Original Article

Impact of Breast Milk Gastric Lavage on Morbidity and Mortality in Preterm Neonates

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ABSTRACT:

The preterm baby has very limited stored energy and needs an adequate supply of nutrient in order to survive beyond a few days. Nutrients can be provided either parenterally or enterally. Hospitalized preterm newborns otherwise on exclusive parenteral fluids were evaluated to see the impact of gastric lavage with breast milk on morbidity and mortality. This was a hospital based randomized controlled trial. In addition to parenteral fluids, sick preterm babies were assigned to receive either gastric lavage with mother's milk within 12 hours of birth and subsequently every 4 hours till tolerance of nutritive enteral feeds (intervention or BML group, n = 40), or remain nil per orally till tolerance of nutritive enteral feeds (control or NPO group, n = 42). The main outcome was the mean number of days till successful tolerance of nutritive enteral feeds and mean number of days to achieve full enteral nutrition. They were also evaluated for mean duration of hospital stay, development of new complications, and mortality. Despite sicker babies in the BML group at baseline, the mean number of days till successful tolerance of nutritive enteral feeds was significantly less (P <.001) in BML (4.68±1.38 days) as compared to NPO group (6.36± 1.43 days). The mean number of days to achieve full enteral feed were also minimum in BML group (9.53±2.77 days) as compared to (13.22±3.11days) NPO group. In the NPO group 73.8% of the babies stayed longer than 2 weeks in hospital compared to only 27.5% in the BML group. The risk of development of new complication specially septicemia after randomization was also significantly less in BML group [RR 1.68 (95% CI 1.01 -2.85) (P=0.042)]. There was no difference in mortality between 2 groups. Early exposure to even small amounts of breast milk in sick preterm neonates significantly reduced the days to tolerate enteral feeds, risk of sepsis and the duration of hospital stay.

Key words: *Breast milk, Gastric lavage, Morbidity, Mortality.*

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INTRODUCTION:

Small preterm babies have greater risk of developing illness in the neonatal period than the mature well grown babies because of immaturity of structures and functions of various organs[1]. The neonatal mortality

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represents the bulk of infant mortality in many developing areas of the world and the association between the incidence of VLBW deliveries and infant mortality is very strong[2]. Approximately 12.5% of births in United States are preterm and preterm infants with very low birth weight who weigh 1500gm or less accounts only for 1.5%[3]. The incidence of LBW is about 22% in Bangladesh and the under five mortality rate is 65, the infant mortality rate is 52 and the neonatal mortality rate is 37 per thousand live births[4-5]. About 60% of the infant deaths occur in the neonatal period. Death of VLBW neonates is 30 times more common than the deaths of newborn of normal weight[6]. The preterm baby has very limited stored energy and needs an adequate supply of nutrient in order to survive beyond a few days. Subsequently, good nutrition is essential to promote the accelerated growth and long term development. Nutrients can be provided either parenterally or enterally but the aim in all infants is to use full enteral feeding as soon as it is safe to do so[7]. Considerable controversy surrounds the timing of initial enteral feeding for the preterm neonates[8]. However it is now believed that feeding should be initiated as soon as clinically possible. Early enteral feeding may promote growth and shorten the duration of parenteral nutrition and hospital stay without increasing the risk of necrotizing enterocolitis(NEC)[9]. Early enteral feeding is associated with better endocrine adaptation, enhanced immune function and gut motility[10]. Despite the positive impact of minimal enteral nutrition (MEN) most practitioners are still in dilemma when and whether to initiate it in sick preterm babies. One study conducted in India showed that the breast milk gastric lavage within 4 hours of birth helps in early tolerance of enteral feeding in sick neonates even who has gastric bleeding and reduces hospital stay[11]. This study was based on the knowledge of effects of early introduction of MEN with different types of initial feeds that improves intestinal function by releasing feed related gut hormones, by increasing intestinal motility and by preventing gut atrophy without adverse effects.

