Efficacy of Oropharyngeal Administration of Pasteurized Colostrum in Very Low Birthweight Newborns in Reducing Late Onset Sepsis at a Tertiary Government Hospital in Manila City: A Randomized Control Trial

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ABSTRACT

Background. Early administration of colostrum is beneficial because of the number of its immunologic components. The problem with very low birthweight (VLBW) patients is the establishment of early, tolerated, and sustained feeding. The study aimed to determine if early initiation of colostrum through oropharyngeal administration within the first hour of life reduces the risk of late-onset sepsis (LOS) among VLBW newborns.

Methods. In this single-blinded randomized control trial, 84 VLBW infants with pediatric aging equal to greater than 28 weeks requiring oxygen support were enrolled. They were allocated to receive either pasteurized colostrum via oropharyngeal administration (treatment group) or none (control group). The occurrence of LOS, duration of ventilator use and oxygen support, time to reach full feeds, length of NICU stay, the occurrence of NEC, and mortality were documented.

Results. A significantly greater proportion of patients who developed LOS were noted in the control group (n=38 (90.4%)) than in the treatment group (n=30 (71.4%)) (p=0.013). The use of colostrum, had a protective effect for LOS (RR=0.77; 95% CI=0.63-0.94). There were no significant differences in the secondary outcomes. Still, there was a trend towards a lower proportion of mortality (p=0.08), shorter duration of ventilator use (p=0.24) and oxygen support (p=0.17), shorter time to reach full feeds (p=0.30), and shorter NICU stay (p=0.33) in the treatment group.

Conclusion. Patients given pasteurized colostrum had significantly less occurrence of LOS. The treatment group had a lower mortality rate, shorter ventilator use and oxygen support duration, faster time to reach full feeds, and shorter NICU stay, but the differences were not statistically significant. Oropharyngeal administration of pasteurized colostrum within the first hour of life reduces the risk of LOS among VLBW infants admitted to the NICU.

Keywords: neonatal late onset sepsis, oropharyngeal, colostrum, very low birth weight

Paper presented in the PSNbM 4th International Conference and 13th Annual Meeting on February 6, 2019, at the Manila Hotel, Manila, Philippines.

Paper presented in the 20th Congress of the Federation of Asia and Oceania Perinatal Societies and 27th Annual Convention of the Perinatal Association of the Philippines, Inc. on August 25, 2018, at the Crowne Plaza, Quezon City, Philippines.

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INTRODUCTION

Late-onset sepsis (LOS) is most frequently defined as an infection developing 72 hours after birth, which is a cut-off time point considered to differentiate LOS adequately from early onset sepsis (EOS) in terms of the spectrum of the causative pathogens.[1] This onset is related to neonatal factors such as mechanical ventilation, intravascular catheterization, the failure of early enteral feeding with breast milk, and prolonged parenteral nutrition and generally affects newborns admitted to NICU. It is acquired in the hospital environment, with the peak incidence being between the 10th to 22nd day of life.[1,2]

The incidence of LOS is inversely associated with birth weight.[1] It is reported to vary from 20 to 50%, depending upon the patient population, with higher rates among lower gestation and lower birth weight infants.[3] Data from the Neonatal Network of the National Institute of Child Health and Human Development in the United States reported that LOS occurred in almost a quarter (21%) of 6,215 very low birth weight (VLBW) infants in two years.[3,4] In Dr. Jose Fabella Memorial Hospital, 871 out of 5,882 live births in 2016 developed late-onset sepsis (14.8 % sepsis rate), but no actual data on how many of these were VLBW neonates.

