Use of topical petroleum jelly for prevention of sepsis in very low-birthweight infants: a prospective, randomised controlled trial

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Background: Emollient therapy is used frequently to prevent nosocomial infection in the management of preterm infants, despite a lack of adequate evidence of its efficacy.
Objective: To assess the efficacy of prophylactic whole-body application of pure preservative-free topical petroleum jelly on the incidence of nosocomial sepsis in very low-birthweight (VLBW) infants.
Study design: A prospective, randomised controlled trial of the application of topical petroleum jelly was conducted. Infants weighing <1250 g at birth and with a gestational age of ≤32 weeks were included. The intervention group received twice-daily topical therapy of 2 g/kg pure, preservative-free topical petroleum jelly until the completion of 34 weeks of gestation. The control group received no topical petroleum jelly treatment. The primary outcome was the incidence of late-onset sepsis during hospitalisation. Other data collected included the pattern of temperature control, weight changes, fluid requirements, serum bilirubin level, electrolyte imbalance and skin condition.
Results: Thirty-five infants in the intervention group and 39 in the control group were recruited. Birthweight, gestational age, gender and perinatal variables were comparable in the two groups. There was a trend towards an increased incidence of culture-proven nosocomial sepsis in the intervention group – 19 episodes (54%) in the intervention group *vs* 16 (41%) in the control group, and an increased rate of NEC – 20% in the intervention group *vs* 8% in the control group. The intervention group had better skin condition throughout their stay and the incubator ambient temperature was lower in the intervention group in the 1st week of life. The fluid balance of the infants in the intervention group was better, as reflected by their mean (SD) shorter time to regain birthweight [12 (5) *vs* 14 (6) days], and there were fewer episodes of hypernatraemia in the 1st week of life, although none of these reached statistical significance. However, there was a significantly lower mean (SD) level of maximum hyperbilirubinaemia [157 (40) *vs* 182 (46) mmol/L, $P=0.02$) in the intervention group.
Conclusion: Although prophylactic topical application of pure, preservative-free petroleum jelly brought substantial improvement of skin condition and temperature control, it was associated with a trend towards an increased rate of nosocomial sepsis.

Keywords: Topical petroleum jelly, Skin care, Nosocomial sepsis, VLBW

Introduction

Skin care is one of the most important management aspects of neonatal intensive care, as effective skin function is essential for the survival of premature infants. Newborn infants of <32 weeks gestational age have an immature epidermis, especially the stratum corneum.[1] The stratum corneum is the barrier that protects the body from pathological environmental hazards, including physical, chemical and infectious factors.[2] It is of primary importance in conserving body contents, especially water, and helps to maintain temperature control. Tremendous acceleration of stratum corneum maturation occurs in the 1st and 2nd weeks of life, even in very premature infants, which may be related to the change from an aqueous to a gaseous environment.[3–5] Protection of the maturing stratum corneum and enhancement of its barrier function by topical application of ointment has been successful in improving skin integrity, decreasing dermatitis and decreasing trans-epidermal water loss (TEWL).[6] Such protection might also decrease bacterial colonisation and therefore the risk of sepsis in the preterm infant. The effect of topical therapy on the incidence of nosocomial sepsis is not clearly established. A systematic review of four randomised trials published by the Cochrane Library showed a significant increase in

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coagulase-negative staphylococcal infection (CONS) with the use of emollient therapy; because of limited data, however, the increase did not reach statistical significance when the overall incidence of nosocomial sepsis was considered.[7]

This study was therefore conducted to augment available evidence of the efficacy or harm caused by emollient therapy in preterm infants. The main objective was to determine the efficacy of prophylactic, whole-body topical application of pure, preservative-free petroleum jelly in very low-birthweight (VLBW) infants (<1250 g) in reducing the incidence of nosocomial sepsis.

Methods

This was a prospective, randomised controlled trial.

VLBW infants admitted to the neonatal intensive care unit (NICU) of King Khalid University Hospital (KKUH) from January 2008 to December 2009 were considered for enrollment. Inclusion criteria were birthweight 501–1250 g and gestational age of ≤32 weeks. Exclusion criteria were major congenital anomalies, skin disease known to interfere with skin integrity, previous treatment with an ointment, outborn infants or small-for-gestational-age (SGA) infants (birthweight <10th centile).

