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Original Paper

Topical Oil Application and Trans-Epidermal Water Loss in Preterm Very Low Birth Weight Infants—A Randomized Trial

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ABSTRACT

Objective: Topical emollient application reduces trans-epidermal water loss (TEWL) in preterm neonates. Coconut oil used traditionally for infant massage in India has not been evaluated for the same.

Patients and Methods: Very low birth weight (VLBW) neonates were randomized at 12 h of age to Oil ($n = 37$) or Control ($n = 37$) groups. Oil group neonates received twice-daily coconut oil application without massage, and Control group received standard care. TEWL was measured every 12 h using an evaporimeter till Day 7 when skin swabs were obtained for bacterial growth and skin condition was assessed using a validated score.

Results: Birth weight (g; mean ± SD: 1213 + 214 vs. 1164 + 208, $p = 0.31$), gestation [week; median (interquartile range): 32 (31–33) vs. 32 (29–33), $p = 0.10$] and other baseline variables were comparable. TEWL was significantly reduced ($g/m^2/h$, mean difference: −6.80, 95% confidence interval: −3.48, −10.15; $p < 0.01$) with better skin condition and lower bacterial growth in the Oil group (20% vs. 60%, $p < 0.01$).

Conclusion: Coconut oil application reduced TEWL without increasing skin colonization in VLBW neonates.

Clinical Trials Registration: NCT01758068

KEYWORDS: neonate, coconut oil, prematurity, very low birth weight, trans-epidermal water loss, skin conditioning score.

WHAT IS KNOWN ON THIS SUBJECT?

Preterm neonates experience high trans-epidermal water loss (TEWL). Therapeutic free fluid replacement increases morbidity in this vulnerable population. Minimizing TEWL is the key to optimal management and improved outcome. Topical emollient application is known to reduce TEWL in preterm neonates.

WHAT THIS STUDY ADDS?

In preterm very low birth weight neonates, twice-daily topical coconut oil application during the first week of postnatal life reduces TEWL. In addition, coconut oil application improves skin condition and its integrity without any increase in bacterial colonization.

INTRODUCTION

Skin of preterm infants is immature and ineffective as an epidermal barrier. Stratum corneum, responsible for epidermal barrier function, does not become mature until 32–34 weeks gestation [1]. An exponential inverse relationship exists between trans-epidermal water loss (TEWL) and gestational age [2]. TEWL is 15 times higher in infants born at 25 weeks of gestation than in full-term infants [3]. Most preterm infants may lose as much as 13% of their body weight as TEWL even at an ambient humidity of 50% [4]. Therapeutic strategies for facilitating epidermal barrier development include topical application of non-physiologic lipids (e.g. Petrolatum), or topical dressings [5]. Emollients that decrease TEWL and form mechanical barrier to bacteria may also affect active lipid metabolism in the epidermis [6]. Emollients benefit premature skin by improving epidermal barrier, leading to decreased heat loss [5, 7], improving skin condition and water balance [8, 9–11] and decreasing incidence of infections [3, 12].

Vegetable oils like safflower and sunflower oils have been observed to decrease morbidity and mortality of low birth weight neonates in developing countries. Coconut oil is used traditionally in India for infant massage. Because of cultural acceptability and low cost, coconut oil and other vegetable oils may emerge as an effective strategy in care of low birth neonates in developing countries. We planned this study to evaluate the efficacy of coconut oil in reducing TEWL in preterm very low birth weight (VLBW) neonates.

HYPOTHESIS AND OBJECTIVES

We hypothesized that twice a day topical application of coconut oil in VLBW neonates for the first week of life beginning at 12 h of life would reduce the TEWL by 20%. The primary objective was to compare the effect of twice a day topical coconut oil application in babies with birth weight 751–1499 g started at 12 ± 6 h of life on reduction of TEWL. The secondary objectives were to assess skin score and incidence of skin colonization at 7 days of life.

PATIENTS AND METHODS

Enrolment of patients, randomization and consent

This randomized controlled clinical trial was conducted from 8 January 2006 to 7 November 2006 in neonatal intensive care unit (NICU) of a tertiary care center. Study was approved by the institute ethics committee.

