Original Article

THE EFFECT OF TOPICAL APPLICATION OF HUMAN MILK, ETHYL ALCOHOL 96%, AND SILVER SULFADIAZINE ON UMBILICAL CORD SEPARATION TIME IN NEWBORN INFANTS

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Background: **Several agents have been used for neonatal umbilical cord care, but we did not find any study evaluating the effect of human milk on umbilical cord separation time.**

The purpose of this study was to compare the effect of topical application of human milk, ethyl alcohol 96%, and silver sulfadiazine on umbilical cord separation time in newborn infants.

This study was undertaken place at a primary-level newborn nursery at a university teaching hospital and a private hospital. Of 373 singleton near- to full-term newborns enrolled in the study, 312 completed the study.

Methods: **Newborns from birth were randomized to either: 1) mother's milk group, 2) alcohol group, 3) silver sulfadiazine group, and 4) control (no treatment) group. Mother's milk for group 1, ethyl alcohol for group 2, and silver sulfadiazine ointment for group 3 were applied to the umbilical stump three hours after birth and continued every eight hours until two days after umbilical cord separation. The time to umbilical cord separation and any discomfort such as infection, hemorrhage, and granuloma formation were reported by mothers. Nothing was applied to the umbilical stump of the control group and they received dry cord care only.**

Results: **It was observed a significant difference in the mean cord separation time among the four group. No significant complications were observed in any group.**

Conclusion: **Breast milk could be substituted for other topical agents for umbilical cord care, but a multicenter study is required in order to advise it for routine umbilical cord care.**

Archives of Iranian Medicine, Volume 9, Number 1, 2006: 33 – 39.

Keywords: Breast milk • ethyl alcohol • newborn • silver sulfadiazine • umbilical cord

Introduction

The umbilical cord is an important site for bacterial colonization.[1] A possible consequence of bacterial colonization is cord stump infection, a factor that can greatly increase morbidity and mortality for infants in developing countries.[2] Because the vessel in the umbilical cord serves as a direct entry site for invasion of pathogenic microorganisms into the circulation of newborn babies, delays in cord detachment may increase risk of bacterial infection. For this reason, umbilical cord care seems to be very important.

In 1998, the World Health Organization (WHO) established umbilical cord care recommendations at birth and after discharge from the hospital that are currently being observed in developed countries.[2]

Although the American Academy of Pediatrics considers no antiseptic treatment to be superior to any other, they confirm its utility.[3] Although application of a topical antimicrobial to the cord stump after cutting the cord once a day for the first

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Accepted for publication: 13 June 2005

3 days may reduce cord colonization, it may delay cord separation time.[4, 5]

In developing countries, umbilical cord infections constitute a major cause of neonatal morbidity and pose significant risks for mortality. Interventions introduced in both developed and developing countries to reduce exposure of the cord to infectious pathogens include clean cord cutting, hand-washing before and after handling the baby, bathing of the infant with antimicrobial agents, and application of antimicrobials to the cord.[6] Despite the importance of umbilical cord care, both traditionally and medically, there have been few randomized trials investigating the impact of different cord care regimens on umbilical cord separation time (UCST), particularly in developing countries.

Current clinical procedures for aseptic cord care are based on research from developed countries. This research does not provide a clear understanding of optimal cord care practices. In developing countries where significant differences exist in resource availability, social customs, environmental cleanliness, and bacteriologic profile, results from developed countries are difficult to apply.

Until data from such trials are available, caution must be exercised in extending conclusions drawn from scarce and inadequately designed trials in developed countries. Specifically, dry cord care alone, which is the current trend in neonatal care in developed as well as developing countries, must be properly evaluated before being further promoted as the best practice.

Several agents have been used for umbilical cord care in newborn infants. The most widely used agents include alcohol, triple dye, chlorhexidine 0.5%, silver sulfadiazine, and bacitracin, but we couldn't find any study to evaluate the effect of topical application of human milk on UCST. There are two reports from KwaZulu-Natal[7] and in some communities in Kenya,[8] in which some women apply expressed breast milk (colostrum) to the cord stump. This could, in fact, be beneficial in view of the antibacterial factors present in breast milk. We carried out a trial to determine the effect of topical application of human milk on UCST in newborn infants.

