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Original Article

To study the effect of early versus late trophic feeding in preterm neonates with mild respiratory distress syndrome

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ABSTRACT

Background: The respiratory distress syndrome in preterm neonates is mostly due to surfactant deficiency. The incidence and severity of respiratory distress syndrome are related inversely to the gestational age of the newborn infant. The early nutritional support, in these preterm neonates with respiratory distress, prevents complications, and maintains positive energy balance. **Objective:** The aim was to study the effect of early versus late trophic feeding in preterm neonates with mild respiratory distress syndrome. **Materials and Methods:** This was a prospective study conducted in babies admitted to neonatal intensive care unit (NICU) from January 2013 to January 2016 in Military Zonal Hospital. A total of 200 babies with a gestational age <37 weeks and birth weight between 1200 and 2000 g were evaluated and divided into the early and late group. In early group, the nutritional support in the form of expressed breast milk 15 ml/kg/day in preterm neonates with mild respiratory distress was given within 24 h of life and in late group after 48 h of life. **Results:** The early nutritional support in preterm neonates with mild respiratory distress decreases the requirement of oxygen and caffeine, helps to reach early full feeds, decrease in the incidence of necrotizing enterocolitis, early weight gain and early discharge from hospital. **Conclusion:** In our study findings, certainly suggest the benefits of early trophic feed compared to late in preterm neonates with mild respiratory distress. It seems that better education of mothers for expressing their milk and handing to NICU for use in trophic feeding is important. However the large randomized controlled trial is required to validate the above findings.

Key words: *Expressed breast milk, Preterm, Respiratory distress, Trophic*

Preterm infants have immature gastrointestinal tracts (including immature motility patterns and delayed transit), so enteral feeding is often delayed by days after birth as a protective strategy for fear of feeding intolerance and to reduce the risk of necrotizing enterocolitis however with lots studies mentioned in the literature suggest to start minimal enteral feed with expressed breast milk to prime the gut to prevent intestinal mucosal atrophy [1].

The early nutritional support within 24 h of life in the form of expressed breast milk 15 ml/kg/day in preterm neonates with mild respiratory distress decreases the requirement of oxygen and caffeine, helps to reach early full feeds, decrease in incidence of necrotizing enterocolitis, early weight gain, and early discharge from hospital [1,2]. The objective of this study was to assess the effect of early versus late trophic feeding in preterm neonates with mild respiratory distress who were hemodynamically stable.

MATERIALS AND METHODS

Sample size

This was a prospective study conducted in babies admitted to neonatal intensive care unit (NICU) from January 2013 to January 2016 in Military Zonal Hospital with an annual delivery rate around 950. Around 200 babies with a gestational age <37 weeks and birth weight between 1200 and 2000 g were evaluated and were divided into the early and late group.

Inclusion criteria

Preterm babies <37 weeks and birth weight between 1200 and 2000 g with mild respiratory distress (Downes score <4) and hemodynamically stable.

Exclusion criteria

Preterm babies with birth weight <1200 g and with severe respiratory distress and those who required total parenteral nutrition. The other causes of respiratory distress were also excluded from the study.

The diagnosis of respiratory distress was made on clinical examination (Downes score) and chest X-ray. Few babies (20 in the early group and 25 in late group) required nasal continuous positive airway pressure (CPAP), and feed was started when CPAP

was weaned to free flow oxygen within 24 h in the early group and after 48 h in late group. The ethical clearance and written informed consent of the parents were obtained before the start of the study. 100 preterm neonates with mild respiratory distress were given 15 ml/kg/day of expressed breast milk by orogastric tube within 24 h of life (early group) which was gradually increased, and other 100 neonates were given enteral feeds after 48 h of life. The feed was started with orogastric tube 15 ml/kg/day divided every 2 hourly and feed residue was checked before each feeds. The feed was gradually stepped up by 10 ml/kg/day as per tolerance. The two groups were similar in terms of birth weight, APGAR score, gestational age, mode of delivery, and diagnosis of respiratory distress syndrome. The outcome was measured in terms of time to reach full enteral feeding, oxygen requirement, weight gain, length of hospital stay, and complications.

The collected data were analyzed using SPSS version 16 (Statistical Package for Social Sciences). For data analysis mean, standard deviation, Student's t-test, and Chi-square test were used. $p<0.05$ with a confidence interval of 95% was considered statistically significant.

