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Hemodynamically stable very low birth neonates weight gain is affected by the early initiation of full enteral feedings compared to standard feeding

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Abstract:

BACKGROUND: Premature babies need to develop similarly to fetuses of the same gestational age. The majority of premature neonates experience a growth-restricted status while in the patent ductus arteriosus (PDA). Extrauterine growth failure is a significant barrier for infants with very low birth weight (VLBW).

MATERIALS AND METHODS: The study was conducted for six months at the Neonatology Unit, Department of Pediatrics, Coimbatore Medical College Hospital, Coimbatore, Tamil Nadu, India. Neonates with VLBW who met the inclusion criteria were assigned randomly to one of two feeding strategies, that is, full enteral feeding or partial feeding, based on the randomization sequence discovered by opening the sealed cover. The duration of stay, weight variation, neonatal variables, feeding intolerance, necrotizing enterocolitis (NEC), septicemia, apnea, newborn hyperbilirubinemia, PDA, hypoglycemia, intracranial bleeding, and mortality of neonatal recruits were all carefully evaluated.

RESULTS: Two thousand two hundred eighty-four neonates were hospitalized throughout the six-month trial period, and 408 had low birth weight. Three hundred forty-two babies were eliminated from the study due to hemodynamic instability, persistent respiratory distress, infections, metabolic issues, and congenital abnormalities. Sixty-six babies met the study's inclusion criteria, and thus participated in the study. Sixty-six newborns weighed between 1.251 and 1.500 kg. Randomly assigning intervention and control groups. Thirty-three newborns were assigned to group A (intervention) and another 33 to group B (control).

CONCLUSIONS: The study concluded that enteral feeding was effective, inexpensive, secure, and feasible. Early full enteral feeding reduced septicemia and infant hyperbilirubinemia. Thus, we must start enteral feeding as soon as possible to avoid inadequate nutrition in neonates with VLBW during a crucial growth period.

Keywords:

Intracranial hemorrhage, low birth weight, mortality, neonates, very low birth weight, weight gain

Introduction

The healthiest and most natural method of nourishing newborns is breastfeeding. This strategy is perfect for a baby's physical and emotional growth and for the mother's recovery. The American Academy of Paediatrics Nursing Work Group recommends exclusively breastfeeding since it provides adequate nutrients to maintain optimum growth, and the first six months of life are primarily devoted in development.[1] Premature babies need to develop similarly to fetuses of the same gestational age. However, most premature

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neonates experience a growth-restricted status while in the neonatal intensive care unit (NICU). Extrauterine growth failure is currently a significant barrier for infants with very low birth weight (VLBW).[2,3] Numerous studies have demonstrated that inadequate nutrition at the most crucial developmental stages of a neonate decreases brain cells and dendritic connections, thereby affecting cognitive and behavioral outcomes.

Numerous studies have found a correlation between early feeding and enhanced neurodevelopmental outcomes. If postnatal "nutritional shocks" are avoided, better results can be anticipated. The start of enteral feedings is frequently delayed out of concern for feeding problems. This leads to inadequate nutrition, which causes the neonate to enter a catabolic state, and growth failure. Regaining birth weight, avoiding growth failure, and achieving positive neurodevelopmental outcomes are all influenced mainly by optimal nutrition.[4,5]

Human milk contains various specific immunological components, and their benefits always outweigh the risks in relation to early feeding in preterm neonates.[6] Mother's milk is the ideal nutrition for neonates[7] because it reduces the incidence of feeding intolerance, necrotizing enterocolitis (NEC), and sepsis. Polyunsaturated fatty acids (PUFAs), platelet-activating factor (PAF)-acetylhydrolase (AH), secretory immunoglobulin A (IgA), lysozyme, and oligosaccharides are some substances in the mother's milk.[8] These elements improve the integrity and maturity of the gut-associated immune system and the gastrointestinal mucosa.[9] There is currently no established protocol for feeding procedures in newborns with VLBW.