METHODS AND METARIALS:

The study was conducted at special care baby unit in Dhaka Shishu (Children) Hospital, which is the largest pediatrics teaching hospital in Bangladesh over a period of 12 months. This was a randomized controlled trial. The sample size was calculated for the main outcome of mean number of days till successful tolerance of nutritive enteral feeds by using 'STATA' statistical software. Considering the previous study, the assumptions were that the mean days in BML would be 5 (SD 2.5) and that in control would be 7 (SD 3). For a two sided alpha of 0.05 and power of 0.9 with equal allocation, the total number would be 82 i.e. 41 in each group. Enrolled babies were randomized into intervention and control group by 'coin flipping' method after taking informed written consent. Certificate from the ethical review committee (ERC) of BICH and Dhaka Shishu Hospital was obtained prior to the trial.

Inclusion criteria:

- Newborn baby aged up to 12 hours.

- Birth weight 1200 gm - 1500 gm.
- Gestational age 28 weeks - 34 weeks.
- Recommended exclusive parenteral fluids on admission by treating physician.

Exclusion criteria:

- Newborn baby aged more than 12 hours.
- Babies with congenital anomalies requiring immediate surgical intervention.
- Critically sick neonate (in need of assistant ventilation, cyanosis with 40% oxygen, RR > 80/ min, severe chest in drawing, audible granting at the time of admission).

Study procedure:

For each baby, a detailed history was recorded in a questionnaire, from the mother or attendants. Information included the baseline assessment of the neonates like the gender, admission weight in grams (measured by baby scale), gestational age in weeks determined from maternal last menstruation period (LMP) and assessment by New Ballard score system and the babies were leveled as small for gestational age (SGA), appropriate for gestational age (AGA) or large for gestational age (LGA). The clinical conditions on admission were assessed and the neonates were classified accordingly. Details of each neonate's condition in hospital were monitored and recorded regularly. Enrolled babies were randomized into two groups: the intervention or breast milk lavage (MBL) group and the control or nil per orally (NPO) group. The BML group received gastric lavage with 5cc of its own mother's milk (EBM) or milk of other mother on admission and subsequently every 4 hours, through No. 5F nasogastrie feeding tube. EBM was kept in stomach for 10 minutes and then aspirated out. When the aspirate was more than 5 ml then the excess amount was replaced parenterally. This was continued till the treating physician decided to initiate the nutritive enteral feeds. The breast milk gastric lavage was given by the investigator during the day time and by the duty nurses during night and holydays. The control group remained "Nil per oral" or NPO and on exclusive parenteral fluids till the same treating physician decided to start the nutritive enteral feeds. For both groups, the daily fluid requirement was also provided parenterally till the nutritive enteral feeds were sufficient enough to provide the daily fluid and caloric requirement. The decisions to initiate nutritive enteral feeds were by the treating physician and not by the study investigators. It was started when baby was hemodynamically stable and had no evidence of shock, clinical sepsis, respiratory distress, abdominal distension, gastric bleeding or bilious aspirate.

In both groups, nutritive enteral feeds were termed as 'successful tolerance' when two hourly three consecutive feeds of 3 ml/kg/feed were tolerated (i.e. absence of abdominal distention or increase in abdominal girth less than 2 cm from baseline and pre feed gastric aspirate less than 25% of previous feed volume). In case of feed intolerance, BML were continued in

interventional group. Serum electrolytes were monitored at least every alternate day during period of gastric laveage. In both the groups, the babies were leveled as 'achieved full enteral feed' when parenteral fluid was stopped. During hospital stay, development of complications like septicemia, necrotizing enterocolitis (NEC), hyperbilirubinemia and dyselectrolytemia were also recorded. The babies were categorized as "improved" if they had complication/s or unstable on admission and improved later on, or "deteriorated" if they were stable on admission and developed new complications or instability, or had complication/s on admission and subsequently developed another new complication. The babies were discharged from the hospital when clinically stable, pink in room air, maintaining temperature, taking full enteral feed by spoon or sucking and gaining weight daily.