Randomisation was undertaken using a random number table. Allocation concealment was ensured using sealed envelopes kept in a closed cabinet and managed by the study coordinator. Premature infants were randomised immediately after birth to receive either prophylactic pure petroleum jelly or routine skin care. The sample size was determined by convenience.

Two g/kg of sterile Vaseline dispensed in sterile syringes was applied by the bedside nurse to all parts of the infants' skin in the intervention group, excluding the scalp, using sterile, non-starch soft gloves once per 12-hour shift. The skin was cleaned before the next application with warm sterile water. The cardiac lead site was cleaned with alcohol. Application of the topical therapy was documented on patients' flow-sheets by the bedside nurse. The control group received routine skin care without emollients. The study medication was continued up to completion of 34 weeks post-conceptional age. All infants were nursed according to the patient's weight group in an environment with 50–80% humidity.

Demographic data, respiratory data (duration of oxygen therapy and ventilation), invasive procedures (umbilical catheterisation, peripheral atrial line and percutaneous central line), episodes of sepsis and antibiotic use were recorded. Sepsis was confirmed by a positive culture from a sterile site (urine, blood and cerebrospinal fluid). Skin examination was performed by one examiner (RB) using a modified scoring system for neonatal dermatitis as per the Lane, Drost Scoring System on day zero, pre-treatment (D_0), day 3 (D_3), day 7 (D_7), then once a week until the end of the study.[8] Fluid balance in the 1st 14 days of life including intake and output and the number of days to regain birthweight were recorded. Days under phototherapy and maximum bilirubin level were documented. Infants' temperatures and incubator settings (temperature, humidity) were also recorded.

The Department of Pediatrics research committee and the KKUH ethics committee approved the study. Written, informed consent was obtained from the parents of all participants.

Statistical analysis

Student's unpaired *t*-test was used to compare continuous data, and Fisher's Exact test for comparative analysis of dichotomous outcomes. Continuous demographic data were presented as means and standard deviations. $P \leq 0.05$ was considered significant.

Results

A total of 93 infants with birthweights <1250 g admitted to the NICU during the study period were screened. Nineteen were excluded: nine were SGA, five died in the 1st 24 hours of life, three were outborn and two had major malformations. The remaining 74 premature infants were included in the study, 35 in the intervention group and 39 in the control group. Three infants, two from the intervention group and one from the control group, died in the 2nd week of the study and were included in the intention-to-treat analysis. The two groups were comparable with regard to baseline demographic data and perinatal variables (Table 1).

There was a trend towards an increased incidence of culture-proven nosocomial sepsis in the intervention group, 19 episodes (54%) in the intervention group and 16 (41%) in the control group. However, this did not reach statistical significance. No difference was seen in the spectrum of pathogens in the two groups. A similar trend towards an increased rate of severe NEC was noted, 20% *vs* 8% in the intervention and control groups, respectively.

There was a clear difference between the skin scores of the two groups (Fig. 1): the intervention group had better skin scores throughout their stay. The incubator ambient temperature was lower in the intervention group (Fig. 2), although this difference was not detected after the 7th day of life.

Parental fluid requirements were similar between the two groups. The mean (SD) fluid requirements on day 3 of life were 144 (23) ml/kg/day in the intervention group *vs* 152 (24) ml/kg/day in the control group, and on day 7 of life were 175 (28) ml/kg/day in the intervention group *vs* 181 (21) ml/kg/day in the control group. There was a trend towards a better fluid balance in the intervention group, reflected by their

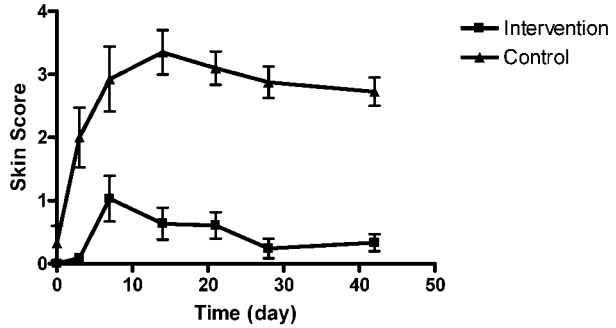

Figure 1 Skin scores, mean (SD)