Regarding the introduction and rate of advancement of enteral meals, feeding techniques vary widely. In neonates with VLBW, there are currently no evidence-based feeding protocols or procedures that are consistently used; rather, the variety of feeding practices is individual-based. The fetus continuously eats amniotic fluid while it is inside the uterus. The growth and development of the gastrointestinal system in pregnancy are significantly influenced by the amniotic fluid.[10] Enteral feedings after delivery encourage gastrointestinal tract motility and aid in hormone secretion. Early acquisition of full enteral feeding is crucial for neonates with very low birth weights. Full enteral nutrition aids in preventing micronutrient deficiencies, late-onset sepsis, liver failure, and growth failure.[11,12] In nations with low resources, where total parenteral nutrition is limited and sepsis is the misleading cause of morbidity and mortality, the early introduction of enteral feeding plays a critical role.

A clinically unclear issue is the initiation and progression of enteral feeding in babies with VLBW. The dread of feeding problems and the possibility of NEC are the main reasons enteral feeding is delayed. A little more than half of the newborns with VLBW develop extrauterine growth restriction (EUGR). Therefore, it is crucial to concentrate on early optimal feeding for infants with VLBW and encourage them to grow appropriately. In neonates with low meagre birth weight, optimal feeding significantly impacts both short- and long-term outcomes. Numerous meta-analyses and systematic reviews advise early initiation of enteral feeding and quick feeding process for gestational age babies and neonates with intrauterine growth restriction (IUGR).[13] Because feeding methods fluctuate across hospitals and even within the same neonatal units, there is a standardized feed deficient for infants with extremely low birth weight in the literature. This results in differences in growth rates, growth failure, and various feed-related issues. The majority of feeding guidelines used in newborn units today are not supported by research; rather, they are solely based on personal experience or unit protocols. This randomized control trial (RCT) was conducted to compare the effectiveness of partial feeding with partial parenteral nutrition in hemodynamically stable babies with VLBW to the risks and advantages of complete enteral feeding beginning on the first day of life.

Therefore, it is imperative to study the attainment of full enteral feeding using just human milk on the first day. This study boosts postpartum women's confidence in lactation maintenance and dispels staff members' misconceptions about various perceived barriers to starting and continuing enteral feedings.

Material and Methods

Study design and setting

The study was conducted as an open-labelled RCT at the Neonatology Unit, Department of Pediatrics, Coimbatore Medical College Hospital, Coimbatore, Tamil Nadu, India for six months.

Study participants and sampling

The sample size was calculated with the hypothesis that initiating full enteral feeding with breast milk on neonates with VLBW was associated with rapid weight gain. It was assumed that neonates who underwent full enteral feeding regained their birth weight in 13 days with a standard deviation of 2 days and neonates who underwent partial feeding regained their birth weight in 15 days with a standard deviation of 2.5 days with a significance level of 5% ($\alpha = 0.05$) and the power of 80% ($\beta = 0.2$). The required sample size for the two groups was 30 in each group. We enrolled 66 neonates in the trial after randomization.

Recruitment and randomization

Before recruiting, parents or caregivers were told the specifics and significance of the study, as well as the intervention and safety. They received written consent in their native language. They were explained the relevance, advantages, and potential negative effects of experimental study.

Both the common language and the individual's native tongue were offered on the consent and information form. Neonatal subjects were randomized and enrolled in the trial after being informed and granted consent.

In accordance with the randomization sequence discovered by opening the sealed cover, neonates with VLBW who met the inclusion criteria were assigned at random to one of two feeding strategies: full enteral feeding or partial feeding. The paper in the envelope, to which the researcher was blinded, revealed whether the neonate belonged to group A (intervention) or group B (control). Neonatal recruits were carefully evaluated for the duration of the stay, weight variation, neonatal variables, intolerance to feeding, NEC, septicemia, apnea, newborn hyperbilirubinemia, patent ductus arteriosus (PDA), hypoglycemia, intracranial bleeding, and mortality.

Results

During the six-month trial period, 2284 neonates were hospitalized, of which 408 were found to have VLBW. These eligibility of these newborns was evaluated. Due to hemodynamic instability, chronic respiratory distress, infections, metabolic problems, and congenital defects, 342 newborns were eliminated. By using inclusion criteria, only 66 newborns were found to be suitable and participated in the study. These newborns were categorized based on their weight at delivery. Twenty-one neonates and 45 neonates under the average weights of 1.251 to 1.500 kg were among the 66 neonates. Thirty-three neonates were included in the full enteral feeding group (group A or intervention group), and the other 33 neonates were assigned to the partial feeding group (group B or control group). Fortunately, neither the intervention group nor the control group experienced any deaths.