Data entry and analysis:

The collected data of the neonates were analyzed thoroughly by SPSS program. In addition to descriptive statistics such as frequency tabulation, mean, standard deviation; statistical tests such as Chi-square test for discrete variables and student's t tests for continuous variables were applied accordingly and $p<0.05$ were considered statistically significant.

RESULTS:

A total of 1214 neonates were admitted into the specialized care neonatal unit during the study period. All the patients were out born, referred from all over the country. Among them, 218 neonates weighed below 1500 gm at birth were screened for eligibility and 89 neonates fulfilled the inclusion criteria of which 82 consented to participate in the trial.

Table I: Baseline characteristics of the study participants

Characteristics	BML (n=40)	NPO (n=42)	Test value	P value
Gestational age (in wks); Mean (± SD)*	31.7 (±1.6)	32.9 (±1.2)	0.44	0.159
Birth weight (in gm); Mean (± SD) *	1343.2 (±86.3)	1360.5 (±74.1)	-0.02	0.327
Sex #				
Male; N(%)	24(60)	22(52.4)	0.483	0.487
Female; N(%)	16(40)	20(47.6)		
Socioeconomic status #				
Lower; N(%)	16(40.0)	20(47.6)		
Middle; N(%)	21(52.5)	17(40.5)	1.32	0.517
Higher; N(%)	3(7.5)	5(11.9)		

Characteristics	BML (n=40)	NPO (n=42)	Test value	P value
Gestational age (in wks); Mean (± SD)*	31.7 (±1.6)	32.9 (±1.2)	0.44	0.159
Multiple pregnancy ¶ Singletone; N(%) Twin; N(%)	31(77.5) 9(22.5)	34(81) 8(19)	0.177 (-.41 to .45)	0.674
Intrauterine growth status ¶ AGA; N(%) SGA; N(%)	34(85) 6(15)	39(92.9) 3(7.1)	0.049 (-.08 to .25)	0.225

* P value generated with student t test

P value generated with χ^2 test

¶ P value generated through comparison of proportion (Z statistics) at 95% CI

Table I shows no statistically significant difference between two groups in the comparison of neonates by baseline characteristics.

Table II: Comparison of associated morbidities on admission

Morbidities	BML (n=40)	NPO (n=42)	Z (95% CI)	P value
Perinatal asphyxia; N(%)	05 (12.5)	06 (14.3)	1.17 (.33 – 4.14)	0.813
RDS; N(%)	08 (20.0)	05 (11.9)	0.54 (.16 – 1.82)	0.316
TTN; N(%)	08 (20.0)	07 (16.7)	0.80 (.26 – 2.46)	0.696
Hypothermia; N(%)	11 (27.5)	07 (16.7)	0.53 (.18 – 1.53)	0.236
Recurrent apnoea; N(%)	02 (5.0)	01 (2.4)	0.46 (.40 – 5.2)	0.528
Shock; N(%)	01 (2.5)	02 (4.8)	1.95 (.17 – 22.4)	0.586
PDA; N(%)	01 (2.5)	02 (4.8)	1.95 (.17 – 22.4)	0.586
With any problem; N(%)	36(90.0)	30(71.43)	2.62(-.023 – 3.9)	0.1056

Comparison of associated morbidities of neonates on admission failed to reveal any statistically significant difference in two groups (p>.05) had been reported in table II.