Materials and Methods

Three hundred and seventy-three singleton well-babies were enrolled in the study. Informed consent was obtained from their parents. Immediately after birth, the umbilical cord was cut and clips applied. In the delivery room, nothing was applied to the umbilical cord, including topical agents or wrapping with sterile gauze. Inclusion criteria for the study were gestational age of 36 – 42 weeks, being appropriate for gestational age and freedom from any diseases or congenital anomalies, requiring immediate evaluation and treatment. Infants with malformations, perinatal asphyxia, respiratory distress, metabolic derangement, and any other problems requiring immediate transfer to a higher neonatal care center were excluded. Infants whose mothers developed significant complications during or after delivery were also excluded from our study. All babies were fed by their own mother's milk, roomed-in with their mothers, and were discharged after 24 hours if born vaginally and 72 hours if born by cesarean section. The neonates were randomly assigned to receive one of the four regimens for umbilical cord care. Group 1 received topical application of human milk to the umbilical stump. Group 2 received ethyl alcohol 96%, by a sterile gauze or swab, to the umbilical stump. Group 3 received silver sulfadiazine ointment (Sobhan Pharmaceutical Company, Iran) topical application to the umbilical stump. Group 4, as the control group, received no topical agent and received just dry cord care.

All mothers were given a leaflet at the time of discharge, containing data related to the protocol assigned to their group. All mothers were asked to record the UCST/date. Then, we called and asked them the time/date of umbilical cord separation and also any discomfort or problem regarding the infants' umbilical cord as well as his/her general condition. All mothers were allowed for follow-up for any problems with their newborns.

The duration for umbilical cord separation was measured from the time/date of birth to the time/date of umbilical cord separation. This duration was expressed in hours. Other perinatal and maternal data were collected by a researcher.

We estimated a sample size of 77 for each group. This sample size detects 2 days difference in UCST with 80% power and 95% confidence interval (CI). The data were analyzed by SPSS software, and were expressed as mean ± SD. Chi-square and Student's *t*-test were used to compare the differences. In statistical analysis, we used the ANOVA model to compare the mean UCST

between four groups and for multiple comparison, we used the Duncan test. A *P* value of less than 0.05 was considered to be statistically significant.

Results

Three hundred and seventy-three eligible neonates were enrolled in the study, but 61 neonates (15 in the silver, 15 in the breast milk, 15 in the alcohol, and 16 in the no treatment groups) were excluded because of concurrent use of two topical agents for cord care, the need for admission to the neonatal ward for treatment with parenteral antibiotics, or for not reporting the time/date of cord separation. Three hundred and twelve neonates completed the study. Perinatal and demographic data for the four groups are detailed in Table 1.

The mean cord separation time in the human milk group was significantly shorter than the other three groups (Table 2) ($P < 0.001$).

By multiple comparisons in Table 3, we showed that the shortest UCST belongs to the human milk group and the longest one belongs to silver sulfadiazine group. We also found that the UCST in the human milk group had significant differences with the other three groups. The UCST in the alcohol group was shorter than that of the silver group ($P < 0.001$). The mean UCST in the alcohol group was not significantly different from that of control group.

According to our findings, the order of mean UCST in the four groups from shortest to longest were human milk, alcohol, control, and silver sulfadiazine groups, respectively.

No cases of complications such as infection (sepsis, omphalitis), umbilical cord hemorrhage, and granuloma formation were seen in any of the groups.

Discussion

This is the first study to evaluate the effect of topical application of expressed human milk on cord separation time and other outcomes in near-term and term newborns. In this study, we examined the efficacy of topical application of human milk, which we have shown to be effective in these infants. We compared human milk with alcohol, silver sulfadiazine, and dry cord care, which the WHO considers one of the most commonly-used practice for umbilical cord care.

Human milk has a lot of immunologic and antiinfective agents. Studies in past decades have proven that human milk is a potent immunocompetent agent containing a variety of rich products, each of which has a role in the immunologic protection of infants.[9] This is not the first report of topical application of human milk in medical practice. The effect of topical application of human breast milk in the prevention of neonatal conjunctivitis was previously determined. In a study in Shiraz University of Medical Sciences, Shiraz, Iran, where 565 newborns were randomized into two groups, the first group consisting of 327 newborns who received topical breast milk prior to each breastfeeding for the first ten days of life. The second group of 238 babies

Table 1. Baseline characteristics of subjects in the four groups under study.