Duration of hospital stay

The duration of hospital stay of the full enteral feeding group was significantly shorter (15.30 ± 2.78 days) than that of the partial feeding group (18.30 ± 3.17 days). This was primarily due to the rapid weight gain in the full enteral feeding group (34.90 ± 6.18 g/day) compared to the partial feeding group (22.89 ± 4.78 g/day). The difference in hospital days between group A and group B was statistically significant [Table 1].

Table 1: Mean duration of hospital stay

	Mean	SD	SE	95% CI for mean		Min.	Max.	Sig.
				Lower	Upper			
Enteral group A	15.3	2.8	0.5	14.32	16.29	10	19	<0.001
Standard group B	18.3	3.2	0.6	17.18	19.43	12	24	
Total	16.8	3.3	0.4	15.99	17.62	10	24	

Neonatal variables

It is possible that a newborn's demographics will affect how quickly they gain weight. Therefore, it is confirmed that these variables were distributed equally and no statistical disagreement between the groups was found [Table 2].

Rate of weight variation in neonates

When compared to newborns with VLBW receiving partial feeding with partial parenteral nutrition, the rate of weight gain at the time of discharge in hemodynamically stable newborns with VLBW receiving full enteral feeding from the first day of life was higher.

Six of the 66 recruited neonates were excluded from the study (two from group A due to feeding intolerance, one from group B due to feeding intolerance, two from Group B due to symptoms of clinical sepsis, one from Group B due to opening up of PAD). As a result, weight variation was calculated from 60 hemodynamically stable neonates with VLBW who remained in their respective groups until the study's conclusion [Table 3].

From the lowest recorded weight after the weight loss phase to the discharge weight, group A (full enteral feeding) gained 34.90 ± 6.18 g per day. By excluding the weight loss phase, this parameter was calculated. From the lowest recorded weight after the weight loss phase to the discharge weight, group B gained 22.89 ± 4.78 g per day.

Observation study of the various clinical conditions of neonate's intolerance to feeding

After the first week of life, two newborns in the complete enteral feeding group and one newborn in the partial feeding group exhibited signs of feeding intolerance. These neonates were removed from the trial due to frequent skipping of meals and the requirement for extensive fluid administration even though subsequent examination did not identify the symptoms of NEC or sepsis. The incidence of feeding intolerance does not statistically differ between the two groups; however, in our study, the complete enteral feeding group experienced more feeding intolerance than the partial feeding group [Table 4].

Necrotizing enterocolitis

In this trial, neither the full feeding group nor the partial feeding group of infants had NEC. Due to the

Table 2: Association of baseline neonatal variables

Variables	Enteral Group A *n*=33	%	Standard Group B *n*=33	%	Sig.
Birth weight (g)	1304.40±124.60		1324.70±180.66		>0.05
Gender					
Male	15	45%	15	45%	>0.05
Female	18	55%	18	55%	
Gestational Age (Weeks)					
28-32	30	91%	23	70%	>0.05
>32	3	9%	9	27%	
<28	0	0%	1	3%	
Growth Status					
AGA (Appropriate For Gestational Age)	28	85%	25	76%	>0.05
SGA (Small for Gestational Age)	5	15%	8	24%	
Mode of Deliveries					
NVD (Normal Vaginal Delivery)	9	27%	5	15%	>0.05
AVD (Assisted Vaginal Delivery	0	0%	0	0%	
LSCS (A Lower Segment Caesarean Section)	24	73%	28	85%	
Apgar Score					
>7 (5 min)	33	100%	33	100%	>0.05
<7 (5 min)	0	0%	0	0%	
High capacity (HC) on admission					
HC on admission	27.88±1.18		28.0±1.54		>0.05
Length on admission					
Length on admission	37.76±1.28		38.17±1.51		>0.05

Table 3: Rate of weight variation of neonates from first day of life to discharge from the clinic

	Groups	Mean	SD	SE	95% CI for Mean		Min.	Max.	Sig.
					Lower	Upper			
Weight gain starts from birth	A	7.71	1.5	0.3	7.15	8.27	5	12	<0.001
	B	9.31	1.7	0.3	8.66	9.96	6	13	
Rate of weight gain from Low birth weight (LRW)	C	34.9	6.2	1.1	32.63	37.16	22	45	<0.001
	B	22.9	4.8	0.9	21.07	24.71	14	34	
Rate of weight gain from birth weight	A	7.69	2.8	0.5	6.66	8.72	4.2	16	<0.05
	B	5.89	2.8	0.5	4.81	6.96	0.5	14	

*Calculated only in the recruited neonates who were not excluded during the study period

possibility of developing NEC with early feeding, the introduction of enteral feeding was generally postponed. Our investigation demonstrated that there was no direct correlation between the occurrence of NEC and early enteral feeding.

