, Assessor-blinded, Randomized Controlled Trial (the Oil in Baby SkincaRE [OBSeRvE] Study)

Alison COOKE[1], Michael J. CORK[2], Suresh VICTOR[3,4], Malcolm CAMPBELL[1], Simon DANBY[2], John CHITTOCK[2] and Tina LAVENDER[1]

[1]School of Nursing, Midwifery and Social Work, [3]Institute of Human Development, The University of Manchester, Manchester, [2]School of Medicine and Biomedical Sciences, University of Sheffield, Sheffield, UK, and [4]Sidra Neonatology Center of Excellence, Sidra Medical and Research Center, Doha, Qatar

Topical oils on baby skin may contribute to development of childhood atopic eczema. A pilot, assessor-blinded, randomized controlled trial assessed feasibility of a definitive trial investigating their impact in neonates. One-hundred and fifteen healthy, full-term neonates were randomly assigned to olive oil, sunflower oil or no oil, twice daily for 4 weeks, stratified by family history of atopic eczema. We measured spectral profile of lipid lamellae, trans-epidermal water loss (TEWL), stratum corneum hydration and pH and recorded clinical observations, at baseline, and 4 weeks post-birth. Recruitment was challenging (recruitment 11.1%; retention 80%), protocol adherence reasonable (79–100%). Both oil groups had significantly improved hydration but significantly less improvement in lipid lamellae structure compared to the no oil group. There were no significant differences in TEWL, pH or erythema/skin scores. The study was not powered for clinical significance, but until further research is conducted, caution should be exercised when recommending oils for neonatal skin. *Key words: infant; skin barrier function; topical oils.*

Alison Cooke, The University of Manchester, Jean McFarlane Building Room 4.336, Oxford Road, M13 9PL Manchester, UK. E-mail: alison.cooke@manchester.ac.uk

Neonatal dry skin is a normal adaptation to the extrauterine environment following birth. The primary function of baby skin is to provide a barrier, firstly to water loss and secondly to penetration from external irritants and allergens (1). Some research has suggested that there is a potential for development of atopic eczema (AE) (synonym atopic dermatitis) if topical products with adverse effects on skin barrier function are used for the prevention or treatment of baby dry skin (2, 3).

AE is a disease resulting from gene environment interactions leading to breakdown of the skin barrier, cutaneous inflammation and allergy (4, 5). Prevalence has increased from 5% of children aged 2 to 15 years in the 1940s (6) to approaching 30% more recently (7). Ap-proximately 60% of diagnoses are made in the first year and 45% in the first 6 months of life (4), a period when midwives and other related health professionals potentially have an influence over parental caring practices. Genetic changes cannot account for this increased incidence, but there has been an increase in potentially linked environmental factors including the increased availability and use of baby skincare products. It has been suggested that certain topical oils instigate a weakness in the skin barrier (2, 8, 9). There may be a link between early use of certain types and formulations of oils on baby skin and the development of AE; this requires further research.

Extra care of baby skin is important due to differences in the biological composition between baby and adult skin. The stratum corneum (SC), a principal component of the epidermal barrier, is 30% thinner, and the overall epidermis is 20% thinner in babies (10). Although newborn skin is sufficiently developed to withstand the extrauterine environment at full term (≥ 37 weeks gestation), its biophysical and biological properties such as corneocytes size, SC hydration and pH, lipid composition and structure, natural moisturising factor (NMF) and water composition continue to be in a transitional state during the early years of life (11–13). Given that babies have a propensity for reduced skin barrier function, careful consideration should be given to topical products used on baby skin to ensure that the developing epidermal barrier is not adversely altered or affected. Alteration in the lipid composition and structure of the SC is linked to reduced skin permeability function and AE (14–16). Only skincare products which are proven to enhance the integrity, barrier and/or immune function of baby skin should be recommended.

There is no national guidance on neonatal skincare. The United Kingdom (UK) Postnatal Care Guidelines (17) briefly mention only cleansing in relation to baby skincare. There is no national or international guidance with regard to using topical oils. The practice of recommending and using topical oils for the prevention or treatment of baby dry skin or for massage has developed as a traditional practice, rather than be based on evidence (18, 19). It has been suggested that there is a readiness to believe that what is 'natural' is 'safe' (20, 21). There

has been a growth in societal interest in 'natural' products (22), particularly for babies (23). Parents follow the advice of health professionals regarding the care of their baby (20). It is necessary to provide evidence from which health professionals can offer the best advice for baby skincare, to avoid harmful practices.

A literature review conducted prior to the study identified 3 studies that investigated the use of topical oils on term newborn babies. One study considered olive oil (24) but the outcome under investigation was detachment of the umbilical cord stump, rather than dry skin. The other studies considered skincare; both being randomized controlled trials (RCTs) (25–27). The BEEP pilot study (26, 27) ($n = 124$) saw a trend toward improved skin barrier function in the intervention group (26) and concluded that a daily full-body emollient therapy from birth can prevent AE (27). Babies randomized to the treatment arm could choose a defined sunflower seed oil with high linoleic acid/low oleic acid content, a specific emollient cream/gel or a specific emollient ointment. Only 23.4% ($n = 15$) of participants in the intervention arm chose sunflower seed oil. Results were provided as a total of participants for the treatment arm so it is not possible to assess results specific to the sunflower oil only, but the study was not powered to detect this. Solanki et al. (25) compared safflower oil (ratio of linoleic acid to oleic acid not reported) to coconut oil to no oil amongst preterm (<34 weeks gestation; $n = 42$ and 34–37 weeks gestation; $n = 30$) and term babies (>37 weeks gestation; $n = 46$). The study was not powered and the main outcome was fatty acid profiling, but clinical observations and AE were also monitored throughout the 5-day treatment period. None of the studies measured TEWL, SC hydration or pH. No trials have considered whether using topical oils is beneficial to healthy term baby skin.