All preterm neonates born at the study center with birth weight between 751 and 1499 g were eligible for enrolment. Exclusion criteria included major congenital malformation(s), severe asphyxia (defined as Apgar score ≤3 at 5 min and cord pH <7.10), hydrops and hypotension needing inotropic support at the time of enrolment. Also excluded were neonates with congenital diseases of skin associated with skin breach or denudation of skin precluding oil application and those with preexisting skin infection. Block randomization sequence was generated by the statistician (V.S.), and random treatment assignments were placed in identical, serially numbered, opaque and sealed envelopes. Written informed consent was obtained from parents of the enrolled neonates.

Intervention

Beginning 12 ± 6 h of age, twice a day for first week of life, neonates in the Oil group received coconut oil application on skin of the trunk below neck. Neonates in Control group received no oil application. During each topical application, staff nurse applied a total of 4 ml coconut oil in four strokes without giving massage. Oil used in the study was procured in small packs to avoid staleness and prevent denaturation. Random samples of oil were collected and checked for any evidence of denaturation. Control group received standard care. Owing to nature of intervention, blinding of clinical care team was not attempted.

Outcome measurement

In Oil group, TEWL was measured immediately before each session of oil application using a portable closed chamber evaporimeter (VapoMeter®, Delfin Technologies limited, Kuopio, Finland). In Control group, TEWL was measured every 12 h for the first week of postnatal life at the same time as the hour of birth. Relative humidity and temperature of NICU (RH_N and T_N) and microenvironment of baby (RH_B and T_B) were also recorded at the time of each TEWL measurement. Skin quality was graded at the end of 1 week of life using the 'Lane and Drost' [11] skin condition score, 1 depicting the best skin state and 9 the worst. Skin swab cultures were obtained at the end of the first week to assess skin colonization. The skin score assessor, microbiologist and the data analyst were blinded to group allocation.

Sample size and statistical analysis

We hypothesized that for being clinically useful, coconut oil should reduce Insensible Water Loss (IWL) by at least 20%. A sample size of 36 in each group was needed to detect 20% reduction in the TEWL from baseline value of $58.4 \pm 15\ g/m^2/h$ with 90% power and 0.05 two-sided significance [3, 13].

Patient information was collected in a pretested proforma. Data entry and analysis were done using Epi-info 2004 (CDC Atlanta, USA) and Stata 9.1 (StataCorp LP, Texas, USA). Continuous data with normal distribution were analyzed by student *t*-test, and categorical data were analyzed by chi-square test. Univariate analysis of variance was done for each TEWL value taking the TEWL at that time point as the dependent variable and building the model using RH_N, T_N, RH_B and T_B at the same time point. *p* value of <0.05 was taken as significant. 'Generalized estimating equation' (GEE) was used as advanced form of multiple regression analysis.

RESULTS

Among 106 neonates screened for enrolment, 32 were excluded owing to various reasons (Fig. 1). A total of 74 neonates were randomized to Oil ($n = 37$) or Control ($n = 37$) groups. Birth weight, gestation, fetal growth group, fluid intake and environmental variables were comparable in the two groups (Table 1). Baseline TEWL was measured before first coconut oil application in Oil group and at 12 h of age in Control group. It was significantly lower in the Oil group (15.76 ± 8.67 vs. 25.64 ± 26.43).

TEWL was significantly lower in Oil group at all measurement points from 12 to 168 h of life. Lower TEWL in the Oil group indicates protective effect of oil on the skin. In view of significant difference in baseline TEWL in the two groups, we conducted additional post hoc analysis. ΔTEWL was calculated as percent decline in TEWL with baseline TEWL value for that group as reference value. ΔTEWL increased steadily from 24 to 84 h of postnatal age (5.59 to 15.09), remained at a plateau from 96 to 120 h (12.54 to 13.29) and thereafter declined precipitously to 5.57 at 132 h and beyond (Table 2). This depicts that epidermal barrier was exquisitely permeable in the initial 4–5 days and that oil application had the maximal effect in reduction of TEWL at this vulnerable time; thereafter, as the skin matured beyond 96–120 h of age, the TEWL decreased irrespective of the oil application.