Table III: Comparison of two groups in relation to outcome

Outcome	BML (n=40)	NPO (n=42)	Mean Difference	't' statistic	P value
Successful tolerance of enteral feeding (days); Mean (± SD)	4.68 (1.38)	6.36 (1.43)	-1.682	5.411	< .001
Achievement of full enteral feeding (days); Mean (± SD)	9.53 (2.77)	13.22 (3.11)	-3.693	5.230	< .001
Hospital stay (days); Mean (± SD)	12.65 (6.57)	17.07 (4.53)	-4.421	5.142	< .001

Table III facilitates the comparison of outcome. Days required for successful tolerance of enteral feeding was 4.68 (±1.38) in BML group and 6.36 (±1.43) in NPO group. Days required for achievement of full enteral feeding was 9.53 (± 2.77) in BML group and 13.22 (±3.11) in NPO group. Both the time required for tolerance (P<.001) and achievement of full enteral feeding (P<.001) was significantly less in neonates of BML group. The average hospital stay of the neonates of BML group was 12.65 (± 6.57) and of NPO group was 17.07 (± 4.53). Neonates treated with BML stayed significantly minimum number of days at hospital (P<.001).

Table IV: Comparison of new complications at hospital

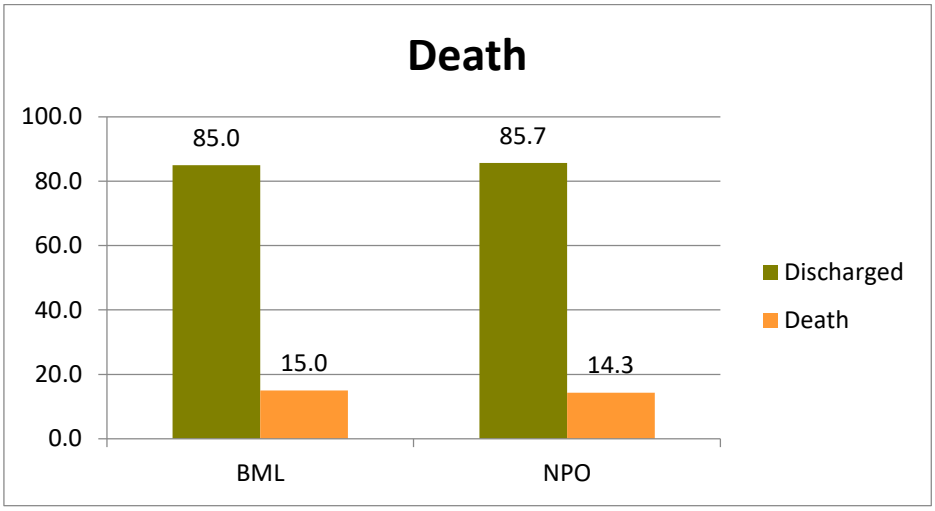
Variables	BML (n=40)	NPO (n=42)	RR (95% CI)	P Value
Septicaemia; N(%)	13 (32.5)	23 (54.8)	1.68 (1.01 -2.85)	.042
Jaundice; N(%)	09 (22.5)	18 (42.8)	1.91 (.97 –3.73)	.051
Electrolytes imbalance; N(%)	02 (5.0)	01 (2.4)	0.46 (.04 – 5.32)	.528
NEC; N(%)	02 (5.0)	02 (4.8)	0.95 (.13 – 7.09)	.960

Comparison of associated morbidities in two groups during treatment at hospital is illustrated in table IV. Intervention with Breast milk gastric lavage was found to be associated with significantly less proportion of septicaemia (P<.05). Among the neonates with BML less proportion developed neonatal jaundice but the difference was found to be marginally insignificant (P=.051). Prevalence of electrolytes imbalance and necrotizing enterocolotis (NEC) was in general low in both groups and the difference of proportion was also not statistically significant (P>.05).