Septicemia

Two newborns in the group receiving partial feeding showed signs of sepsis, and additional testing revealed septicemia. None of the newborns in the group receiving full enteral feeding experienced septicemia.

Apnea

One incident of apnea occurred in one newborn from each group, but it was resolved with the right placement and stimulation. Therefore, those receiving full feeding and those receiving limited feeding have an equal likelihood of developing apnea. The incidence of apnea did not differ statistically significantly in our study.

Newborn hyperbilirubinemia

From three to six days of life, 10 newborns in the complete feeding group and nine in the enteral feeding group developed neonatal hyperbilirubinemia (NNH), necessitating only short-term phototherapy. These newborns were not disqualified from the investigation. The incidence of NNH in the partial feeding group was twice as high as in the full feeding group, which was a statistically significant difference between the two groups. This may be explained by the full enteral feeding group's improved enterohepatic circulation which lowers the incidence of NNH.

Patent ductus arteriosus

One baby in the partial feeding group experienced ductal opening on the third day of life. Because of the neonate's unstable hemodynamic condition, she was removed from the study and placed on a fluid restriction regimen. No neonates in the full enteral feeding group experienced these problems, which could be attributed to increased

Table 4: A study of observations of the different clinical conditions on newborns

Variables	Enteral Group A *n*=33	%	Standard Group B *n*=33	%	Sig.
Duration of hospital stay	15.30±2.78		18.30±3.17		<0.001
Feeding intolerance					
No	31	94%	32	97%	>0.05
Yes	2	6%	1	3%	
Hypoglycemia					
No	32	97%	32	97%	>0.05
Episode 2	1	3%	1	3%	
Episode 3	0	0%	0	0%	
Sepsis					
No	33	100%	31	94%	<0.05
Yes	0	0%	2	6%	
NEC					
No	33	100%	33	100%	>0.05
Yes	0	0%	0	0%	
ICH					
No	33	100%	33	100%	>0.05
Yes	0	0%	0	0%	
PDA					
No	33	100%	32	97%	>0.05
Yes	0	0%	1	3%	
NNH					
No	23	70%	13	39%	<0.05
Yes	10	30%	20	61%	
Apnea					
No	32	97%	32	97%	>0.05
Positioning and Stimulation	1	3%	1	3%	
PPV (Positive presser ventilation)	0	0%	0	0%	
Intubation	0	0%	0	0%	

intravascular volume in group B neonates who received less enteral feed (20 ml/kg/day) and more intravenous fluid administration (60 ml/kg/day) on the first day compared to group A neonates who received a total of 80 ml/kg/day as enteral feeding. Group B neonates also experienced gradual enteral feeding progression, necessitating intravenous fluid.

Hypoglycemia

Out of 66 neonates, one from each group experienced asymptomatic hypoglycemia once. These infants was treated according to the unit's procedure, and they were kept in their designated group and under close observation; no other cases of hypoglycemia were noted.

Intracranial bleeding

Throughout the trial period, there were no intracranial hemorrhages in either group of newborns. In our study, there was no correlation between feeding methods and the occurrence of cerebral bleeding.

Mortality

No recruited neonate died during the study period, in either the full enteral feeding or partial feeding groups [Table 5].

Table 5: Mortality in study subjects

Parameter	Enteral Feeding Group A *n*=33	%	Standard Feeding Group B *n*=33	%	Sig.
Mortality	0	0%	0	0%	>0.05

Discussion

This RCT compared the full enteral feeding strategy with the partial feeding strategy in hemodynamically stable neonates with VLBW and found that the full enteral feeding group's rate of weight gain was noticeably higher. As a result, the full enteral feeding group's hospital stay was shorter. With no appreciable change in the incidence of hypoglycemia, apnea, feeding intolerance, NEC, cerebral hemorrhage, or death, complete enteral feeding can be deemed as quite safe. Septicemia, PAD opening, and NNH were more common in the partial feeding group compared to the full enteral feeding group.