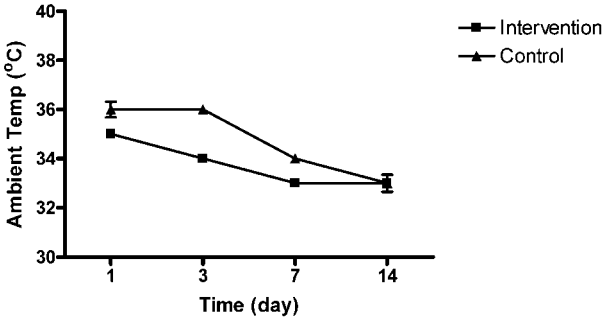

Figure 2 Ambient incubator temperature during the 1st 2 weeks of life, mean (SD)

mean (SD) shorter time to regain birthweight [12 (5) *vs* 14 (6) days] and fewer episodes of hypernatraemia (13 *vs* 23); however, these differences did not reach statistical significance. A significantly lower maximum bilirubin level was noted in the intervention group [157 (40) mmol/L] compared with the control group [182 (46) mmol/L, $P=0.02$]. Other short-term neonatal outcomes were similar in the two groups (Table 2).

Discussion

In 1954, Hoath *et al*. posed a question regarding the skin care of neonates: 'How can we facilitate bacterial colonisation while avoiding infections with pathogens? What is the best skin care practice for the newborn infant?' He concluded: 'time will tell what the next 50 years will bring.'[9] Today, 50 years later, several studies have sought to establish the optimum skin care for neonatal intensive care.[2,4,7,8,10–13]

This study sought to determine whether the use of topical petroleum jelly for skin care of VLBW infants was associated, as an occlusive material, with significant improvement in the incidence of sepsis. The patterns of temperature control, weight changes, fluid requirements, electrolyte imbalance and skin condition were also monitored. Pure preservative-free petroleum jelly was used to decrease exposure of these infants to chemicals and therefore reduce the risk of subsequent allergic or irritant dermatitis.

This prospective, randomised study demonstrated that topical application of petroleum jelly to the skin of VLBW infants resulted in a trend towards better fluid balance status, faster return to birthweight and significantly lower maximum bilirubin levels in the intervention group, which could be explained by less TEWL. Consistent with the literature, however, the intervention was associated with a trend towards an

Table 1 Baseline characteristics

Category	Intervention group ($n=35$)	Control group ($n=39$)	*P*-value
Gestational age, wks, mean (SD)	27 (2)	27 (2)	1.00*
Birthweight, g, mean (SD)	874 (217)	858 (183)	0.73*
<1000 g, *n* (%)	23 (66)	26 (67)	1.00†
Male:female	16:19	16:23	0.81†
Antenatal antibiotics, *n* (%)	10 (29)	14 (36)	0.62†
Antenatal corticosteroids, *n* (%)	28 (80)	31 (79)	1.00†
Chorio-amnionitis, *n* (%)	2 (6)	3 (8)	1.00†
Spontaneous vaginal delivery, *n* (%)	18 (51)	23 (59)	0.64†

* Unpaired *t*-test; † Fisher's Exact two-tailed test.

Table 2 Short-term neonatal outcomes

Category	Intervention group ($n=35$)	Control group ($n=39$)	*P*-value
Culture-proven sepsis, *n* (%)	19 (54)	16 (41)	0.35*
Fluid requirement, ml/kg/d, mean (SD):			
Day 3	144 (23)	152 (24)	0.15†
Day 7	175 (28)	181 (21)	0.3†
Days to regain birthweight, mean (SD)	12 (5)	14 (6)	0.13†
Episodes of hypernatraemia (Na >145 mmol/L), *n* (%)	13 (37)	23 (59)	0.07*
Maximum bilirubin, mean (SD)	157 (40)	182 (46)	0.02†
Patent ductus arteriosus, *n* (%)	12 (34)	9 (23)	0.31*
Chronic lung disease at 36 wks, *n* (%)	9 (26)	15 (38)	0.32*
Intraventricular haemorrhage, all grades, *n* (%)	4 (11)	4 (10)	1.00*
Necrotising enterocolitis, *n* (%)	7 (20)	3 (8)	0.18*
Length of stay, days, mean (SD)	84 (36)	95 (50)	0.29†
Survival to discharge, *n* (%)	30 (86)	37 (95)	0.24*