Early initiation of breast milk feeding reduces neonatal and early infant mortality.[5] Human milk has various antimicrobial factors and immunologically active mediators beneficial to premature infants who are immune deficient and clinically unstable. Compared with term maternal milk, preterm milk contains lower proinflammatory cytokines and higher levels of anti-inflammatory cytokines and immunoglobulin A.[6] Secretory immunoglobulin A (sIgA) inhibits pathogen attachment to the respiratory and intestinal mucosal epithelial barrier, maintains intestinal mucosal integrity, and provides specific barrier protection against pathogens that cause respiratory and gastrointestinal infections. The interleukin-6 cytokine, on the other hand, stimulates the growth and differentiation of B lymphocytes into IgA-secreting plasma cells. Lactoferrin is a glycosylated protein with potent bactericidal, bacteriostatic, antiviral, anti-inflammatory, and immunomodulatory properties. It may protect against infection by inhibiting the attachment of pathogenic bacteria to cells lining the oropharyngeal mucosa.[7]

Colostrum, the milk produced in the first few days after birth, has higher concentrations of sIgA, growth factors, lactoferrin, anti-inflammatory cytokines, oligosaccharides, antioxidants, and other protective components than matured milk.[8] Moreover, recent studies suggest an inverse relationship between the concentration of protective immune factors in the colostrum and the duration of pregnancy; hence many of these factors are more highly concentrated in the colostrum of mothers who deliver infants with lower birthweights.[9]

Since there are concerns regarding increasing the risk of necrotizing enterocolitis (NEC) and tolerance issues, enteral feedings are often delayed in VLBW infants. Trophic feeding or minimal enteral feeding/ priming feeding has been a strategy in attempting to overcome the absence of enteral stimulation while exerting minimal stress on the immature gut. It is generally defined as an enteral milk intake with a small volume of up to 24 mL/kg/d. It has been shown to reduce the risk of LOS.[1] Decreasing LOS will also lessen the stay in the NICU, hence, cutting the hospital expenses.

Likewise, enteral feedings are typically prevented in extremely low birth weight (ELBW) infants because of the underdeveloped gastrointestinal tract and the presence of prematurity-associated morbidities that compromise gastrointestinal perfusion. The delay in feeding then can lead to intestinal atrophy, which augments the risk of localized inflammation, feeding intolerance, NEC, and nosocomial infections. The oropharyngeal route is an alternative method of administering colostrum.[7]

This study determined if oropharyngeal administration of colostrum at birth reduces late-onset neonatal sepsis in VLBW newborns admitted to the NICU. It also aimed to determine if this can reduce secondary outcomes in terms of mortality, duration of ventilator use and oxygen support, length of NICU stay, and occurrence of NEC. This was a relatively easy and safe method of administering colostrum and possibly providing its beneficial components to these patients who were not allowed to feed or feed in small amounts initially.

METHODS

Subjects

This was a single-blinded randomized control trial done from April to October 2017. The protocol was reviewed by the Ethics Committee of the Dr. Jose Fabella Memorial Hospital and the Manila Central University Institutional Review Board. Eighty-four (84) VLBW neonates born at the institution with pediatric aging equal to or greater than 28 weeks (including term newborns), with birth weights between 1,000 to 1,499 grams, admitted to the Neonatal Intensive Care Unit (NICU) of Dr. Jose Fabella Memorial Hospital, requiring oxygen support at birth were included in the study. The NICU of this DOH-retained tertiary government hospital is duly accredited to provide level 1-3 care for neonates. Excluded were newborns with 1) low APGAR score less than five at 10 minutes, 2) with the presence of metabolic acidosis on admission (with pH less than 7.2 or base deficit less than 12), 3) with major congenital abnormalities incompatible with life, or those with little or no life expectancy such as bilateral renal agenesis, Potter syndrome, acrania/anencephaly, skeletal dysplasia, trisomy 13 or 18, and alobar holoprosencephaly.

Clinical data collected at birth were gestational age, weight, sex, APGAR score, oxygen support, and presence of central lines (PICC; venous or arterial line). The neonates were randomly allocated to receive either colostrum via oropharyngeal administration or none. Data were obtained

regarding outcome measurements of occurrence of sepsis, length of NICU stay, duration of ventilator use and oxygen support, use of enteral nutrition, and time to reach full oral feeds. Occurrence of adverse events such as NEC (definite and advanced) and mortality was also documented.

