

A Comparative Analysis of 4% Chlorhexidine Versus Methylated Spirit as Prophylaxis of Omphalitis and Sepsis in Newborns

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Abstract

Objective: To compare the effectiveness of 4% chlorhexidine and methylated spirit in newborns for prevention of omphalitis and neonatal sepsis.

Material and Methods: This open label randomized control trial was carried out in neonatal unit of Shaikh Zayed Hospital Lahore from 1st September 2020 to 30th August 2021. After meeting the inclusion criteria, 300 neonates were enrolled. In group A 4% chlorhexidine was applied for cord care and in group B methylated spirit was used. Neonates were followed till 10th day of life, none was lost to the study. Careful examination was done for cord separation and for any signs of omphalitis or sepsis.

Results: In Chlorhexidine group omphalitis was present in 56(37.3%) patients and in Methylated spirit group 66(44%) patients had omphalitis (p-value=0.240). In Chlorhexidine group 36(24%) patients while in Methylated spirit 50(33.3%) developed sepsis (p-value=0.074).

Conclusion: Methylated spirit and 4% chlorhexidine are equally effective in newborns for prevention of omphalitis and neonatal sepsis.

Keyword: Omphalitis, Neonatal Sepsis, 4% Chlorhexidine, Methylated Spirit

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Introduction

Neonatal sepsis is one of the leading causes of death in neonates in developing countries. Infection of the umbilical cord often leads to infection in the blood. WHO recommends 4% chlorhexidine to prevent omphalitis and neonatal sepsis.¹ In Pakistan we use methylated spirit for prophylaxis of omphalitis as 4% chlorhexidine is not available and expensive to use. Some commercial gels containing 2% chlorhexidine are available, but these are not as effective as methylated spirit.

Chlorhexidine gel is an antiseptic agent with broad-spectrum bactericidal and bacteriostatic properties effective

against gram-negative bacteria and fungi with rapid pathogen killing rates. Methylated spirit on the other hand is both bactericidal, mycobactericidal, fungicidal and viricidal.²⁻⁵ In Pakistan Staphylococcal aureus is common pathogen in umbilical discharge. Some low cost prevention therapy should be used. Methylated spirit is commonly used for cord care. A study was conducted to explore about cord care practices in African setting which showed that 73.2% respondents consider methylated spirit as most important agent for cord care.⁶

Chlorhexidine is available in different concentrations for antiseptic purpose. Efficacy of all concentrations is comparable but 4% chlorhexidine concentration is more effective in inhibiting organism's flora as compared to 2% chlorhexidine. Since then, multiple studies were done to compare methylated spirit and 4% chlorhexidine. Methylated spirit is equally safe where 4% chlorhexidine is unavailable.⁷ In Pakistan 57% deaths occur in neonatal period. Pakistan has highest neonatal mortality rate of 42 per 1000 live births.⁸ In developing countries

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neonatal sepsis is aggravated by home deliveries, antibiotic resistance and less medical staff. The most important way to decrease mortality and morbidity due to infections is prevention at an early stage.⁹ Various antiseptics used in neonatal intensive care units include chlorhexidine, alcohol, iodine, hexachlorophene & octenidine. Each agent having its own advantages and adverse effects.¹⁰ However best antiseptic is yet to be determined.¹¹ WHO recommends application for 4 percent chlorhexidine in high neonatal mortality area while methylated spirit is commonly used agent for cord care.¹² One study conducted shows that applying chlorhexidine on cord in neonatal intensive care unit decreases mortality rate and decreases time of separation of cord.¹³

Methylated spirit and chlorhexidine both have comparable efficacy and can be used in areas of non-availability of chlorhexidine and whenever chlorhexidine is not safe to use as in very preterm neonates. In Pakistan there is no population based study published on this issue this study aimed to compare the effectiveness of methylated spirit and 4% chlorhexidine from prevention of omphalitis and neonatal sepsis. This study will help to establish the use of methylated spirit in prevention of omphalitis and neonatal sepsis at low price and easy availability.