GEE, an advanced form of regression analysis, was applied to evaluate temporal change in TEWL and to adjust for the baseline difference in the TEWL at 12 h of age (i.e. before oil application). The results of GEE population-averaged model application adjusting for the baseline variables (birth weight, sex, gestation, fetal growth group, booking status of the mother, presence of Preterm Premature Rupture Of Fetal Membranes (PPROM)) and evaluating the role of other co-variates like antenatal steroids, temperature of the nursery, temperature of the baby, relative humidity of the nursery and relative humidity of the baby revealed that TEWL was statistically significantly lower in the Oil group as compared with Control group at all time points with a mean difference of $6.8\ g/m^2/h$ (95% confidence interval: 3.48, 10.15).

Skin condition was good in both the groups, with worst score being 3. However, skin score was significantly better in the Oil group (Table 3). In Oil group, 81% of the skin swab cultures were sterile as against 43% in Control group (Table 4).

DISCUSSION

In this randomized controlled trial, we have demonstrated that coconut oil application accelerates the

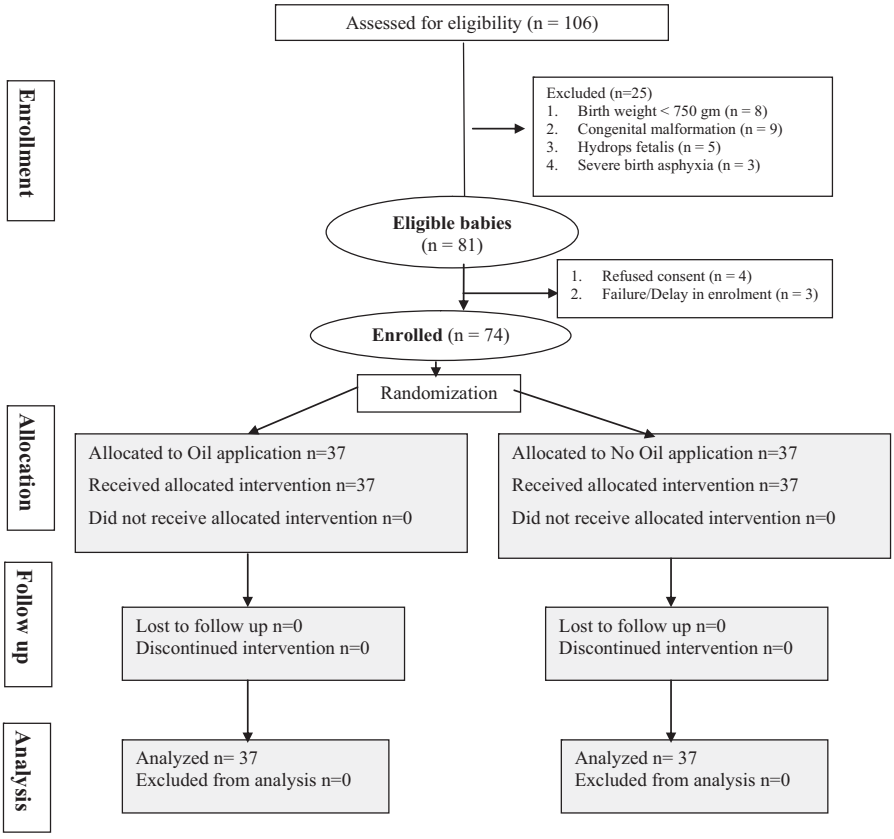

Fig 1. Trial flow of the study.

physiological decline in TEWL during first week of life, reduces skin colonization and results in a better skin condition.

Although effect of emollients in reducing TEWL has been investigated previously, there are no such studies using vegetable oils. Rutter and Hull [14] applied a paraffin mixture and reported decreased water loss by 40–60% after topical application. Wananukul *et al.* [15] studied the evaporation rate from the skin of jaundiced preterm infants under phototherapy and observed that application of an ointment resulted in decreased TEWL without effect on serum bilirubin. Similarly, Nopper *et al.* [9] found a decrease of 34–67% in TEWL with twice-daily topical ointment application. Despite beneficial effect of reduction in TEWL, paraffin-based ointments have not found much use because of increased rate of bacterial colonization. Safflower and sunflower oils have been observed to decrease morbidity by absorption of lipids, resulting in improved skin integrity. We chose coconut oil to study its effect on TEWL because of its easy availability and cultural acceptability in India.