RESULTS

There were no statistically significant differences in the clinical characteristics of infants in the two groups (Tables 1 and 2). However, there was statistically significant difference in outcome. The time to gain birth weight 12.00 (6-36) days versus 22.00 (19-33) days ($p<0.021$), age at maximal weight loss 12 (5-15) days versus 17 (15-21) days ($p=0.027$), duration of oxygen requirement 12.00 (7-22) days versus 25 (22-40) days ($p<0.012$), caffeine requirement 22 (6-33) days versus 40 (26-52) days ($p=0.006$), time to reach full feeds 14.2 (10-22) days versus 24 (20-36) days ($p=0.002$), hospital stay 22.00 (20-30) days versus 35 (32-40) ($p<0.036$)) were significantly shorter in early compared to late trophic feeding group (Table 3). The complications such as chronic lung disease 03 versus 06 ($p=0.003$), retinopathy of prematurity (ROP) 03 versus 08 ($p=0.002$), necrotizing enterocolitis 3 versus 5 ($p=0.045$), patent ductus arteriosus 03 versus 07 ($p=0.271$), intraventricular hemorrhage (IVH) 02 versus 05 ($p=0.018$) compared to late group, sepsis 10 versus 23 ($p=0.012$) (Table 4).

Table 1: Clinical parameters of preterm neonates of early versus late group

Clinical parameters	(n=100)		p value
	Early group	Late group	
Gestational age (weeks)			
Mean±SD	30.2±1.9	30.4±1.8	0.76
Median (range)	30 (30-36)	30 (30-34)	0.66
Birth weight (g)			
Mean±SD	1216±240	1200±240	0.74
Median (range)	1240 (1200-2000)	1210 (1200-1700)	0.72
Apgar (1 min)	5	5	0.73
Median (range)	4-8	3-9	
Apgar (5 min)	7	8	0.75
Median (range)	6-9	6-9	
Mode of delivery			
Normal	75	70	0.49
LSCS	25	30	
Male/female	60/40	65/35	
Respiratory distress (mild)	100	100	

LSCS: Lower segment Cesarian section, SD: Standard deviation

DISCUSSION

To determine the best method for feeding in preterm neonates admitted to the NICUs remains a big challenge for the caregiver. Preterm infants often experience feeding difficulties primarily because of the immaturity of their gastrointestinal systems. It has been well-established that inadequate provision of enteral nutrition in very low birth weight neonates leads to suboptimal growth at discharge. Early introduction of enteral feeding in preterm infants is associated with improved growth, better nitrogen balance, and maintenance of the intestinal barrier and better outcome. The introduction of early trophic feeds (within 24 h of birth) in the form of expressed breast milk in the amount of 15 ml/kg/day in hemodynamically stable preterm babies with mild respiratory distress have many beneficial outcome. Lack of enteral nutrients may diminish gastrointestinal functional and structural integrity by diminishing hormonal activity, growth of intestinal mucosa, and nutrient absorption. A prolonged delay in starting feeds in preterm neonates may be partly responsible for the common problem of feeding intolerance in these tiny newborns [3]. These problems may then hinder the transition from parenteral to enteral nutrition, and thus prolonged hospital stay [4,5]. In our study, we introduced trophic feeds (expressed breast milk) by orogastric tube within 24 h of life in early group (range 4-24 h) and after 48 h in late group (range 48-72 h) (Table 2). The gestational age and weight in early group (30-36 weeks/1200-2000 g) and late group (30-34 weeks/1200-1700 g) with male preponderance are shown in Table 1. There were no statistically significant differences in the clinical characteristics of infants in the two groups (Tables 1 and 2). The time to regain birth weight was significantly lower in early group than late group ($p<0.021$) which is comparable to study conducted by Troche et al. [6], which mentions the early weight gain in more than 90% of neonates who were given early trophic feeds. The current study represented that preterm neonates that fed early their mean birth weight was significantly faster than those fed late. These results consistent with Salhotra and Ramji [7] who reported that infants fed early regained their birth weight faster than those fed lately, with a statistically significant difference between the two groups. In addition, these current results are consistent with Dunn et al. [8] who mentioned that low birth weight neonates who were fed earlier with minimal feeds had gained weight faster as compared to neonates who were fed late. In contrary, Leaf et al. [9] reported that early trophic feeds had no significant effect on weight gain. The other advantages were age at maximal weight loss was earlier ($p=0.027$), duration of oxygen requirement was lesser ($p<0.012$), caffeine requirement for lesser days ($p=0.006$),