Study Intervention

Before delivery, mothers with obstetric data suggestive of an estimated fetal weight of less than 1,500 grams were asked for consent after explaining the study protocol. The mothers were assisted during colostrum extraction via hand expression or breast pump. Once delivered and the entry criteria were fulfilled, the infant was enrolled in the study. Randomization was done using the RALLOC software. The allocation was placed inside sealed opaque envelopes, and the topmost envelope was selected for each enrolled patient. Patients were assigned to a group, indicated on each envelope, either in the treatment or the control group. All newborns were provided with the standard care practiced in the institution regarding medical management and feeding and were either placed on NPO or started on trophic feeding as appropriate. Newborns randomized to the treatment group received pasteurized colostrum from the human milk bank, starting from the first hour and continuing until the 7th day of life.

For standardization in the study, pasteurized colostrum was used since all mothers might not uniformly be able to produce colostrum immediately after delivery, especially in the first hour when the procedure would be started. The containers with pasteurized colostrum were stored in the refrigerator at 2-8°C. Tuberculin syringes were each filled with 0.2 mL colostrum and properly labeled with the subject's name/date/time of preparation. Twelve syringes were filled with colostrum for the entire 24-hour period per day, and these were stored in the body of the refrigerator. The procedure for administration was as follows: The colostrum-filled syringe was held with the needle-less tip positioned along the right buccal mucosa of the newborn with the needle directed posteriorly towards the oropharynx, then administered 0.1 mL of colostrum. Another 0.1 mL was administered on the left buccal side. The syringes were properly disposed of after each administration. This initial administration of 0.2 mL colostrum was done within the first hour of life. The procedure was repeated every 2 hours and continued for seven days, regardless of feeding status. All administrations were recorded on individual monitoring sheets. The primary investigator was blinded on the subjects included in the treatment or control group.

Sepsis work-up for all newborns consisting of CBC and blood culture were done at birth. Repeat CBC and blood culture was done on the fourth to the fifth day of life and were recorded and analyzed. LOS was operationally defined as the occurrence of sepsis after 72 hours of life manifested by a combination of clinical signs plus a positive repeat blood culture result or parameter derangement in CBC.

Sample Size

The number of samples was collected using a 95% confidence level and 80% power, with an estimated reduction in LOS of 50% and 17.3% between the treatment and the control group based on a previous study by Manzoni et al.[10] At least 42 subjects per group were needed, using the sample size computation on inference about two proportions.

$$n = \frac{[z_\alpha \sqrt{(2pq)} + z_\beta \sqrt{(P_1Q_1 + P_2Q_2)}]^2}{(P_1-P_2)^2}$$

$$n = \frac{\{1.96 \sqrt{[2(0.34)(0.66)]} + 1.28 \sqrt{[(0.5)(0.5) + (0.173)(0.827)]}\}^2}{(0.5 - 0.173)^2}$$

Where:
z_α= 95% confidence level
z_β= 80% power of the study
P_1 = estimated reduction in LOS in treatment group
$Q_1 = 1-P_1$
P_2 = estimated reduction in LOS in the control group
$Q_2 = 1-P_2$
$p= (P_1+P_2)/2$
$q = 1-p$

Statistical Analysis

Data were encoded and tallied in SPSS version 10 for Windows. Descriptive statistics were generated for all variables. For nominal data, frequencies and percentages were computed. For numerical data, mean ± SD were generated. The different variables were analyzed using the T-test to compare two groups with numerical data, Mann Whitney U test, the Chi-square test to compare/associate nominal (categorical) data, and the Fisher Exact test for the 2x2 table, when there were expected frequencies <5. Statistical analyses were completed according to the intention to treat.

RESULTS

Table 1 shows the demographic profile. Eighty-four (84) subjects were included in the study, randomly assigned into two groups. The baseline characteristics of both groups were comparable.

Table 2 shows the occurrence of sepsis in the two groups. The difference between subjects with EOS between the two groups was not statistically significant. Initial blood cultures were likewise not significant. More patients in the control group developed LOS than in the treatment group (36 (85.7%) vs 28 (66.7%), p = 0.013). Also, more subjects had positive blood cultures in the control group compared to the treatment group (32 (67.2%) vs. 24 (57.1%), p = 0.036). Three subjects died before 72 hours of life and were not included in the analyses of LOS outcomes and cultures.