Material & Methods

It was an open label randomized controlled trial done at the Neonatology unit, Department of Pediatrics, Shaikh Zayed Hospital, Lahore, IRB: SZMC/ IRB/ INTERNAL/MD/130/19, for a period of 12 months from 1st September 2020 to 30th August 2021. The hypothesis was methylated spirit is equally effective as 4% chlorhexidine in preventing omphalitis and sepsis in neonate. 300 newborns were included with simple random sampling by lottery method in study with 150 newborns in each group with confidence interval of 95% and margin of error 5%. Randomization was done by computer software which automatically generated numbers to the participants in an allocation ratio of 1:1 to each group, it helped to remove the selection bias. Sample size was calculated using Raosoft sample size calculator. Assumption for sample size estimation was the hypothesis test for difference of two proportions (two sided test). The estimated sample size is sufficient to detect the difference of 20% among the two groups at significance level 5% and power of study 90%. The estimated sample size was 150 for each group. Trial registration number NCT: 06002295 after approval from hospital ethical committee, neonates fulfilling

inclusion and exclusion criteria were selected. Term neonates of either gender born via cesarean section or spontaneous vaginal delivery at Shaikh Zayed Hospital were included. After taking informed consent of parents. Antiseptic agent started from 1st day of life & continued up to 10 days without missing dose. Newborns with congenital defects or cord anomalies, Laboratory or clinical evidence of sepsis, preterm newborns having very low birth weight <1.5 kg. Any evidence of asphyxia during birth were excluded. Full instructions to avoid confounding variables like maintaining temperature, hygiene of newborn, frequent diaper change, avoidance of herbal tonics and cow milk were given to mothers.

In group "A" mothers were advised the topical application of 4% chlorhexidine generously over cord along with base of cord stump and surrounding skin thrice a day. In group "B" clean cotton swab dipped in methylated spirit was used to clean cord along with cord clamps and base thrice a day. Mother of both groups were advised to report after three days or immediately if the baby developed fever, redness or discharge of cord till 10 days of life. On each visit careful examination was done for cord separation and any signs of omphalitis or sepsis. Primary outcome measure was omphalitis which was characterized by locally inflamed cord. Secondary outcome measure was sepsis which was characterized by signs and symptoms such as fever, reluctance to feed, respiratory difficulty, irritability. Treatment success was labelled if there was no evidence of omphalitis or sepsis. If omphalitis or evidence of sepsis was present, the patient was treated as per hospital protocol. Data was collected according to proforma.

Data was entered in SPSS v.23.0 and was analyzed through it. The numeric variables like birth weight and gestational age at birth were presented as mean \pm standard deviation, while the categorical variables like gender of the neonate, omphalitis and sepsis were presented as frequency (%). Both groups were compared for omphalitis and sepsis by using the chi-square (χ^2) test. P-value ≤ 0.05 was kept as significant. Data was stratified for gender of the neonate, birth weight and gestational age at birth to deal with the effect modifiers. Post-stratification, Chi-Square test was applied to compare both groups for omphalitis and sepsis in each strata. P-value ≤ 0.05 was kept as significant.

Results

A total of 300 patients participated in this study and all

completed the follow-up. There were 141 (47%) male neonates and 159 (53%) female neonates, giving a male to female ratio of 0.8:1. These patients were divided into two groups. Group A patients were treated with chlorhexidine and group B patients with methylated spirit. In group A, 63 (42%) patients were male and in group B 78 (52%) patients were male, rest was females. Overall omphalitis was present in 122(40.67%) patients while sepsis was present in 86(28.67%) patients. In group A, the omphalitis was present in 56(37.3%) patients and in group B the omphalitis was present in 66 (44%) patients (p-value=0.240). In group A, the sepsis was present in 36(24%) patients and in group B the sepsis was present in 50(33.3%) patients (p-value=0.074). In the study, most common sign of sepsis was respiratory distress, followed by irritability, hypotension, jaundice and apnea. There was statistically no significant difference

Table 1: Comparison between study groups.

Outcome	Study Groups		Total	p-value	
	A	B			
Gender	Male	63	78	141	0.083
		42.00%	52.00%	47.00%	
	Female	87	72	159	0.24
		58.00%	48.00%	53.00%	
Omphalitis	Present	56	66	122	0.24
		37.30%	44.00%	40.70%	
	Absent	94	84	178	0.074
		62.70%	56.00%	59.30%	
Sepsis	Present	36	50	86	0.074
		24.00%	33.30%	28.70%	
	Absent	114	100	214	0.903
		76.00%	66.70%	71.30%	
Signs and symptoms	Jaundice	3	11	14	0.903
		8.30%	22.00%	16.30%	
	Respiratory Distress	14	14	28	
		38.90%	28.00%	32.60%	
	Hypotension	9	7	16	
		25.00%	14.00%	18.60%	
Apnea		0	2	2	0.903
		0.00%	4.00%	2.30%	
Irritability		10	16	26	0.903
		27.80%	32.00%	30.20%	

Group A = Chlorhexidine: **Group B** = Methylated spirit

rence in the two groups, i.e. p-value=0.903.