We applied coconut oil and recorded the TEWL every 12 h with the measurements done immediately before next oil application. This is in contrast to other studies, which have recorded TEWL within minutes to few hours after application of oil. We believe that immediate measurements may reflect the effect of 'a film of oil' or 'waterproofing' on the measurements rather that the true TEWL measurement. We observed that with advancing postnatal age, TEWL decreased in both the groups but the reduction was significantly higher in the Oil group, being 42% in the Oil group as against 32% in the Control group.

'Lane and Drost' [11] skin condition score has been used by many workers evaluating preterm skin, allowing easy comparisons between interventions aimed at preserving the skin integrity. The skin score was statistically significantly better in the Oil group

Table 1. Characteristics of enrolled neonates and environment of NICU

Variable	Oil ($n = 37$)	Control ($n = 37$)	p value
Birth weight (g)[a]	1213.54 (214.38)	1163.65 (208.87)	0.31
Gestation (weeks)			
a	31.89 (2.21)	31.00 (2.45)	0.10
b	32 (31–33)	32 (29–33)	0.10
Apgar score 1 min[b]	7.00 (7.0–8.0)	7.00 (7.0–8.0)	0.20
Apgar score 5 min[b]	8.00 (8.0–9.0)	8.00 (7.0–8.0)	0.21
Apgar score 10 min[b]	9.00 (8.0–9.0)	8.00 (8.0–9.0)	0.21
Fetal growth group[c]			
Appropriate for date	23 (62)	25 (68)	0.63
Small for date	14 (38)	12 (32)	
Sex[c]			
Male	17 (45.9)	18 (48.6)	0.82
Female	20 (54.1)	19 (51.4)	
Fetation[c]			
Single	27 (73)	26 (70)	0.90
Twin	8 (22)	8 (22)	
Triplet	2 (5)	3 (8)	
Resuscitation[c]			
None	33 (89.2)	29 (82.9)	0.48
Bag and mask	1 (2.7)	1 (2.9)	
Intubation	2 (5.4)	5 (14.2)	
Chest compression	1 (2.7)	0 (0.0)	
Nursery temperature[a]	27.08 (0.59)	27.27 (0.73)	0.23
Baby temperature[a]	28.29 (0.51)	28.43 (0.80)	0.39
Nursery relative humidity[a]	63.51 (7.85)	63.05 (8.55)	0.81
Baby bassinet relative humidity[a]	43.83 (8.34)	45.78 (9.83)	0.36

[a]Mean (SD).
[b]Median (interquartile range).
[c]*N* (%).

as compared with the No oil group. Nopper *et al.* [9] applied topical ointment twice daily in preterm VLBW neonates for the first 2 weeks and assessed the skin condition by the same score at D7 and D14 and found significantly superior skin scores in ointment-treated babies. Pabst *et al.* [5] studied the effects of twice-daily application of Aquaphor®, an occlusive ointment, on the skin of infants of 26–30 weeks gestation for 2 weeks, and Edwards *et al.* [10] studied the effect of Aquaphor® ointment vs. routine skin care in extremely low birth weight (ELBW) neonates. Both reported better skin condition in Aquaphor®-treated group. Lane and Drost [11] originally proposed this skin condition score and reported less dermatitis and better skin condition in preterm infants randomized to receive water in oil emollient application.

We compared the incidence of skin colonization and found statistically significant differences between the Oil and Control groups. (Table 4) Lane and Drost [11] evaluated the effect of water in oil emollient cream on 29–36 weeks preterm infants and found no difference in bacterial or fungal cultures. Nopper *et al.* [9] reported decreased skin colonization in preterm VLBW neonates with Aquaphor® similar to our results. Pabst *et al.* [5] evaluated the effect of Aquaphor® on 26–30 weeks preterm neonates and found no difference in skin cultures.