Prior to the study we conducted a national survey of UK maternity and neonatal units. The survey found that routine practice was to recommend topical olive oil or sunflower oil to new parents for their baby's dry skin (19). We therefore conducted a pilot RCT to compare the topical use of a specific sunflower oil (high linoleic acid, low oleic acid) to a specific olive oil (low linoleic acid, high oleic acid) to no oil. We hypothesized that the regular application of the specific sunflower oil, when compared to no oil or specific olive oil, would improve the skin barrier function of newborn term babies. From the study design stage we involved a Trial Steering Committee made up of independent specialists in nursing, midwifery, pediatrics, clinical trials, dermatology, and patient user groups including a representative from the National Eczema Society and a parent representative.

The pilot was designed to address the following aspects in the design of a definitive study: proof of concept of what, if any, effect oils have on baby skin barrier function, the suitability of Attenuated Total Reflectance Fourier Transform Infra-red spectroscopy (ATR-FTIR) as an outcome measure, optimal primary outcome measure, sample size calculation, optimal trial design (recruitment rates, protocol adherence and acceptability), and optimal trial management processes (patient information provision, consent, data recording).

METHODS (for complete details see Appendix S1[1])

Study site and population

A pilot, assessor-blinded, RCT was conducted in St. Mary's Hospital, Manchester, North West England. We set a target sample size of 100 babies to allow for 30 per group after a 10% anticipated loss to follow-up. We included those with and without a family history of AE. The sample size was considered to be sufficient to explore differences in outcomes and provide data capable of determining feasibility for a definitive trial (28). The trial was approved by Greater Manchester East Research Ethics Committee (13/NW/0512).

Recruitment and randomization

Babies of women who gave consent were randomized to one of the intervention groups or the control group within 72 h of birth. Randomization was 1:1:1 via a central telephone-based service provided by The Christie Hospital NHS Foundation Trust Clinical Trials Unit. The randomization sequence was computer generated. Randomization was stratified according to whether or not there was a family history of AE, where at least one of father, mother, or sibling had a medical diagnosis of AE and had been prescribed topical steroid treatment. The randomization was in blocks within eczema history strata (yes, no) and the block size varied at random between 6 and 15 (i.e. 6, 9, 12 or 15) to guard against predictability. Allocation was concealed from the participant and independent research midwife until the point of allocation. Babies were randomized to one of 3 groups: olive oil, sunflower oil or no oil (control). The study was assessor-blinded, and participants in the intervention groups were blinded to which oil they were using; oils were labelled X and Y. Participant blinding was impossible for the control group as there is no control oil that we could be confident was safe to apply and would have no effect on skin barrier function (29).

Intervention

Olive oil and sunflower oil of specific defined formulation (William Hodgson and Co, Congleton, United Kingdom; see Table I) were provided for the intervention groups as appropriate. Parents began using the oil as instructed from the day after the initial assessment. Parents applied 4 drops of oil to their baby's left forearm, left thigh and abdomen, twice a day. No oils were applied on the day of assessment to avoid any

---

Table I. *Specifications of natural oils used in the Oil in Baby SkincaRE (OBSeRvE) study*

Fatty acid/Carbon number	Content (%)	
	Olive oil	Sunflower seed oil
Palmitic acid/C16: 0	11.5	6.0
Oleic acid/C18: 1	72.8	29.3
Linoleic acid/C18: 2	10.8	59.2
Linolenic acid/C18: 3	0.2	0.1

interference with results that may have been caused by oil residues, and to maintain assessor blinding. Parents in all 3 groups were asked not to use any other skincare products on the 3 study sites; water only was advocated.

Assessment of trial outcomes

All measurements were taken by the investigator who remained blind to the treatment allocation. Data were collected at two time points. The first assessment was conducted at baseline prior to discharge from the hospital. A second assessment was made at 4 weeks ± 5 days.

Primary outcomes

ATR-FTIR spectroscopy. The change in structure of the lipid lamellae, a determinant of SC permeability barrier function (30), was assessed between 48 h and 4 weeks following birth using ATR-FTIR spectroscopy. This technique has been used previously to demonstrate the effect of oleic acid on skin barrier (8). At each spectroscopy measurement site on the skin surface an absorbance spectrum was collected on intact skin and following the application and removal (tape-stripping) of 3 consecutive D-Square discs (CuDerm Corporation, Dallas, TX, USA) to reassess the deeper corneocyte layers of the SC. Data analysis of absorbance spectra was performed in Omnic 9.0 and TQuant (Thermo Fisher Scientific Inc., Waltham, USA). The difference in the quantity of lipids and lipid esters in the skin was determined based upon the change in peak intensities of the spectral regions centred on ~2,920 and ~2,850 wavenumbers (31). Lipid chain conformation ($v_{asym}CH_2$ COG) was based on the location (centre of gravity: COG) of the peak between ~2,853 and ~2,848 wavenumbers, corresponding to the asymmetric stretching of the CH_2 bond of lipids (32, 33). Lateral chain packing was determined from the second derivative reflectance spectra by measuring the full width at half maximum (FWHM) of the spectral region centred at 1,468 wavenumbers (30). The difference in the quantity of surfactants in the skin, measured to assess adherence regarding use of wash products, was determined based upon the change in peak intensity of the spectral region centred on 1,240 wavenumbers, corresponding to the sulphur group of surfactants found in wash products (34).

Trans-epidermal water loss (TEWL). This outcome measured the rate of change of basal trans-epidermal water loss (TEWL) between 48 h and 4 weeks after birth. TEWL, a validated measure of skin barrier function (35), was measured using a closed chamber TEWL instrument (Biox Aquaflux Model AF200). The lead investigator took the measurements at both time points, at each study site twice, before and after tape-stripping, in accord with published guidelines for TEWL measurements (36).