Table 2: Trophic feeding administration in early and late feeding group

Parameters	n=100	
	Early group (EBM within 24 h)	Late group (EBM after 48 h)
Hours of life for EBM administration	10 h (4-24 h)	50 h (48-72 h)
PICC line (number of neonates)	25	35
UV line	10	15
Surfactant (administration h)	1 (0.5-3.0) n=15	2 (1.8-6) n=16
Initial fluid administration (ml/kg/day)	80 (60-80)	85 (60-100)
Caffeine administration (days)	30 (25-40)	45 (35-60)
NCPAP (number of babies)	20	25

UV: Umbilical vein, PICC: Peripherally inserted central catheter, NCPAP: Nasal continuous positive airway pressure

Table 3: Outcome parameters of early versus late group

Parameters	n=100		
	Early group	Late group	p value
Time to reach full feeds (days)	14.2 (8.2-28.2)	24 (20-36)	0.001
Time to reach minimal enteral feeds (80 ml/kg/day)	10.2 (10-22)	30 (25-30)	0.002
Oxygen requirement (days)	12 (7-22)	25 (22-40)	0.012
Caffeine requirement no of babies	22	40	0.006
Age at maximal weight loss (days)	12 (5-15)	17 (15-21)	0.027
Weight gain after d-10 of life in g	25 (10-36)	20 (10-24)	0.021
Regain birth weight (days)	12 (10-18)	22 (19-33)	0.001
Hospital stay required (days)	22 (20-30)	35 (32-40)	0.036

Table 4: Complications of early versus late group

Disease Condition	n=100		
	Early group	Late group	p value
Chronic lung disease	03	06	0.003
ROP	03	08	0.002
Necrotising enterocolitis	03	05	0.045
Patent ductus arteriosus	03	07	0.271
Intraventricular haemorrhage	02	05	0.018
Sepsis	10	23	0.012

ROP: Retinopathy of prematurity

time to reach full feeds was early (p=0.002), lesser hospital stay (p<0.036) in early than late trophic feeding group (Table 3).

Two systematic reviews on the matter revealed that trophic feeding resulted in significant reduction in stay days [10,11]. In the current study, neonates in early group were associated with a decreased mean in length of hospital stay than late group which is a valuable finding. The complications such as chronic lung disease (p=0.003), ROP (p=0.002), necrotizing enterocolitis (p=0.045), patent ductus arteriosus (p=0.271), IVH (p=0.018) compared to late group, sepsis (p=0.012) (Table 4) were higher in late group than early group which is similar to study done by Ho et al. [12]. The high incidence of IVH in late group could be sepsis or prematurity-related; however, it was Grade 1 which resolved without active intervention. Furthermore, the ROP was Stage 1 which gradually resolved on follow-up. Bombell S reviewed the literature regarding early nutritional support in preterm very low birth weight infants and concluded that early nutritional support acted as a mediator between critical illness the 1st weeks of life and later growth and outcomes which include bronchopulmonary dysplasia, late onset sepsis, hospital stays, neurodevelopmental impairment, cognition, and death [13].

In our study, the introduction of trophic feeds within 24 h of life in preterm neonates with mild respiratory distress has made a significant difference in the outcome compared to the late group. This study is one of the different studies compared to those mentioned in the literature; however, more randomized controlled trials (RCTs) considering enteral feeding initiation in different time zones after birth are recommended. This study has few limitations: (1) The other causes of respiratory distress were not included in the study, (2) the sample size is small and further RCT is required to validate the findings.

CONCLUSION

In our study findings, certainly suggest the benefits of early trophic feed compared to late in preterm neonates with mild respiratory distress. Thus, early trophic feeds in preterm neonates with mild respiratory distress shorten time to gain birth weight, early feed tolerance, less duration of oxygen requirement, lesser hospital stay, and lesser complications. It seems that better education of mothers for expressing their milk and handing to NICU for use in trophic feeding is important. However, large RCT is required to validate the above findings.

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