Table 3 shows the comparison of the secondary outcomes between the two groups. No significant difference was seen in mortality and NEC, duration of oxygen support, duration of ventilator use, time to full enteral feeds, and length of

Table 1. Demographic Characteristics between the Two Groups

	Control group (n=42)	Treatment group (n=42)	*p*-value*
***Ballard Score** (in weeks)*			
Mean ± SD	31.06 ± 2.11	30.92 ± 2.14	0.76 (NS)
***Birthweight** (in grams)*			
Mean ± SD	1267.74 ± 154.62	1279.29 ± 138.43	0.72 (NS)
Sex			
Male	21 (50.0%)	19 (45.2%)	0.66 (NS)
Female	21 (50.0%)	23 (54.8%)	
Type of Delivery			
CS	25 (59.5%)	26 (61.9%)	0.82 (NS)
NSD	17 (40.5%)	16 (38.1%)	
Maternal Risk Factors			
With risk factors	13 (31%)	13 (31%)	
Fever	1 (2.4%)	0	
PROM	5 (11.9%)	4 (9.5%)	1.00 (NS)
URTI	4 (9.5%)	3 (7.1%)	
UTI	3 (7.1%)	6 (14.3%)	
Without risk factors	29 (69.0%)	29 (69.0%)	
APGAR Score at 5 min.			
Mean ± SD	7.98 ± 0.78	8.24 ± 0.73	0.12 (NS)
Admitting Diagnosis			
Pneumonia	18 (42.9%)	26 (61.9%)	0.08 (NS)
RDS-S	24 (57.1%)	16 (38.1%)	
Oxygen Support			
Cannula	1 (2.4%)	1 (2.4%)	
NCPAP	2 (4.8%)	4 (9.5%)	
NIPPV	2 (4.8%)	0	0.45 (NS)
ETCPAP	1 (2.4%)	0	
SIMV	36 (85.7%)	37 (88.1%)	
Central Lines			
Yes	42 (100%)	42 (100%)	1.00 (NS)
Feeding Initiated			
Yes	33 (78.6%)	36 (85.7%)	0.39 (NS)
No	9 (21.4%)	6 (14.3%)	
***Age Feeding Initiated** (in hours)*			
Mean ± SD	(n=33) 19.85 ± 18.34	(n=36) 16.28 ± 13.99	0.36 (NS)

** p>0.05 – Not significant; p ≤0.05 – Significant*

Table 2. Occurrence of Sepsis between the Two Groups

	Control group (n=42)	Treatment group (n=42)	*p*-value*
Sepsis			
Early Onset Sepsis			
Yes	20 (47.6%)	13 (31.0%)	0.12 (NS)
No	22 (52.4%)	29 (69.0%)	
Late Onset Sepsis (LOS)			
Yes	38 (90.4%)	30 (71.4%)	0.013 (S)
No	2 (4.8%)	11 (26.2%)	
Not included (died < 72 hrs)	2 (4.8%)	1 (2.4%)	
Blood Cultures			
Positive Blood Culture Growth (EOS)			
Yes	16 (38.1%)	11 (23.2%)	0.24 (NS)
No	26 (61.9%)	31 (73.8%)	
Positive Blood Culture Growth (LOS)			
Yes	32 (76.2%)	24 (57.1%)	0.036 (S)
No	8 (19.0%)	17 (40.5%)	
Not included (died < 72 hrs)	2 (4.8%)	1 (2.4%)	