Secondary outcomes

Stratum corneum hydration and skin surface pH. The change in SC hydration and skin surface pH between 48 h and 4 weeks were measured at the same times and sites as the primary outcome measures using a Corneometer® Model CM825 [Courage & Khazaka electronic GmbH, Köln, Germany] and skin pH meter® Model PH905 [Courage & Khazaka electronic GmbH].

Clinical observations. Changes in the skin were observed and recorded by the investigator at baseline and follow-up (erythema, dryness and scaling, need for medical products/ attention) between 48 h and 4 weeks. The investigator assessed the babies' skin according to a modified Neonatal Skin Condition Score (NSCS; 37). Erythema was measured using a Mexameter® Model MX18 probe at each visit [Courage & Khazaka electronic GmbH].

Analysis

Data were double-entered into IBM SPSS Statistics version 20 and analysed in version 22, with the two data files cross-checked for errors. In accordance with recommended practice for pilot studies (28), the main analyses were descriptive, involving the estimation of recruitment rates, attrition rates, adherence rates, means and standard deviations of primary and secondary outcomes by group at baseline and 4 weeks, and 95% confidence intervals (CI) for differences of means of change scores of primary and secondary outcomes between groups at 4 weeks. Missing values at 4 weeks were not carried forward or imputed; descriptive analysis at 4 weeks was based on complete data, compared by randomization group. The latter comparisons were confirmed by analysis of covariance.

RESULTS

Data were collected between September 2013 and July 2014. We approached 1,037 mothers and 115 consented to participate (recruitment rate: 11.1%). The recruitment flow chart is illustrated in Fig. S1[1], which includes detail of reasons for declining and loss to follow-up. Baseline characteristics were homogenous across the 3 groups (Table SI[1]). Approximately 32% of infants had a family history of AE; stratification ensured that these were evenly distributed across the 3 groups. There were no differences in ambient conditions across the groups for each visit (Table SII[1]).

Protocol adherence

Protocol adherence was explored for the assessment of feasibility, both to treatment allocation regime and regarding other product use. Adherence was measured from the ATR-FTIR sebum data and mother's self-reporting in the weekly telephone questionnaires and final follow-up questionnaire. The most adherent group was the control group for both treatment use and product avoidance. The proportion of lipid esters in the SC was elevated in the two oil groups compared to the no oil group on all test sites (data not shown), evidencing the use of oils, which both contain high levels of lipid esters on the skin. The weekly ranges of adherence for treatment use were 79% to 93% of participants for the olive oil group, 83% to 94% for the sunflower oil group and 100% for the no oil group (Table SIII[1]). The ranges for other product avoidance were 57% to 89%, 70% to 87% and 74% to 100%, respectively (Table SIII[1]). Overall, there were no significant differences in adherence across the groups. However, there was a noticeable decrease in compliance with regard to product use in week 4 for all groups. The actual number of mothers using alternative products on their babies may be higher as adherence was self-reported. Analysis of the ATR-FTIR spectra supported the data collected from the mothers by indicating no significant differences in the change in proportion of sulphur groups in the skin at 4 weeks between the groups (data not shown), suggesting no difference in the

use of cleansers containing sulphate surfactants, which represent the largest class of cleansers in skincare (34).

Primary outcomes

As shown in Table SIV[1], there were no significant differences for TEWL between the trial arms for all body sites. The ATR-FTIR spectroscopy data showed that both oil groups contained a significantly higher proportion of lipids within the SC, compared to the no oil group. All groups exhibited improvement in lipid chain conformation and lateral packing over the 4 week treatment period, as indicated by a shift in $v_{asym}CH_2$ COG to a lower wavenumber and an increase in the FWHM, respectively. However the extent of this improvement was significantly reduced in the groups using oils compared to the no oil group. For olive oil compared to no oil, there was a difference in lipid chain conformation and lateral packing pre tape-stripping (e.g. at the abdomen: lipid chain conformation mean difference = 1.02, 95% CI 0.66–1.38, $p < 0.001$; lateral chain packing mean difference = –0.92, 95% CI –1.40 to –0.44, $p < 0.001$) and post tape-stripping (conformation mean difference = 0.85, 95% CI 0.46–1.23, $p < 0.001$; packing mean difference = –0.95, 95% CI –1.50 to –0.40, $p = 0.001$), suggesting a more persistent fluid-like (less ordered) state. For sunflower oil compared to no oil, these differences occurred pre tape-stripping (e.g. at the abdomen: lipid chain conformation mean difference = 0.88, 95% CI 0.52–1.25, $p < 0.001$; lateral chain packing mean difference = –1.27, 95% CI –1.82 to –0.73, $p < 0.001$) but were not so marked post tape-stripping (conformation mean difference = 0.54, 95% CI 0.15–0.93, $p = 0.007$; packing mean difference = –0.49, 95% CI –1.12–0.14, $p = 0.121$) indicating that they may be more restricted to the superficial layers of the SC. There were no significant differences between the two oil groups in lipid chain conformation or lateral chain packing. Full results can be viewed in Table SIV[1].

Secondary outcomes

As shown in Table III, both oil groups were significantly more hydrated than the no oil group at all 3 body sites. There were no significant differences for skin surface pH between the trial arms for all body sites. However, CI only just crossed the line of no difference. With regard to the clinical observations of the skin, none of the infants had severe dryness and/or scaling or rash and very few had mild to moderate dryness and/or scaling or rash (see Table II). The majority had no or slight dryness and/or scaling or rash. At 4 weeks, skin condition score (NSCS) had improved overall. There were no significant differences across treatment groups for erythema at baseline or 4 weeks (see Table III).