Discussion

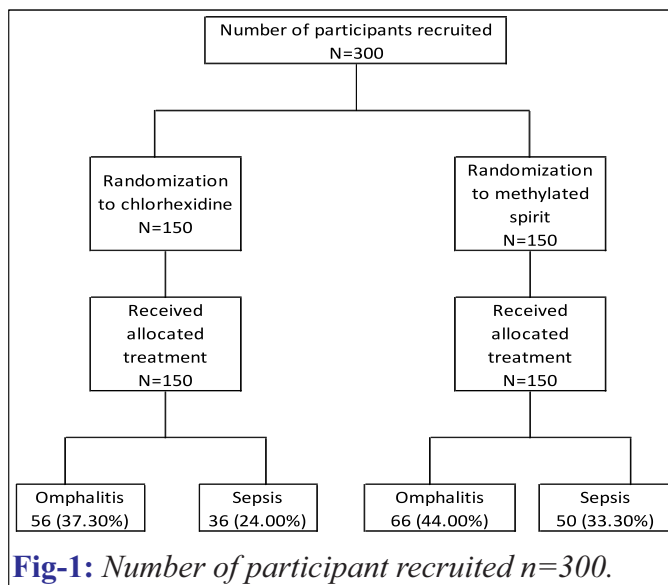


Fig-1: Number of participant recruited n=300.

Neonatal sepsis due to omphalitis is a leading cause of morbidity and mortality in neonates, especially in developing countries, accounting for 10%–19% deaths. According to a study conducted in Karachi, omphalitis is 217.4/1000 live births from which moderate-severe omphalitis is 170/1000 live births and associated with sepsis is 20.4/1000 live births.²

Omphalitis results mostly due to unhygienic cord cleaning practices. Chlorhexidine is a WHO approved antiseptic for cord care and is available in different formulations i.e. 2, 4 and 7.1%. In high-mortality situations, a topical application of 7.1 percent chlorhexidine to the umbilical cord has been shown to decrease newborn mortality and omphalitis. A study conducted in Peshawar showed that a single application of 4% chlorhexidine was superior to dry cord in prevention of omphalitis.³ Data regarding use of other formulations of chlorhexidine or methylated spirit in low to middle income countries is scarce. The methods of cord care differ in various countries depending on income status and cultural practices, with the bottom line being a desire to promote healing and hasten cord separation. Whatever the substance, its use has not been studied for as to determine its frequency of application, both in number of days or the times per day.¹⁴ To give an example, cord cleaning decreased invasive organisms such as Escherichia coli (49 percent, 64 percent, and 42 percent less), Klebsiella pneumoniae (46 percent, 53 percent, and 33 percent less) and Staphylococcus aureus (46 percent, 53 percent, and 33 percent less) on days 1, 3, and 6 respectively.¹⁵ In this study, chlorhexidine and methylated spirit were compared for cord cleaning. It was shown that in Chlor-

hexidine group, omphalitis occurred in 56 (37.3%) patients while in Methylated spirit group, omphalitis was present in 66 (44%) patients (p-value=0.240). Similarly in Chlorhexidine group, sepsis was present in 36 (24%) patients and in Methylated spirit group, the sepsis was present in 50 (33.3%) patients (p-value=0.074). A similar study done in Islamabad showed that methylated spirit resulted in a significantly less cord sloughing time than chlorhexidine (p-value = 0.001) and both treatments had equal efficacy in prevention of omphalitis.¹⁶ D D Shwe et al in a similar study earlier had mentioned no difference in the risks of neonatal sepsis and mortality among those treated with methylated spirit compared to those exposed to chlorhexidine gel (RR:1.0;95% CI=0.984-1.017; P=1.000) and (RR: 1.0;95% CI=0.994-1.018; P=0.986) respectively.¹⁷ A study conducted in African setting has shown methylated spirit to be effective in 73.2% patients for cord care.⁶