** p>0.05 – Not significant; p ≤0.05 – Significant*

Table 3. Secondary Outcomes between the Two Groups

	Control group (n=42)	Treatment group (n=42)	*p*-value*
Mortality	(n= 42)	(n=42)	
Yes	26 (61.9%)	18 (42.9%)	0.08 (NS)
No	16 (38.1%)	24 (57.1%)	
***Duration of Oxygen Support** (in days)*	(n=42)	(n=42)	0.17 (NS)
Mean ± SD	13.71 ± 13.25	10.19 ± 9.86	
***Duration of Ventilator Use** (in days)*	(n=42)	(n=42)	0.24 (NS)
Mean ± SD	8.52 ± 9.54	6.35 ± 8.45	
***Time to Full Enteral Feeds** (in days)*	(n=18)	(n=25)	0.30 (NS)
Mean ± SD	14.50 ± 9.84	11.6 ± 8.08	
***Length of NICU Stay** (in days)*	(n=42)	(n=42)	0.33 (NS)
Mean ± SD	18.02 ± 16.76	15.9 ± 11.42	
NEC			
No	42 (100%)	42 (100%)	1.00 (NS)

** p>0.05 – Not significant; p ≤0.05-Significant*

NICU stay. However, a trend toward a lower proportion of mortality, shorter duration of O_2, time to reach full feeds, and NICU stay was noted in the treatment group than in the control group. Subjects included in the analysis of the time to reach full enteral feeds were only those who reached full feeds during the hospital course.

DISCUSSION

Among the patients enrolled, fewer subjects developed LOS in the treatment group compared with the control group (28 (66.7%) vs. 36 (85.7%), p = 0.013), and this was statistically significant. The oropharyngeal administration of colostrum is hypothesized to protect infants from infection through these mechanisms: 1. the potential interaction of cytokines in colostrum with lymphoid cells within the oropharyngeal associated lymphoid tissue (OFALT) system; 2. the mucosal absorption of immunologically-derived factors; and 3. the barrier protection afforded by human milk oligosaccharides against respiratory pathogens that can penetrate the oropharyngeal mucosa. OFALT stimulation is crucial since it may lead to systemic immuno-stimulatory effects. But this opportunity to use own mother's colostrum (OMC) to stimulate OFALT is often delayed for up to eight weeks post-birth for ELBW infants until "per oral"

feeds can be safely introduced.[11] This may hold true in VLBW infants. Feeding via gavage tube bypasses OFALT structures, and OMC cytokines never come in contact with lymphoid cells within OFALT.[11]

This significant result is similar to that of the study by OuYang et al. In this single-center randomized control trial conducted among preterm neonates less than 32 weeks gestational age; there was a lower incidence of LOS in the colostrum group (6 (4.7%) vs. 17 (13.6%, p = 0.1).[12] Results of other studies showed otherwise. On analysis of neonates <1500 grams and <34 weeks gestational age from a randomized, double-blinded, control trial in Brazil, no significant difference was found between the colostrum group and the placebo group (21 (51%) vs 34 (51%), OR = 0.7602, CI 95% 0.3-1.6).[13] The randomized control trial by Sharma et al., which included subjects with birthweight ≤ 1,250 grams, 30 weeks gestational age, or both, gave a nonsignificant difference between the intervention group and control group (8 (13.5%) vs. 10 (17.2%), p = 0.61).[14]