Family history of atopic eczema

Analysis of covariance found no significant effect for family history of AE in any of the primary or secondary outcomes apart from erythema on the thigh ($p = 0.007$). Mean erythema scores at follow-up were consistently numerically higher in babies without a family history at all 3 body sites for both oil groups and also on the abdomen and thigh for babies in the no oil group. This agreed with clinical observation of rash at follow-up, where a slight or mild rash was observed in 11/61 babies with no family history of AE compared with 2/31 babies with a family history. A similar pattern occurred in each study arm and while there was no significant effect for family history in this small study, it would have to be monitored in further research.

DISCUSSION

Data generated in the OBSeRvE study provided evidence that specific topical oils may have an adverse effect on skin barrier function, and informed the feasibility of

Table II. *Clinical skin assessment (tool adapted from Lund et al. [37]; assessed and recorded by midwife)*

	Baseline Count (%)			4 weeks Count (%)		
	Olive oil group $n = 38$	Sunflower oil group $n = 38$	No oil group $n = 39$	Olive oil group $n = 27$	Sunflower oil group $n = 30$	No oil group $n = 35$
Dryness and/or scaling						
No evidence of dryness or scaling	12 (31.6)	13 (34.2)	5 (12.8)	11 (40.7)	19 (63.3)	17 (48.6)
Slight dryness and/or scaling	20 (52.6)	20 (52.6)	31 (79.5)	16 (59.3)	11 (36.7)	17 (48.6)
Mild–moderate dryness to severe dryness and/or scaling	5 (13.2)	4 (10.5)	1 (2.6)	0 (0)	0 (0)	1 (2.9)
Moderate–severe dryness and/or scaling	1 (2.6)	1 (2.6)	2 (5.1)	0 (0)	0 (0)	0 (0)
Severe dryness and/or scaling	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Rash						
No evidence of rash	34 (89.5)	30 (78.9)	35 (89.7)	23 (85.2)	26 (86.7)	30 (85.7)
Slight rash–slight erythema and/or scaling	4 (10.5)	8 (21.1)	3 (7.7)	4 (14.8)	3 (10.0)	5 (14.3)
Mild rash–moderate to severe erythema and/or scaling, slight papules and oedema	0 (0)	0 (0)	1 (0.9)	0 (0)	1 (3.3)	0 (0)
Moderate rash–moderate to severe erythema and/or scaling, moderate ulceration, moderate to severe papules and oedema	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Severe rash–severe erythema and/or scaling, severe ulceration, papules, and oedema	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table III. *Secondary outcome assessments*

| | Baseline | | | 4 weeks | | | 95% CI for difference in mean change from baseline | | |
	Olive oil n=38 Mean (SD)	Sunflower oil n=38 Mean (SD)	No oil n=39 Mean (SD)	Olive oil n=27 Mean (SD)	Sunflower oil n=30 Mean (SD)	No oil n=35 Mean (SD)	Olive oil–sunflower oil Mean [CI] (p-value)	Olive oil–no oil Mean [CI] (p-value)	Sunflower oil–no oil Mean [CI] (p-value)
Hydration									
Arm	17.65 (4.42)	19.13 (5.00)	16.22 (3.82)	50.12 (10.06)	51.80 (9.77)	41.79 (9.65)	−1.27 [−6.63–4.09] (0.636)	5.81 [0.91–10.71] (0.021)*	7.08 [1.88–12.28] (0.008)*
Abdomen	25.61 (5.89)	26.90 (6.99)	24.26 (6.99)	58.34 (9.81)	58.97 (10.29)	49.25 (9.32)	−0.07 [−6.54–6.41] (0.984)	7.19 [1.71–12.68] (0.011)*	7.26 [0.85–13.67] (0.027)*
Thigh	19.92 (4.98)	20.38 (5.77)	17.94 (4.76)	41.23 (9.30)	41.40 (9.83)	32.36 (7.79)	−1.28 [−6.42–3.86] (0.620)	5.91 [1.26–10.56] (0.014)*	7.19 [2.44–11.94] (0.004)*
Erythema									
Arm	463.28 (85.44)	467.14 (83.30)	437.05 (85.93)	439.42 (78.45)	406.40 (73.93)	412.36 (74.05)	20.22 [−31.07–71.51] (0.433)	−6.44 [−53.08–40.20] (0.783)	−26.67 [−76.77–23.43] (0.291)
Abdomen	402.75 (75.23)	380.79 (58.69)	385.15 (74.03)	393.12 (60.29)	373.92 (66.23)	387.75 (81.71)	−32.33 [−67.34–2.68] (0.070)	−29.00 [−67.42–9.41] (0.136)	3.32 [−36.51–43.16] (0.868)
Thigh	472.76 (90.39)	460.73 (72.79)	457.30 (77.35)	414.10 (87.90)	390.40 (64.92)	389.73 (62.03)	0.64 [−48.45–49.74] (0.979)	1.55 [−43.53–46.63] (0.945)	0.90 [−47.30–49.11] (0.970)
Skin pH									
Arm	5.90 (0.49)	5.80 (0.42)	6.10 (0.57)	4.98 (0.31)	4.93 (0.31)	4.98 (0.34)	−0.04 [−0.30–0.22] (0.733)	0.18 [−0.11–0.46] (0.220)	0.22 [−0.06–0.50] (0.115)
Abdomen	6.18 (0.56)	6.03 (0.46)	6.39 (0.50)	5.02 (0.39)	4.94 (0.31)	5.02 (0.35)	0.01 [−0.30–0.31] (0.973)	0.22 [−0.07–0.51] (0.133)	0.22 [−0.07–0.50] (0.131)
Thigh	5.91 (0.50)	5.97 (0.58)	6.29 (0.56)	5.29 (0.61)	5.20 (0.43)	5.13 (0.38)	0.18 [−0.19–0.54] (0.338)	0.47 [0.13–0.81] (0.007)*	0.29 [−0.02–0.61] (0.066)

*p<0.05.

a definitive trial with regard to recruitment, retention, protocol adherence, choice of optimal primary outcome measure and trial design.