Okpaleke et al also found that there is insignificant difference regarding the occurrence of umbilical cord infection after the use of chlorhexidine or methylated spirit. Their study however showed a greater noncompliance in the use of chlorhexidine gel (21.1 percent) as compared to methylated spirit (9.6 percent) (p-value=0.001)¹⁸. Similar observations have been made by other researchers regarding the use of either methylated spirit or chlorhexidine gel for cord cleaning in neonates. In fact, methylated spirit was found to be a safer substitute in a clinical setting where the topical chlorhexidine gel was not accessible due to pricing or was contraindicated / unsafe to use.^{7,19} Apart from local irritation, chlorhexidine has been shown to cause various allergic reactions.²⁰ One study has even shown detectable levels of chlorhexidine in the blood of preterm infants after its local application. This may inhibit L1-mediated neurite outgrowth of cerebellar granule neurons, thus it can be a neurotoxic for developing brain.²¹

Whatever the choice, use of appropriate antiseptic agent by health care workers is vital to promote neonatal health and reduce mortality due to neonatal sepsis.²² It is high time that WHO should make alternative low price recommendations to chlorhexidine use for cord cleaning or otherwise mothers in low income countries will keep using harmful home remedies. One such recommendation can be use of methylated spirit. The limitation of this study is that it was a single center study and it did not include comparison with 2% chlorhexidine or its other formulations. On the other hand, this study has an advantage of easy to perform, not having any invasive

parameters on follow up except for those who develop septicemia. It is suggested that in future, further studies should be done with larger sample size and studies should be done at multicenter setting to control the bias. Evidence-based interventions are needed to achieve Sustainable Development Goal 3.2. This will help in reducing neonatal mortality. Currently, umbilical cord care coverage is measured by population-based household survey programs such as the Demographic and Health Surveys (DHS) Program and Multiple Indicator Cluster Surveys (MICS), typically conducted every 2–5 years. There is a need to conduct such surveys regarding cord care especially in rural areas. Mother should also be counselled /taught to recognize fever, redness or swelling of the umbilicus and report to the hospital immediately.

Conclusion

This study concluded that both groups 4% chlorhexidine and methylated spirit are statistically equally effective in newborns for prevention of omphalitis and neonatal sepsis.

Conflict of Interest

None

Source of Funding

None

References

1. World Health Organization. WHO recommendations on Newborn Health. Geneva: World Health Organization. 2017;4.
2. Mir F, Tikmani SS, Shakoor SS, Warraich HJ, Sultana SA, Ali SA, et al. Incidence and etiology of omphalitis in Pakistan: a community-based cohort study. *J Infect Dev Ctries.* 2011;5:828-833. doi:10.3855/jidc.1229.
3. Ishaq M, Noor B, Ahad A, Muhammad N, Bibi R. Chlorhexidine for the Prevention of Omphalitis in neonates with a single dose. *Pakistan Journal of Medical & Health Sciences.* 2023 May 6;17(04):141-. doi: <https://doi.org/10.53350/pjmhs2023174141>
4. Lachapelle JM. Antiseptics and Disinfectants. In: John S, Johansen J, Rustemeyer T, Elsner P, Maibach H, editors. *Kanerva's Occupational Dermatology.* Cham: Springer; 2020. p. 36. doi:10.1007/978-3-319-68617-2_36. doi: https://doi.org/10.1007/978-3-319-68617-2_36
5. Andleeb Kanwal Za, Akram M, Anwar S, Pirzada S. Cord Care Methods in Neonates. *World Health.* 2020 Dec;6:7 doi: <https://doi.org/10.53350/pjmhs2115103509>