There was a lower number of positive-culture cases among patients who developed late-onset sepsis in the treatment group compared with those in the control group, and this was statistically significant (24(57.1%) vs. 32(76.2%), p = 0.036). The study by OuYang also showed a significantly lower incidence of proven sepsis in the colostrum group (3 (2.4) vs. 11 (8.8), p = 0.03).[12] These results oppose the findings in a randomized control trial by Abd-Elgawad et al. done in Egypt. Their results showed no statistically significant difference in infants delivered at <32 weeks gestational and <1500 gram birthweight who developed culture-proven nosocomial sepsis (8 (8%) vs. 8 (13%), p = 0.35) between the 'oropharyngeal administration of mother's milk group and the regular group.[15] Another randomized control trial in subjects with birth weight less than or equal to 1,500 grams conducted in 2015 by Zhang et al. showed no difference in proven sepsis between the study group and control group (3 (11.1%) vs. 6 (21.4%), p = 0.17).[16] The non-blinded randomized control trial conducted by Aggarwal et al. in India likewise showed nonsignificant results in culture-positive LOS between the colostrum group and placebo group (20 (15.6%) vs. 16 (12.5%), p = 0.47).[17] Glass et al. also had a pilot trial involving VLBW subjects in Pennsylvania, with nonsignificant results (p = 0.37).[18] In a 2009 retrospective descriptive study by Thibeau and Bourdeaux among mechanically ventilated preterms weighing 1500 g or less who were given oral care with mothers' milk (not just the colostrum), the results also showed that the rate of positive blood cultures was not statistically significant (p = 0.15), which may be due to lack of experimental design.[19] Since it was a chart review, there was insufficient accuracy in the dose of oral care because of a lack of control of the milk administered. There was also a lack of control over confounding variables such as hospital-acquired infection prevention practices.[19] The cotton swabbing technique was less accurate than our method of using a syringe for application. Cotton swabs could absorb up to 97% of the milk during 10 seconds of swabbing, and repeatedly dipping a swab into a container of mother's milk can contaminate the milk with hospital pathogens, further increasing the risk of infection.[20] Using a syringe, on the other hand, minimizes the absorption of milk into the swab, and thus more administered milk remains on the mucosa.[20] The trend, however, showed a reduced sepsis rate after implementation of oral care with mothers' milk, probably due to the potential benefits of the oropharyngeal route itself.

In a retrospective chart review by Flidel-Rimon et al. in 2004, 163 (42%) of the 385 VLBW infants included developed LOS. Feeding was started at a significantly earlier mean age in infants who did not develop nosocomial sepsis (2.8 ± 2.6 days vs. 4.8 ± 3.7 days, p = 0.0001).[9] However, the route was enteral, and the milk used was either breastmilk or a standard preterm formula. This was initiated as soon as the infant's condition was considered to be stable by the attending neonatologist. This decrease in infection rate with early enteral feeding was attributed possibly to gastrointestinal atrophy prevention, intestinal bacterial contamination, decreased parenteral nutrition use, decreased need for intravenous devices hence less opportunity for entry of pathogenic organisms, and mucosal immunity.[9] In our study, feeding was started, on average, within 24 hours. There was no significant difference in the initiation of feeding (in hours) between the treatment and control group (16.28 ± 13.99 vs. 19.85 ± 18.34, p = 0.36), further strengthening the efficacy of the oropharyngeal route in the reduction of LOS in our study.

The secondary outcomes considered were not significantly different between the two groups. Still, lower cases of mortality, shorter ventilator use duration, shorter oxygen support duration, shorter time to reach full feeding, and shorter NICU stay were seen in the treatment group. This may be because the sample size computation was based on the sepsis outcome, not the parameters.

In the study by Thibeau and Bourdeaux, the number of days on a ventilator for patients was not statistically significant ($X2$ (46, n = 115) = 46.22, p = 0.46).[19] The studies by Ferreira et al. (2 (0-5) vs. 2 (0-7) days, p = 0.75) and Ouyang et al. (1.02 ± 3.02 vs. 1.94 ± 9.29 days, p = 0.29)also had no significant results in ventilator days.[12,13] Our result between the treatment and control group (6.35 ± 8.45 days vs. 8.52 ± 9.54 days, p = 0.24) was likewise not significant. Duration of oxygen support was shorter in the treatment group than in the control group but not significant (10.19 ± 9.86 days vs. 13.71 ± 13.25 days, p = 0.17). The study by Abd-Elgawad et al., on the other hand, had a significant result on oxygen support duration (12(9-17) vs. 19(7-25) days, p = 0.01).[15]

In a randomized control trial in sixteen ELBW infants by Rodriguez et al. that aimed to determine whether OMC has an immunostimulatory effect when administered via oropharyngeal using tuberculin syringes, there were no statistically significant differences in immune markers found between or within groups, possibly because of the small sample size. However, it was found that patients reached

full enteral feedings (150 mL/kg/day) 10 days earlier compared to those in the placebo group (M = 14.3 ± 5.7 vs 24.2 ± 8.7 days; p = 0.032).[11] According to the authors, the mechanism for this finding is unclear. Still, it may be because of factors that enhance intestinal motility and promote maturation, including growth factors and enzymes in OMC. This may have been absorbed mucosally or traveled to the gastrointestinal tract, providing local maturational effects at the mucosal surface.[11]