Proof of concept

The primary purpose of conducting this study was to provide proof of concept that using specific types of defined topical oils have an effect on baby skin barrier function and the magnitude of that effect, and to assess the feasibility of conducting a robust definitive RCT of specific types of defined topical oils versus no oil for newborn term babies. This is the only trial we are aware of to investigate and compare the effect of the two most commonly recommended topical oils in the UK on term baby skin barrier function. The ATR-FTIR data provided evidence that topical oils may have a negative effect on baby skin. Significant differences in lipid structure were found in both oil groups, compared to the no oil group. All groups displayed an increased ordering of the lipids, both on the surface and within the SC, over the 4 weeks following birth, but this improvement was significantly less in the groups using the topical oils. This suggests that the oils may impede development of the lamellar lipid structures of the permeability barrier from birth. Reduction in the ordering of lipids throughout the SC is statistically significantly associated with decreased skin barrier function (30); this may increase the risk of developing AE. Moreover the skin of patients with AE, who display a skin barrier defect, is characterized by reduced ordering of SC lipids determined using the same technique employed here (15, 16). No significant change in skin barrier function between the two oil groups was reported, but this pilot study was not sufficiently powered to detect such a difference. In adults, using a minimally invasive technique not suitable for the assessment of baby skin, a significant adverse effect of olive oil on TEWL was observed (2). Free fatty acids, like oleic acid that accounts for the greatest proportion of the fatty acid components of olive oil triglycerides, are well-documented penetration enhancers that increase TEWL when applied to the skin (38–40). Whilst triglycerides themselves do not penetrate the skin, as indicated by the sharp reduction in lipid esters in the skin following tape-stripping, lipases derived from the resident skin flora breakdown triglycerides to release glycerol and free fatty acids such as linoleic acid and oleic acid (41, 42). Glycerol is an important moisturising factor (humectant) found in the SC, increased levels of which increase skin hydration (43). Notably both oil groups exhibited elevated skin hydration compared with the no oil group. The process of triglyceride lipolysis helps explain why the topical oils appear to both hydrate the SC and disrupt the lipids of the lipid lamellae. The types of fatty acids derived from olive oil and sunflower

seed oil are distinct; olive oil containing predominantly oleic acid and sunflower seed oil containing more linoleic acid. It is this different content of oleic and linoleic acid that has been implicated in positive and negative effects of different oils on the skin barrier (2, 9). No significant differences in the effects of the two topical oils in this pilot study were found, but due to the limited sample size no conclusions can be drawn from this. The clinical importance of the difference found between the oil groups and no oil is unknown.

This study provides important pilot data which considers for the first time the impact of using the two most commonly recommended topical oils in the UK, olive oil and sunflower oil, for the prevention or treatment of baby dry skin or baby massage. These oils continue to be recommended by midwives, health visitors and other neonatal health professionals as there is a common, but unfounded, belief that what is 'natural' is also 'safe' (20, 21). Our pilot data demonstrates that these oils may have a negative effect on skin barrier function. Further research to establish clinical importance is absolutely necessary, particularly in view of the potential link with the increasing prevalence of AE in children aged 2 to 15 years (7). One recent randomized study of neonates using topical oil compared newborns washed with water only ($n=52$) to newborns washed daily with liquid baby cleanser and moisturized with topical almond oil ($n=42$) (44). It is unclear if the study was powered, the level of protocol adherence or how homogenous the groups were. Contrary to our findings, there was a statistically significant difference in TEWL between the groups at day 10; higher in the intervention group. The intervention group alone used the cleansing agent so the specific effect of the oil cannot be determined. Cleansing may have adversely affected skin barrier function, resulting in higher TEWL values. The authors conclude that cleansing and moisturizing with oil may delay the natural maturation of skin barrier function. One study (45; $n=118$) addressing prevention of AE has suggested, like Simpson et al. (27), that the use of a daily emollient therapy from birth reduces the incidence of AE in those with a family history of the condition. The Simpson et al. (27) and Horimukai et al. (45) studies only recruited babies at high risk of developing AE. Application of particular defined oils to skin of newborn babies predisposed to a defective skin barrier and AE may have different effects to those with no genetic predisposition to develop a defective skin barrier and AE. Topical oils are routinely recommended to healthy newborn babies who have dry skin or for baby massage. It is not known what number of these healthy babies may go on to develop AE and whether the two factors are linked. It is important to establish whether this link exists. Future studies should consider the effects of defined oils on the skin of babies with and without a genetic predisposition to AE.

Our hypothesis stated that the regular application of sunflower oil, when compared to no oil or olive oil, improved the skin barrier function of newborn term babies. This was not demonstrated by our pilot data. Sunflower oil was found to have a similar effect to olive oil on skin barrier function, both oils having a statistically significant negative effect compared to the no oil group. This negative effect of sunflower oil was unexpected in view of the existing evidence base highlighting the beneficial effects of topical sunflower oil in adults (2) and preterm infants (29, 46, 47). A recent study of topical sunflower oil with preterm infants (48), although a small sample ($n=22$), found that sunflower oil may impede skin barrier development. This supports our findings and contrasts with the work of Darmstadt, who suggested that the positive effect of sunflower oil was linked to a barrier-enhancing effect. The positive effect found by Darmstadt may have more to do with the antimicrobial effect of sunflower oil. Unlike the Darmstadt population, our term baby population were not faced with a significant fatal infection risk. We suggest that whilst sunflower oil may not be a great barrier enhancing topical agent (perhaps the opposite), this does not detract from the very positive effect it has in situations where infection is a great risk. As these studies were not designed to determine the antimicrobial action of sunflower oil, it would be prudent to explore this in future studies.