Table V: Comparison of progress of neonates at hospital with or without BML

Category	BML	NPO	OR (95% CI)	P value
Improved; N (%)	18 (5 0.0%)	12 (40%)	1.2 (0.52 - 2.8)	P = 0.67
Deteriorated; N (%)	21(52.5%)	30 (71.43%)	0.9 (0.4 - 1.8)	P = 0.89

On admission, 30 and 36 neonates had some associated morbidities in NPO and BML group respectively. Among them 12/30 (40.0%) in NPO group and 18/36 (50.0%) in BML improved though it was not statistically significant (p >.05). On the other hand 30/42 (71.43%) in NPO group and 21/40 (52.5%) in BML group deteriorated which was statistically insignificant (p>.05).



χ^2=.008 df=1 P=.927

Figure 1: Comparison of fatalily

DISCUSSION

The current study had been carried out in special care baby unit at Dhaka Shishu Hospital. Patients usually came to this hospital for treatment from all over the country, so it can be assumed that medical problems among the preterm neonates of this study would reflect the scenario of Bangladesh. A total 82 preterm neonates were enrolled in this trial. Preterm neonates up to 12 hours of postnatal age were included in this study. Patel et al[11] and Barua et al[12] in their trail included preterm neonates within 4 hours of age. As there is no obstetric unit attached to this hospital and patients are referred from different canters, so age limit were extended up to 12 hours.

In this study, 40 neonates were allocated in to BML group and 42 in NPO group randomly by coin flipping method. Patel et al[11] randomized in their trail by computerized random number generator. The coin flipping

method was adopted in this trial with a view to allocate similar intervention in case of twin pregnancy. Total 17 neonates came from multiple pregnancies, among them 8 were in NPO group and 9 in BML group. In NPO group 52.4% were male and in BML group 60% were male, however no statistically significant difference was found in sex distribution in two groups (P>.05). This male preponderance was almost similar to Rashid et al[13] but reverse to the Patel et al[11] trial which showed female preponderance, 58% in NPO group and 53% in BML group were female respectively. Males are more cared in our society and this may be the cause of male preponderance of current study. In BML arm 40.0% were of low, 52.5% were of middle and 7.5% were of high socio-economic status. In NPO arm 47.6% were of low, 40.5% were of middle and 11.9% were of high socioeconomic status. No statistically significant difference was found in two groups in socioeconomic status (P>.05). Overal in both the groups most of the patients came from low and middle class family which is consistent with Islam et al[14] and there was also no statistically significant difference in place of residence distribution in two groups. Besides, both birth-weight and gestational age were also statistically similar in two groups in this trial. However the mean gestational age of BML group was 31.7 (±1.6) weeks and NPO group was 32.9 (±1.2) weeks; and mean birth weight was 1343.2 (±86.3) grams in BML group and 1360.5 (±74.1) grams in NPO group. But in compare to Patle's trial both the birth-weight and gestational age was found less in this study. In Patle's trial, mean gestational age was found 32.87(±2.02) weeks and 32(±2.3) weeks in BML and NPO group respectively and mean birth weight was found 1.43(±0.198) Kg and 1.37(±0.21) Kg. Regarding intra-uterine growth status, in NPO group 92.9% neonates were AGA and only 7.1% neonates were SGA; in BML group 85% neonates were AGA and 15% neonates were SGA. Statistical test failed to reveal any statistically significant difference in two groups. Comparison of associated morbidities was made between the two groups of neonates on admission. None of the prevalence of perinatal asphyxia, RDS, TTN, Hypothermia, Recurrent apnea, PDA and Shock differed between NPO and BML group statistically. Moreover in BML group had higher number of babies (90%) in compare to NPO group (71.43%) who were associated with some complications on admission, although the difference was statistically insignificant (Table II). These findings were also consistent with Patle's trial[11].