6. Afolaranmi TO, Hassan ZI, Akinyemi OO, Sule SS, Malete MU, Choji CP, et al. Cord care practices: a perspective of contemporary African setting. *Front Public Health*. 2018;6:10. doi: 10.3389/fpubh.2018.00010
7. Shwe D, Abok I, Diala U, Egbodo C, Toma B, Nathan S, et al. Methylated spirit versus 4% chlorhexidine gel in neonatal umbilical cord infection: A short report of a randomized, open-labelled, parallel-group trial. *Niger J Paediatr*. 2018;45:118-122. doi: 10.4103/njcp.njcp_535_20
8. Demographic and Health Survey. Available from: <https://dhsprogram.com/pubs/pdf/PR109/PR109.pdf> [Accessed 2021].
9. Celik IH, Hanna M, Canpolat FE, et al. Diagnosis of neonatal sepsis: the past, present and future. *Pediatr Res*. 2022;91:337-350. doi: <https://doi.org/10.1038/s41390-021-01696-z>
10. Asma'u A, Oloche OB, Ridwan JM, Muhammad A, Mohammad AU, Omeneke IK, Kehinde IP, Omoshalewa UM, Fatima JB, Ilah GB. Determinants of Umbilical Cord Care Practices among Mothers of Neonates Admitted into Special Care Baby Unit of Usmanu Dan Fodiyo University Teaching Hospital, Sokoto, Nigeria. 2021. doi: <http://dx.doi.org/10.21276/ijcmr.2021.8.4.3>
11. Ponnusamy V, Venkatesh V, Clarke P. Skin antisepsis in the neonate: what should we use? *Curr Opin Infect Dis*. 2014;27:244-250. doi: 10.1097/QCO.0000000000000064
12. Osuchukwu EE, Ezeruigbo C, Eko J. Knowledge of standard umbilical cord management among mothers in Calabar South local government area, Cross River State, Nigeria. *Int J Nurs Sci*. 2017;7:57-62. doi: 10.5923/j.nursing.20170703.01
13. Okoye CF, Okoh EE, Ager T, Ikpeama OJ, Ogbodo IJ, Aguyi I, Okoye AO, Kakwi J, Udeogu K, Ifeadike CO, Kingsley AP. A Cross Sectional Comparative Study of Methylated Spirit and Chlorhexidine in Preventing Neonatal Cord Infections in a Local Hospital, Jos-Plateau State, Nigeria. *Trop J Med Res [Internet]*. 2022 Nov. 15 [cited 2023 Aug. 19];21(2):85-92. doi: <https://doi.org/10.5281/zenodo.7792906>
14. Umbilical cord-care practices in low- and middle-income countries: a systematic review. *BMC Pregnancy Childbirth*. 2017 Feb;17(1):68. DOI: 10.1186/s12884-017-1250-7.
15. Zaman SB, Siddique AB, Ruysen H, et al. Chlorhexidine for facility-based umbilical cord care: EN-BIRTH multi-country validation study. *BMC Pregnancy Childbirth*. 2021;21(Suppl 1):239. doi:10.1186/s12884-020-03338-4. doi: <https://doi.org/10.1186/s12884-020-03338-4>
16. Hussain I, Wahid S, Qureshi MA, Hashmi FUI, Fahim M. Comparison of the Impact of Topical Chlorhexidine Versus Methylated Spirit on Umbilical Cord Sloughing Time in Neonates. *Pak Armed Forces Med J*. 2022; 72(4): 1392-1396. DOI: 10.51253/pafmj.v72i4.6542.
17. Shwe DD, Afolaranmi TO, Egbodo CO, Musa J, Oguche S, Bode-Thomas F. Methylated spirit versus chlorhexidine gel: A randomized non-inferiority trial for prevention of neonatal umbilical cord infection in Jos, North-Central Nigeria. *Niger J Clin Pract*. 2021; 24: 762-769. doi: 10.4103/njcp.njcp_535_20
18. Okpaleke M-H, Ndikom CM, Bulama KU. Incidence of umbilical cord infection in neonates receiving 7.1% chlorhexidine gel and methylated-spirit in Ibadan. *J Neonatal Nurs*. 2019;25:20-25. doi: 10.1016/j.jnn.2018.07.002
19. Metzler M, Coffey PS. Using consumer data to inform marketing strategies for chlorhexidine for umbilical cord care programming in Kenya and Nigeria. *Soc Mark Q*. 2018;24:235-248. doi: 10.1093/inthealth/ihad061
20. Kefala K, Ponvert C. Allergic contact dermatitis to chlorhexidine-containing antiseptics and their excipients in children: A series of six cases. *Pediatr Dermatol*. 2023; 40(1):151-153. doi: 10.1111/pde.15127
21. Milstone AM, Bamford P, Aucott SW, Tang N, White KR, Bearer CF. Chlorhexidine inhibits L1 cell adhesion molecule-mediated neurite outgrowth in vitro. *Pediatr Res*. 2014;75:8-13. doi: 10.1038/pr.2013.175
22. Mullany LC, Saha SK, Shah R, Islam MS, Rahman M, Islam M, et al. Impact of 4.0% chlorhexidine cord cleansing on the bacteriologic profile of the newborn umbilical stump in rural Sylhet District, Bangladesh: a community-based, cluster-randomized trial. *Pediatr Infect Dis J*. 2012;31:444-450. doi: 10.1186/1471-2458-13-S3-S15

Authors Contribution

LR, MA: Conceptualization of Project
MJ, AZW: Data Collection
MA, AMN: Literature Search
MJ, AMN: Statistical Analysis
AT: Drafting, Revision
AT, LR, MJ: Writing of Manuscript