Optimal primary outcome measure

This trial presents one of the largest neonatal datasets of novel information provided by the use of infrared spectroscopy. ATR-FTIR is important from an ethical perspective for a neonatal population as it provides a method to detect changes in the molecular composition of the SC before those changes are visible to the naked eye. There were some challenges with regard to the ATR-FTIR equipment: size, the need for liquid and dry nitrogen to operate the equipment, and the need for mothers to leave the postnatal ward to visit the assessment room for baseline assessment and return to the hospital with their 4-week-old baby for follow-up assessment as the equipment was not portable. However, having determined that the outcome measure provides useful and informative biological data within a short treatment period, the technology is available to provide the FTIR equipment in a smaller, portable, bespoke device which would not require the use of liquid or dry nitrogen. Our study found that ATR-FTIR spectroscopy is suitable as an outcome measure. TEWL is a validated measure of skin barrier function (35). Although our data did not show any significant differences in TEWL between groups, it was not powered to detect this. TEWL as an outcome measure would still be recommended for a study with

a larger sample size as it has been shown previously to detect changes in skin barrier function with the use of topical oils (2, 38–40).

Optimal trial design

The original target sample of 100 was increased to 115 due to the higher than anticipated loss to follow-up in order to recruit 30 per group with baseline and follow-up data. Only two home follow-up visits took place. The decision not to offer more home visits to increase retention was made due to the requirement to collect ATR-FTIR spectroscopy data at follow-up. Using a bespoke portable ATR-FTIR device would undoubtedly enhance recruitment and retention; baseline assessment could be conducted at the bedside on the postnatal ward and home visits could be offered as a choice at follow-up. This helped to reduce attrition rates substantially in a previous similar trial (49). Loss to follow-up in the OBSeRvE pilot study compared favourably to a previous pilot study (20% vs. 58% (49)). Loss to follow-up of less than 10% would be optimal; this was achieved in a definitive trial when home visits were offered (50). Loss to follow-up was lowest in the no oil group. This may have been because there was no treatment regime to follow. Qualitative data to assess maternal satisfaction, from this study, suggests that women in the no oil group found their allocation 'easy', but women in the oil groups conversely liked the 'routine' of applying oil. Qualitative data analysis is ongoing and will be published later.

Babies were originally recruited within 48 h after birth to reduce the risk of infants having been bathed prior to baseline assessments. Even with a 48 h restriction in place some infants had already been bathed. The extension of the recruitment period to 72 h was deemed to have little effect on outcome data, but it increased the number of infants eligible to take part. The screening process was also amended to allow the lead investigator to identify eligible postnatal women from the hospital in-patient software (BedMan) by comparing each one against the eligibility criteria rather than the clinical team having to do this task. The lead investigator then approached the clinical midwife with the list of identified women to confirm if there was any reason not to approach them. This reduced the burden of time on the clinical team, and made the process of eligibility screening more efficient. Nevertheless, the overall recruitment rate was poor (11.1%). During a review of recruitment at the end of the study, the Trial Steering Committee agreed that it would not be necessary to exclude babies undergoing phototherapy treatment from a future study as the duration of phototherapy treatment is short and trial treatment could commence after this had ended. In addition, the clinical assessment room was only available on alternate days. This affected recruitment as babies could not be assessed on the day following recruitment, which was often the parent's preference. Addressing both of these issues would improve the recruitment rate.

Protocol adherence was fairly evenly distributed across the treatment groups but appeared to reduce with regard to alternative product use in the 4th week of the trial. This also occurred in a previous skincare trial (49) which suggested that a primary endpoint prior to 4 weeks may be beneficial. The first follow-up assessment could be conducted at 3 weeks in a future study; however, adherence may still remain an issue. One solution would be to include a control soap for parents to use to bathe and cleanse their baby, however this would be problematic. If a good cleanser was used, the effects of the oils may be masked. If a poor cleanser was used, the negative effects could overwhelm the effect of the oils.

The OBSeRvE pilot study was conducted to test the feasibility of a superiority hypothesis, that the regular application of defined sunflower oil, compared to no oil or defined olive oil, improved the skin barrier function of newborn term babies. However, our data suggest that this was not the case. The sunflower oil was found to have a similar effect on skin barrier function to olive oil. Results were not powered to identify the optimal treatment for baby dry skin or massage; findings should therefore be interpreted with caution. A future study must address clinical importance. Our findings suggest that using olive oil or sunflower oil may have the potential to damage the skin barrier function of neonatal skin. This could consequently increase the development of AE. However, we cannot draw firm conclusions about the long-term effects of these topical oils as the relationship between the outcomes we assessed and clinically important outcomes is unknown. It is necessary to investigate the link between use of defined topical oils from birth and development of AE. AE can develop at any age, with earliest diagnosis not usually before 4–6 months of age. This suggests that a longitudinal observational study is necessary to explore the natural course of AE over a number of years following the use of topical oils together with more mechanistic studies in term babies to determine the biological relevance of the changes in lipid lamellae when topical oils are used from birth. These studies would inform a possible future definitive RCT. The optimal trial design should not only assess skin barrier function, but also the diagnosis of AE. The definitive trial should be designed with clinical outcomes to generate data that can inform clinical practice.

Conclusions

Our study provides valuable baseline data on the newborn skin barrier using a novel technique. It also provides informative data on optimal trial processes. Our findings suggest that a definitive RCT may not be the optimal design for the next study about this topic. Be-

fore moving to further RCTs it is important to establish the biological importance of using defined topical oils from birth in babies with and without a genetic predisposition to AE, and whether there is a link between this practice and the development of AE. We suggest that the immediate way forward is to conduct a long-term observational study to observe whether and when AE develops naturally depending on the use of topical oils from birth, together with further mechanistic studies to consider the optimal formulation.