This study concluded that the rate of weight gain in neonates of the full enteral feeding group was 34.90 ± 6.18 g/day during the weight gaining phase while that of the partial feeding group was 22.89 ± 4.78 g/day ($P < 0.001$). This disparity was statistically remarkable.

According to Sanghvi *et al*.,[14] newborns receiving full enteral nutrition and weighing between 1200 and 1500 g gained weight at an astonishingly rapid rate, regaining their birth weight seven days earlier than neonates in the control group. In our study, full enteral feeding neonates gained an average of 35.25 ± 6.07 g per day compared to the control group's average weight growth of 23.20 ± 5.14 g per day.

Statistically speaking, it is notable that neonates in the partial feeding group spent more time in the hospital than those in the full enteral feeding group. In comparison to the partial feeding group, which was hospitalized for 18.30 ± 3.17 g/days, the full enteral feeding group was hospitalized for 15.30 ± 2.78 g/days. This was most likely caused by the intervention group's high pace of weight gain and the control group's lower frequency of morbidities.

Caple *et al*.[15] compared rapid and slow feeding progression for hospital stay and intravenous (IV) fluid days. He concluded that neonates in the rapid feeding progression group spent fewer days in the hospital and required fewer IV fluids than the slow feeding progression group, though the difference was not statistically significant.

Although the partial feeding group was more likely to develop septicemia than the full enteral feeding group, the difference was statistically insignificant. This vulnerability was likely brought on by the requirement for an IV catheter, higher handling, a lack of aseptic IV fluid preparation, and receiving less breast milk which contained immunomodulatory factors in the partial feeding group. Compared to other studies of a comparable nature, our study's incidence of septicemia was very low. This may have been because only breast milk was utilized in the full enteral feeding and partial feeding groups.

Lavoie *et al*.[16] studied the relationship between initiation of early enteral feeding and coagulase-negative staphylococci (CoNS) septicemia in a trial involving infants with VLBW. He demonstrated that early enteral nutrition reduced the risk of CoNS septicemia and that these neonates were able to take in a full feed earlier than control groups. When the early enteral feed began using formula milk, this study also provided a significant conclusion that there was no difference in the incidence of CoNS bacteremia compared to the control group.

In neither of the groups of newborns that we studied did NEC occur. The exclusive use of human milk may have been the cause.

Limitations and recommendation

Our unit's supply of pasteurized donor human milk (PDHM) was not divided between term and pre-term milk. Therefore, changes in the protein and caloric content of PDHM may have had an effect on the study's primary and secondary outcomes. A larger sample size may have accurately represented the occurrence of the morbidities investigated in our experiment. In our trial, the long-term neurological prognosis was not examined. We excluded long-term anthropometric parameters from our analysis.

Only a small number of investigations were carried out utilizing only human milk. One of them was our study. Our neonatal unit's human milk bank provided the necessary amount of breast milk for the investigation. Our research was a well-planned RCT with a sizeable sample. The full enteral feeding group can be distinguished from the partial feeding group by their strict adherence to the feeding strategies.

Implications for practice

In newborns with VLBW and who are hemodynamically stable, full enteral feeding can be initiated from the first day of life with caution and close monitoring. Early complete enteral feeding with standardized methods lowers the incidence of morbidities related to feeding. The policy of exclusive breastfeeding would be supported by the strategy of full feeding from the baby's first day of life. Pre-term and term milk categories in human milk banks will aid in more precise distribution to the right candidate. This low-cost approach to premature neonatal care is crucial in environments with limited resources.

Conclusions

Early complete enteral feeding with only breast milk from the first day of life increases the weight growth rate in hemodynamically stable neonates with VLBW. Necrotizing enterocolitis and other morbidities are not more common when complete enteral feeding is started earlier. The study found that implementing a full enteral feeding plan is effective, affordable, secure, and practical. Practices that encourage complete enteral feeding earlier in life decrease the risk of septicemia and newborn hyperbilirubinemia. Our analysis concluded that this tactic had unintended advantages. The results of this early complete enteral feeding technique are superior even for small for gestational age (SGA) and IUGR infants. Therefore, it would be wise to start complete enteral feeding as soon as possible to prevent inadequate nutrition during a crucial growth period.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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