Characteristics	Breast milk group Mean ± SD *n* = 79	Alcohol group Mean ± SD *n* = 78	Silver group Mean ± SD *n* = 77	Control group Mean ± SD *n* = 78	*P* value
Sex					
Male	37 (46.8)	43 (55.1)	42 (55.1)	42 (54.5)	0.53
Female	42 (53.2)	35 (42.3)	35 (42.3)	35 (45.5)	
Birth weight (g)					
Mean ± SD	3224 ± 467	3313 ± 413	3268 ± 493	3235 ± 540	0.28
Gestational age					
Term	43 (92.4)	73 (93.6)	75 (97.4)	72 (92.3)	
Preterm	3 (3.8)	2 (2.6)	1 (1.3)	4 (5.1)	
Postterm	3 (3.8)	3 (3.8)	1 (1.3)	2 (2.6)	0.77 NS
Type of delivery					
NVD	45 (57)	22 (28.2)	11 (14.3)	25 (32.1)	0.001
CS	34 (43)	56 (71.8)	66 (85.7)	53 (67.9)	
Parity					
Mean ± SD	1.9 ± 1.2	1.7 ± 0.8	1.8 ± 0.9	1.8 ± 1.3	0.58
Maternal age (yr)					
Mean ± SD	25.7 ± 5.5	27.2 ± 5.5	26.7 ± 5	27.9 ± 5.6	0.29

NVD = normal vaginal delivery; CS = cesarean section, NS = not significant, SD = standard deviation.

Table 2. The mean ± SD and 95% CI of UCST in the four groups.

Groups	Mean ± SD (hours)	Mean ± SD (days)	95% CI of UCST	*P* value
Breast milk	124 ± 43	5.16 ± 1.79	114 – 134	
Alcohol	154 ± 47	6.41 ± 1.95	144 – 165	< 0. 001
Silver	251 ± 87	10.45 ± 3.62	231 – 271	
Control	158 ± 52	6.58 ± 2.16	147 – 170	

CI = confidence interval.

received no treatment and served as a control group. Conjunctivitis appeared in 9.1% of the newborns in group one and 25.6% of the newborns in the control group ($P < 0.001$). As environmental microorganisms are the main cause of conjunctivitis in newborns and because human milk has antiinflammatory and antimicrobial properties, the topical application of breast milk is recommended as a prophylactic measure in neonatal conjunctivitis.[10]

Umbilical cord separation is a complex process. The umbilical cord dries and becomes mummified. Histological study has revealed that polymorphonuclear leukocytes infiltrate the area between the drying cord stump and the vital tissues of the abdominal wall, forming a demarcation zone.[11] Breast milk may enhance the umbilical cord separation through polymorphonuclear leukocytes, proteolytic enzymes, or other immunologic agents.

UCST may be influenced by some prenatal factors. The separation time of the umbilical cord was studied in 98 healthy Indonesian newborns with the aim of determining the normal time of separation and evaluating factors which may influence cord separation. None of the factors analyzed, including sex, birth weight, gestational age, parity of the mother, and nutrition of the newborn, had a statistically significant influence.[12] Nowak and colleagues reported that infants born by cesarean section were found to have an increased interval for cord separation when compared to infants born vaginally (mean ± SD, 15.9 ± 5.0 days vs. 12.9 ± 1.2 days).[13] But on examination of 293 healthy term newborns, Rais-Bahrami et al found no significant differences when comparing the mode of delivery, sex, or race of an infant, with respect to the time interval for their cord separation.[14]

Although, in our study there was a significant difference between the four groups in terms of the type of delivery, using covariant analysis, we found that difference in UCST was not affected by this factor.