Our study was not designed to provide definitive answers on whether or not specific defined olive or sunflower oils should be used on babies' skin. The data suggested that the skin of babies who used the oils in this trial may be better hydrated; however the lipid structure of the skin barrier appeared altered, the clinical importance of which is unknown at present. Given that interventions should only be recommended if shown to do more good than harm, it would be difficult to support the use of sunflower or olive oils, based on our data. Further research is required to inform future practice.

ACKNOWLEDGEMENTS

REFERENCES

1. Lewis-Jones S. Dry Skin in Childhood and the Misery of Eczema and Its Treatments. In: Treatment of Dry Skin Syndrome. Edited by Loden M, Maibach H. Berlin: Springer-Verlag; 2012.
2. Danby S, Al Enezi T, Sultan A, Lavender T, Chittock J, Brown K, et al. Effect of olive and sunflower seed oil on the adult skin barrier: implications for neonatal skin care. Pediatr Dermatol 2013; 30: 42–50.
3. Silverberg J, Lee-Wong M, Silverberg N. Complementary and alternative medicines and childhood eczema: a US population-based study. Dermatitis 2014; 25: 246–254.
4. Bieber T. Atopic Dermatitis. N Engl J Med 2008; 358: 1483–1494.
5. Danby S, Cork M. The Skin Barrier in Atopic Dermatitis. In: Textbook of Pediatric Dermatology. Edited by Irvine A, Hoeger P, Yan A. Oxford: Blackwell Publishing; 2011.
6. Taylor B, Wadsworth J, Wadsworth M, Peckham C. Changes in the reported prevalence of childhood eczema since the 1939–45 war. Lancet 1984; 2: 1255–1257.
7. Gupta R, Sheikh A, Strachan D, Anderson H. Burden of allergic disease in the UK: secondary analyses of national databases. Clin Exp Allergy 2004; 34: 520–526.
8. Naik A, Pechtold L, Potts R, Guy R. Mechanism of oleic acid-induced skin penetration enhancement in vivo in humans. J Control Release 1995; 37: 299–306.
9. Darmstadt G, Mao-Qiang M, Saha S, Ziboh V, Black R, Santosham M, et al. Impact of topical oils on the skin barrier: possible implications for neonatal health in developing countries. Acta Paediatr 2002; 91: 546–554.
10. Stamatas G, Nikolovski J, Luedtke M, Kollias N, Wiegand B. Infant skin microstructure assessed in vivo differs from adult skin in organization and at the cellular level. Pediatr Dermatol 2010; 27: 125–131.
11. Nikolovski J, Stamatas G, Kollias N, Wiegand B. Barrier function and water-holding and transport properties of infant stratum corneum are different from adult and continue to develop through the first year of life. J Invest Dermatol 2008; 128: 1728–1736.
12. Stamatas G, Nikolovski J, MC. M, Kollias N. Infant skin physiology and development during the first years of life: a review of recent findings based on in vivo studies. Int J Cosmet Sci 2011; 33: 17–24.
13. Fluhr J, Darlenski R, Lachmann N, Baudouin C, Msika P, DeBelilovsky C, et al. Infant epidermal skin physiology: adaptation after birth. Br J Dermatol 2011; 166: 483–490.
14. Janssens M, Van Smeden J, Gooris G, Bras W, Portale G, Caspers P, et al. Lamellar lipid organization and ceramide composition in the stratum corneum of patients with atopic eczema. J Invest Dermatol 2011; 131: 2136–2138.
15. Janssens M, van Smeden J, Gooris G, Bras W, Portale G, Caspers P, et al. Increase in short-chain ceramides correlates with an altered lipid organization and decreased barrier function in atopic eczema patients. J Lipid Res 2012; 53: 2755–2766.
16. Higgs-Bayliss T, Brown K, Chittock J, Cork M, Danby S. Noninvasive assessment of the lipid structure and water holding properties of the stratum corneum in vivo by ATR-FTIR using a fibre optic probe in patients with atopic dermatitis and healthy controls. Br J Dermatol 2014; 170: e29.
17. National Institute for Health and Care Excellence. NICE clinical guideline 37: Postnatal care. London: NICE; 2014.
18. Walker L, Downe S, Gomez L. A survey of soap and skin care product provision for well term neonates. Br J Midwifery 2005; 13: 768–773.
19. Cooke A, Cork M, Danby S, Lavender T. Use of oil for baby skincare: A survey of UK maternity and neonatal units. Br J Midwifery 2011; 19: 354–362.
20. Lavender T, Bedwell C, Tsekiri-O'Brien E, Hart A, Turner M, Cork M. A qualitative study exploring womens' and health professionals' views of newborn bathing practices. Evid based Midwifery 2009; 7: 112–121.
21. Bedwell C, Lavender T. Newborn skin care – a review of evidence and practice. Eur J Obstet Gynaecol Sup 2012: 18–21.
22. Allemann I, Baumann L. Botanicals in skin care products. Int J Dermatol 2009; 48: 923–934.
23. Cottingham M, Winkler E. The organic consumer. In: The handbook of organic and fair trade food marketing. Edited by Wright S, McCrea D. Oxford: Blackwell Publishing Ltd.; 2007.
24. Erenel A, Vural G, Efe S, Özkan S, Özgen S, Erenoğlu R. Comparison of olive oil and dry-clean keeping methods in umbilical cord care as microbiological. Matern Child Health J 2010; 14: 999–1004.

25. Solanki K, Matnani M, Kale M, Joshi K, Bavdekar A, Bhave S, et al. Transcutaneous absorption of topically massaged oil in neonates. Indian Pediatr 2005; 42: 998–1005.