Current study facilitates the comparison of time required for successful tolerance of enterall feeding, achievement of full enteral feeding and duration of hospital stay in two groups. Neonates of BML group required fewer days (4.7±1.4) for successful tolerance to enteral feeding than the NPO group (6.4±1.4 days) and it was found statistically significant (p<.05). This finding was abeit longer than Patle's trial which showed 3.9±1.5 days and 5.4±2.6 days in BML and NPO group respectively. Days required for achievement of full enteral feeding was also less (9.53±2.7) in BML group than in NPO group (13.2±3.1) and it was also found

statistically significant. Most importantly neonates treated with BML stayed significantly fewer days at hospital than those in the NPO group. The average hospital stay of the neonates of BML group was 12.7 (± 6.6) and NPO group was 17.1 (± 4.5) days respectively.

There is clear evidence that promoting early enteral nutrition is beneficial. Pietz et al also shown that early enteral feeding prevents gut atrophy, appears to stimulate maturation of the gastrointestinal system, may actually enhance eventual feeding tolerance, and may reduce the incidence of NEC, especially when colostrums and human milk are used[15]. Among different theories, explaining the plausibility of early enteral feeding for low birth weight preterm neonates antioxidant theory is notable. Groneck and Speer[16] illustrated that premature infants are exposed to many possible sources of oxygen free radical production including high concentrations of inspired oxygen, frequent alterations in blood flow to major organs, and inflammation with accumulation of neutrophils and macrophages. Moreover, premature infants are known to have a poorly developed antioxidant system and may be at increased risk of radical damage[17].

Comparison of associated morbidities in two groups during treatment at hospital showed that intervention with breast milk gastric lavage was found to be associated with significantly less proportion of septicaemia (32.5%) than NPO group (54.8%). Similar low prevalence of jaundice is seen in BML group. This finding was consistent with Patle et al and Barua et al. Patle's trail found septicemia 55% in NPO group and 30% in BML group; and Barua's trail found septicemia 55% in NPO group and 22% in BML group. The low proportion of infection might be translated into the protective effect of such treatment against infection, and is attributable to immunologic and antimicrobial properties of breast milk and also supports the hypothesis that gut is often portal of entry in neonatal sepsis. Similar results of lowered rate of sepsis have been shown in studies that have used early MEN or early feeding by breast milk[18]. Lavage can also contribute by reducing adhesion of bacteria to the gut mucosa by virtue of presence of an array of oligosaccharide and glycoconjugates in breast milk thereby decreasing their entry into the circulation[19]. It also has the potential to prevent gastric bleeding, promote early resolution of an inflamed mucosa, protect against mucosal permeability and entry of organisms from inflamed gastric mucosa due to the anti-inflammatory properties of breast milk used for lavage. This shows that gastric bleeds need not be a deterrent to introduction of breast milk. On the contrary lavage with breast milk could assist recovery. The presence of milk in stomach may also stimulate release of enteral hormones particularly gastrin which has trophic effect on gastrointestinal tract thereby improving feeding tolerance later[20].

On admission, 30 and 36 neonates had some associated morbidities in NPO and BML group respectively. Of these 40.0% neonates in NPO group and 50.0% in BML showed improvement. Conversely, proportion of neonates experienced deterioration was also

more in NOP group (71.43%) than in BML group (52.5%). The consequence is likely to translate in to fatality. However comparison of fatality illustrates no significant difference in two groups. There were 6 deaths in each group. However, two in NPO group were due to NEC, one due to RDS and three due to sepsis; whereas in BML group two due to NEC, two due to RDS and two due to sepsis.

CONCUSSION:

Neonates of BML group required fewer days for successful tolerance of enteral feeding than the NPO group. Days required for achievement of full enteral feeding was also low in this group. Moreover they stayed significantly fewer days at hospital than those in the NPO group. Intervention with BML was found to be associated with significantly less proportion of septicaemia and low prevalence of jaundice. In course of treatment proportion of neonates experienced deterioration was more in NPO group than in BML group. However comparison of fatalily illustrates no significant difference in two groups. Hence comments can be inferred as BML starting within 12 hours of birth doesn't affect the fatal outcome of the premature neonates but it significantly raises the probability of improvement in health condition of low birth weight neonates by reducing morbidity.

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