In a non-randomized interventional study of 100 neonates born at < 32 weeks gestational age and weighing less than 1500 grams by Moreno-Fernandez et al., infants in the colostrum group reached full enteral feedings also sooner compared to the control group (7.2 ± 0.6 vs. 9.1 ± 0.7, p = 0.04), and this was the only outcome in the study that was statistically significant.[21] The study by OuYang also had an earlier age of achieving full enteral feeding in the intervention group (11.1 ± 2.1 vs. 15.57 ± 1.9 days, p = <0.01).[12]

Although not statistically significant, the results of our study also revealed a shorter time to reach full feedings in the treatment group (11.6 ± 8.08 days vs. 14.5 ± 9.84 days, p = 0.30). Two patients in the control group and one in the treatment group who died but reached full feeds were included in the analysis of the said parameter.

The length of NICU stay in days was shorter in the treatment group (15.9 ± 11.42 days vs. 18.02 ± 16.76 days, p = 0.33). Non-significant results were also seen in the studies between treatment and control groups by Rodriguez et al. (101.43 + 44.26 days vs 85.33 + 32.96 days, p = 0.78) and Thibeau and Bourdeaux (X2 (75, n = 115) = 78.78, p = 0.36).[11,19] Significant results were seen in the studies by Sharma et al. (34.2 ± 5.7 vs. 41.5 ± 6.7 days, p = 0.04) and Abd-Elgawad et al. (46 ± 5 vs. 61.6 ± 9 days, p = <0.01).[14,15]

This is probably related to the earlier achievement of discharge criteria such as relatively shorter oxygen therapy duration, shorter days to full oral feeding, shorter time to reach the required weight, and decreased sepsis and VAP incidence in the intervention group.[14,15]

The trial by OuYang yielded a statistically significant result of decreased NEC in the colostrum group (3 (2.36%) vs. 13 (10.4%), p = 0.01), the probable reason for which was attributed to a large colostrum dosage (0.4 mL), long duration (10 days) and high frequency (every 3 hours) of colostrum administration.[12] On the other hand, the study of Seigel et al. reported NEC cases, which may be due to lower birth weights (ELBW) and gestational age of the included subjects and the relatively later administration of human milk via oropharyngeal and enterally. The percentage of infants with medical NEC (7% vs. 6%, p = 0.80), surgical NEC (4% vs. 7%, p = 0.62), and spontaneous perforation (11% vs. 10%, p = 0.53) were statistically similar between colostrum protocol group and pre-colostrum protocol group.[6] Other studies also showed nonsignificant results for NEC.[6,14-18] In our study, there was no definite nor surgical NEC occurrence in the treatment and control groups.

Most clinical studies had statistically nonsignificant results in mortality.[14,15,17] In the study by Seigel et al., there was a lower number of deaths in the colostrum group but not statistically significant (15% vs. 20%, p = 0.35), and this trend was attributed to the direct effects of exposure to the cytokines and growth factors found in colostrum.[6] Results from our study showed the same trend toward lower mortality in the treatment group (40.5% vs. 57.1%, p = 0.12).

CONCLUSION

Oropharyngeal administration of pasteurized colostrum within the first hour of life reduces the risk of LOS among VLBW infants admitted to the NICU (RR = 0.77; 95% CI = 0.63 – 0.94). There was a trend of lower mortality rate, shorter duration of ventilator use, shorter duration of oxygen support, shorter time to reach full feeds, and shorter NICU stay in the treatment group.

More extensive randomized control trials may be needed to yield significant conclusions on the effects of early colostrum administration in reducing mortality, NEC, ventilator use, oxygen support duration, and NICU stay.

Statement of Authorship

All authors contributed in the conceptualization of work, acquisition and analysis of data, drafting and revising, and approved the final version submitted.

Author Disclosure

No financial grants were involved in this study, and all authors declared no conflicts of interest.

Funding Source

This study has no funding support.

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