26. Simpson E, Chalmers J, Hanifin J, French M, Lubianski T, Samrao A, et al. Barrier enhancement for eczema prevention – the BEEP feasibility study. J Invest Dermatol 2012; 132: S90.

27. Simpson E, Chalmers J, Hanifin J, Thomas K, Cork M, McLean W, et al. Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention. J Allergy Clin Immunol 2014; 134: 818–823.

28. Lancaster G, Dodd S, Williamson P. Design and analysis of pilot studies: recommendations for good practice. J Eval Clin Pract 2004; 10: 307–312.

29. Darmstadt G, Saha S, Ahmed A, Chowdhury M, Law P, Ahmed S, et al. Effect of topical treatment with skin barrier-enhancing emollients on nosocomial infections in preterm infants in Bangladesh: a randomised controlled trial. Lancet 2005; 365: 1039–1045.

30. Damien F, Boncheva M. The extent of orthorhombic lipid phases in the stratum corneum determines the barrier efficiency of human skin in vivo. J Invest Dermatol 2010; 130: 611–614.

31. Brancaleon L, Bamberg M, Kollias N. Spectral differences between stratum corneum and sebaceous molecular components in the mid-ir. Appl Spectrosc 2000; 54: 1175–1182.

32. Mendelsohn R, Flach C, Moore D. Determination of molecular conformation and permeation in skin via IR spectroscopy, microscopy, and imaging. Biochim Biophys Acta 2006; 1758: 923–933.

33. Boncheva M, Damien F, Normand V. Molecular organization of the lipid matrix in intact Stratum corneum using ATR-FTIR spectroscopy. Biochim Biophys Acta 2008; 1778: 1344–1355.

34. Hoppel M, Baurecht D, Holper E, Mahrhauser D, Valenta C. Validation of the combined ATR-FTIR/tape stripping technique for monitoring the distribution of surfactants in the strateum corneum. Int J Pharm 2014; 472: 88–93.

35. Fluhr J, Feingold K, Elias P. Transepidermal water loss reflects permeability barrier status: validation in human and rodent in vivo and ex vivo models. Exp Dermatol 2006; 15: 483–492.

36. Rogiers V. EEMCO guidance for the assessment of transepidermal water loss in cosmetic sciences. Skin Pharmacol Appl 2001; 14: 117–128.

37. Lund C, Kuller J, Lane A, Wright-Lott J, Raines D, Thomas K. Neonatal skin care: evaluation of the awhonn/nann research-based practice project on knowledge and skin care practices. J Obstet Gynecol Neonatal Nurs 2001; 30: 30–40.

38. Jiang S, Hwang S, Choi E, Elias P, Ahn S, Lee S. Structural and functional effects of oleic acid and iontophoresis on hairless mouse stratum corneum. J Invest Dermatol 2000; 114: 64–70.

39. Sinha V, Kaur M. Permeation enhancers for transdermal drug delivery. Drug Dev Ind Pharm 2000; 26: 1131–1140.

40. Correa M, Mao G, Saad P, Flach C, Mendelsohn R, Walters R. Molecular interactions of plant oil components with stratum corneum lipids correlate with clinical measures of skin barrier function. Exp Dermatol 2014; 23: 39–44.

41. dos Santos Rodrigues J, Pinto T, de Oliveira C, de Sousa Freitas I, do Socorro Vieira Pereira M, de Souza E, et al. Lipolytic activity of Staphylococcus aureus from human wounds, animals, foods, and food-contact surfaces in Brazil. J Infect Dev Ctries 2014; 8: 1055–1058.

42. Sharma M, Singh S, Maan P, Sharma R. Biocatalytic potential of lipase from Staphylococcus sp. MS1 for transesterification of jatropha oil into fatty acid methyl esters. World J Microb Biot 2014; 30: 2885–2897.

43. Choi E, Brown B, Crumrine D, Chang S, Man M, Elias P, et al. Mechanisms by which psychologic stress alters cutaneous permeability barrier homeostasis and stratum corneum integrity. J Invest Dermatol 2005; 124: 587–595.

44. Roberta R, Patrizi A, Cocchi G, Faldella G, Raone B. Comparison of two different neonatal skin care practices and their influence on transepidermal water loss in healthy newborns within first 10 days of life. Minerva Pediatr 2014; 66: 369–374.

45. Horimukai K, Morita K, Narita M, Kondo M, Kitazawa H, Nozaki M, et al. Application of moisturizer to neonates prevents development of atopic dermatitis. J Allergy Clin Immunol 2014; 134: 824–830.

46. Darmstadt G, Badrawi N, Law P, Ahmed S, Bashir M, Iskander I, et al. Topically applied sunflower seed oil prevents invasive bacterial infections in preterm infants in Egypt. Pediatr Infect Dis J 2004; 23: 719–725.

47. Darmstadt G, Saha S, Ahmed A, Ahmed S, Chowdhury M, Law P, et al. Effect of skin barrier therapy on neonatal mortality rates in preterm infants in Bangladesh: a randomized, controlled, clinical trial. Pediatrics 2008; 121: 522–529.

48. Kanti V, Grande C, Stroux A, Bührer C, Blume-Peytavi U, Garcia Bartels N. Influence of sunflower seed oil on the skin barrier function of preterm infants: a randomized controlled trial. Dermatology 2014; 229: 230–239.

49. Lavender T, Bedwell C, O'Brien E, Cork M, Turner M, Hart A. Infant skin-cleansing product versus water: A pilot randomized, assessor-blinded controlled trial. BMC Pediatr 2011; 11: 35.

50. Lavender T, Furber C, Campbell M, Victor S, Roberts I, Bedwell C, et al. Effect on skin hydration of using baby wipes to clean the napkin area of newborn babies: assessor-blinded randomised controlled equivalence trial. BMC Pediatr 2012; 12: 59.