The other factor, which may influence cord separation time is the topical agent used for cord care. The efficacy of alcohol or water in promoting umbilical cord separation was compared in a randomized controlled trial. Time-to-cord separation, rates of colonization, and species of organisms that colonized were compared between groups. Cords that were cleaned with sterile water separated more quickly than those cleaned with alcohol ($P = 0.002$). Between-group differences in colonization rates were not found ($F = 1.59$, $df = 2$, $P = 0.205$). Bacterial colonization of the umbilical area and surrounding skin occurs over time in healthy term neonates. Cleaning with alcohol increases the length of time from birth to cord separation but will not prevent colonization of the umbilical area.[15]

Golombek and colleagues compared the cord separation times between infants treated with triple dye followed by daily alcohol application with infants treated with daily alcohol application alone. Infants in the alcohol alone group had a shorter cord separation time by 3 days (10 vs. 13 days) ($P < 0.001$). There was no reported increase in infection, and monetary savings were noted. They concluded that alcohol applied once a day appears to be a safe and effective means of promoting cord detachment.[16]

The effect of topical cord care in preventing cord infection, illness, and death was assessed by Zupan and his colleagues through a search of the Cochrane pregnancy and childbirth group trials register and the Cochrane central register of

Table 3. Multiple comparison of the mean difference (MD) of UCST between different groups.

Multiple comparison	Mean difference (MD)	95% CI of UCST	*P* value
Breast milk vs. alcohol	–30	–54.6 – 5.2	0.1%
Breast milk vs. silver	–127	–151.2 – 101.7	< 0.001
Breast milk vs. control	–34	–58.5 – 9.2	0.002
Alcohol vs. silver	–96	–121.4 – 71.7	< 0.001
Alcohol vs. control	–3	–28.7 – 20.8	0.98 NS
Silver vs. control	92	73.6 – 111.6	< 0.001

CI = confidence interval.

controlled trials.[17] Randomized and quasi-randomized trials, all from developed countries, compared trials of topical cord care with no topical care and compared different forms of care. Although the study concludes that bacterial colonization could be reduced with antimicrobial applications, the review did not find any evidence that antimicrobials are superior to dry care only in reducing infection.[17]

In our study, UCST in the alcohol group had no significant difference with the dry cord care group. Also, no difference was demonstrated between cords treated with alcohol compared with natural dry cord care.[18]

In another study, Pezzati and his colleagues [19] evaluated the effect of 8 cord-care regimens for 1,535 healthy term infants on cord separation time and other secondary outcomes (omphalitis, sepsis, death, cord bleeding, compliance, umbilical cord colonization, and satisfaction or dissatisfaction with regard to the type of treatment). The 8 cord-care regimens studied were: 70% alcohol, natural drying, salicylic sugar powder, triple dye, micronized green clay powder, colloid silver-benzyl-peroxide powder, neomycin-bacitracin powder, and 1% basic fuchsin. None of the newborns developed sepsis or died and only sporadic cases of omphalitis were detected. With regard to cord separation time, the best results were obtained with salicylic sugar powder (5.6 ± 2.3 days) and green clay powder (6.7 ± 2.2 days). Both forms of treatment proved to be more effective ($P < 0.05$) than the others. They found that salicylic sugar powder allows for early cord detachment resulting in excellent parental treatment compliance and a reduction of their concern, notwithstanding higher percentages of cord bleeding. The rate of positive umbilical swabs was low and was significantly higher only than the results obtained with neomycin-bacitracin powder treatment. This study demonstrates that, in hospital nurseries in developed countries, salicylic sugar powder can be effectively and safely used for the umbilical cord care of healthy term infants.[19]

Extra vigilance against infection is needed for umbilical cord stumps that are not treated with antibacterial agents, according to the study,[20] "To Dye or Not to Dye: A Randomized, Clinical Trial of a Triple Dye/Alcohol Regime Versus Dry Cord Care." Traditionally, umbilical cord stumps have been treated with triple dye and alcohol, which cleaned and dried the stump and restricted bacterial growth. But many hospital maternity units have abandoned this regimen in favor of spot cleaning with soap and water, referred to this as "dry care." This is because of the medical concerns about the toxicity of the dye, as well as parental concerns about the appearance and brittleness of the stump. But, the study on infants receiving both kinds of care two or three days after hospital discharge, found significantly more bacteria and signs of infection in the dry care group.[20]

Further research in developed countries, including follow-up beyond hospital discharge, is required before advising on best cord care practices. The paucity of published reports from developing countries indicates the need to investigate the impact of antimicrobial applications on cord and systemic infections in a community-based, prospective manner.[21]

In low-income countries the policy of dry cord care needs to be evaluated. In these communities, breast milk, a readily-available and antiinfective agent, is traditionally used for topical cord care by some people. Firm conclusions regarding the effect of topical applications of human milk on UCST and on reducing infection await large, well-designed, and sufficiently powered investigations.

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