* Unpaired *t*-test; † Fisher's Exact two-tailed test.

increased rate of nosocomial sepsis and severe NEC.[7,8,10–12]

A systematic review of four randomised controlled trials[7,8,10–12] which enrolled around 1300 infants concluded that prophylactic emollient applied to the skin of preterm infants improved skin condition, and decreased TEWL in treated infants. However, there was a 31% increase in CONS and a 21% increase in any infection in treated infants.[7] One of the studies enrolled 1191 ELBW infants, and it alone showed no effect of topical treatment on nosocomial sepsis. However, the treated group overall still had a higher rate of CONS sepsis.[10]

The mechanism of increased CONS sepsis in treated infants is unclear. Contamination during the application process could have resulted in this observation. A more likely explanation, however, is that emollients serve as a conductive environment for the proliferation of bacterial pathogens when applied to the fragile epidermis of preterm infants.[7]

On the other hand, a randomised trial conducted in preterm infants (<33 weeks gestation) in Bangladesh demonstrated a 41% decrease in the rate of sepsis in infants massaged with sunflower oil.[13] The use of Aquaphor ointment, purified petrolatum (Beiersdorf, Norwalk, CT), had no effect on the overall rate of sepsis, which suggests that the effect of emollient therapy might be related to the components of the products used.[13]

Limitations of this study are the small sample size, the inclusion of relatively larger infants (>1000 g), and the fact that it was unblinded. The assessment of skin condition in particular was prone to bias since it was performed by one examiner who was unblinded to study assignment. Nosocomial infection is associated with many factors, some of which are related to the host and others to the care provided in the NICU. Therefore, imbalance in co-interventions or exposures beyond randomisation, i.e. random variables, could not be ruled out.

Although prophylactic topical application of a pure preservative-free petroleum jelly showed significant improvement of skin condition and temperature control, it was associated with a trend towards an increased rate of nosocomial sepsis.

References

1 Rutter N. The immature skin. Eur J Pediatr. 1996;155:18–20.
2 Rutter N, Hull D. Reduction of skin water loss in the newborn. 1. Effect of applying topical agents. Arch Dis Child. 1981;56:669–72.
3 Doty SE, McCormack WD, Seagrave RC. Predicting insensible water loss in premature neonates. Biol Neonate. 1994;66:33–44.
4 Darmstadt GL, Saha SK, Ahmed AS, Choi Y, Chowdhury MA, Islam M, *et al.* Effect of topical emollient treatment of preterm neonates in Bangladesh on invasion of pathogens into the bloodstream. Pediatr Res. 2007;61:588–93.
5 Darmstadt GL, Dinulos JG. Neonatal skin care. Pediatr Clin North Am. 2000;47:757–82.
6 Darmstadt G, Saha S, Ahmed A, Khatun M, Chowdhury M. The skin as a potential portal of entry for invasive infections in neonates. Perinatology. 2003;5:205–12.
7 Conner JM, Soll RF, Edwards WH. Topical ointment for preventing infection in preterm infants. Cochrane Database Syst Rev. 2004;CD001150.
8 Lane AT, Drost SS. Effects of repeated application of emollient cream to premature neonates' skin. Pediatrics. 1993;92:415–19.
9 Hoath SB, Narendran V. Skin care of the newborn infant. J Pediatr. 1954;44:258–63.
10 Edwards WH, Conner JM, Soll RF. The effect of Aquaphor Original Emollient Ointment on nosocomial sepsis rates and skin integrity in infants of birthweight 501 to 1000 grams. Pediatr Res. 2001;49:388A.
11 Nopper AJ, Horii KA, Sookdeo-Drost S, Wang TH, Mancini AJ, Lane AT. Topical ointment therapy benefits premature infants. J Pediatr. 1996;128:660–9.
12 Pabst RC, Starr KP, Qaiyumi S, Schwalbe RS, Gewolb IH. The effect of application of aquaphor on skin condition, fluid requirements, and bacterial colonization in very low birthweight infants. J. Perinatol 1999;19:278–83.
13 Darmstadt GL, Saha SK, Ahmed AS, Chowdhury MA, Law PA, 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;365:1039–45.