Table 2. Percent decline in TEWL from baseline value (ΔTEWL)

Age (h)	Oil group ($n = 37$)	Control group ($n = 37$)	Mean difference (95% confidence interval)	p value
24	5.91 (1.50, 10.32)	0.33 (−4.78, 5.44)	5.59 (−1.05, 12.23)	0.09
36	13.92 (7.63, 20.21)	5.05 (−0.39, 10.49)	8.88 (0.69, 17.05)	0.03
48	16.75 (10.09, 23.41)	8.39 (2.05, 14.73)	8.36 (−0.68, 17.39)	0.06
60	18.38 (11.52, 5.25)	8.22 (1.41, 15.02)	10.17 (0.67, 19.67)	0.03
72	22.05 (15.99, 28.09)	7.99 (−0.09, 16.06)	14.06 (4.14, 23.97)	0.01
84	26.87 (20.46, 33.27)	11.77 (3.69, 19.85)	15.09 (4.96, 25.23)	0.00
96	28.72 (21.08, 36.37)	16.18 (10.01, 22.35)	12.54 (2.89, 22.20)	0.01
108	29.97 (22.34, 37.59)	18.67 (13.02, 24.31)	11.30 (1.98, 20.63)	0.01
120	34.67 (28.05, 41.29)	21.38 (14.65, 28.11)	13.29 (4.016, 22.57)	0.01
132	33.34 (26.16, 40.52)	27.77 (22.05, 33.49)	5.57 (−3.45, 14.60)	0.22
144	35.02 (28.21, 41.83)	29.50 (23.82, 35.17)	5.53 (−3.21, 14.26)	0.21
156	36.33 (27.60, 45.06)	30.06 (23.81, 36.30)	6.28 (−4.32, 16.88)	0.24
168	41.99 (34.81, 49.17)	32.81 (26.37, 3 9.26)	9.19 (−0.32, 18.68)	0.06

Table 3. Skin condition score on D7

Skin score D7	Group		
	Oil Number (%)	No oil Number (%)	Total Number (%)
1	20 (54.05)	4 (10.81)	24 (32.43)
2	16 (43.24)	26 (70.27)	42 (56.76)
3	1 (2.7)	7 (18.92)	8 (10.81)
Total	37 (100)	37 (100)	74 (100)

Fisher's exact = 0.000.

Table 4. Skin colonization on D7 in 'Oil group' vs. 'No oil group'

Skin colonization D7	Group		
	Oil Number (%)	No oil Number (%)	Total Number (%)
No growth	30 (81.08)	16 (43.24)	46 (62.16)
Gram Positive Cocci (GPC)	7 (18.92)	16 (43.24)	23 (31.08)
Gram Negative Bacilli (GNB)	0 (0.00)	4 (10.81)	4 (5.41)
Mixed growth	0 (0.00)	1 (2.7)	1 (1.35)
Total	37 (100)	37 (100)	74 (100)

Fisher's exact = 0.002.

Edward *et al.* [10] evaluated the effect of Aquaphor® in preterm ELBW infants and found increased incidence of nosocomial sepsis by coagulase negative staphylococcus. Darmstadt *et al.* [12] evaluated the effect of sunflower seed oil (SSO) application in infants <34 weeks gestation and reported better skin scores and decreased incidence of nosocomial infection. Darmstadt *et al.* in another randomized trial compared the effect of SSO application with Aquaphor® and routine care and found lower incidence of nosocomial infection in the SSO group [12]. Even though most of the authors have found either no difference or a slightly increased incidence of nosocomial infection with the use of Aquaphor® ointment, none of the studies done with vegetable oil have reported such an outcome.

Based on significantly lower TEWL, favorable skin scores and low colonization rate in the Oil group in this study population of preterm VLBW neonates, it can be concluded that coconut oil application reduces TEWL and improves skin maturity and integrity without compromising the sterile milieu of the baby and thus can be recommended to be used in small preterm neonates in the NICU. We recommend routine use of coconut oil in babies weighing 750–1500 g.

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