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IMPACT OF EARLY TROPHIC FEEDING VERSUS DELAYED INITIATION OF FEEDING IN VERY PRETERM, VERY LOW BIRTH WEIGHT BABIES ON INCIDENCE OF SEPSIS

Neonatology

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ABSTRACT

OBJECTIVE: The objective of the study is to evaluate the impact of feed introduction and feed advancement on the rate of sepsis and duration of NICU stay

DESIGN: Prospective, hospital based, observational study

SETTING: Tertiary referral centre with level 3 neonatal care. Study period was one year, from June 1st 2017 to May 31st 2018 and included a total of 102 neonates (preterm babies <= 32 weeks gestational age and birth weight <= 1500 grams) who were admitted in neonatal intensive care unit

RESULTS: Out of the 102 preterm neonates included in the study , 37 babies had sepsis (probable sepsis + culture proven sepsis = 36.2%). Mean gestational age in the study population was 29.9 weeks (SD = 2.02) and mean birth weight was 1220.75 gm (SD=241.09). In the late feeding group , 22 out of 35 babies (62.8%) had sepsis whereas in early feeding group , 15 out of 67 babies (22.38%) had sepsis. Among the late feeders , 5 out of 35 babies died (14.28%) whereas only 1 baby out of 67 early feeders did not survive (1.49%).

CONCLUSON: Early introduction of enteral feeds in very preterm , very low birth weight babies resulted in decreased incidence of sepsis. This, in turn , has decreased duration of hospital stay and improved survival

KEYWORDS

Neonatal sepsis, Gestational Age

INTRODUCTION

The term 'neonatal sepsis' is described as a systemic condition of bacterial, viral, or fungal (yeast) origin that is associated with haemodynamic changes and other clinical manifestations and results in substantial morbidity and mortality. Neonatal sepsis is an important cause of significant morbidity and mortality. Precise estimates of neonatal sepsis burden vary by setting. Differing estimates of disease burden have been reported from high-income countries compared with reports from low-income and middle-income countries.

Preterm babies and Babies with low birth weight are particularly vulnerable for infection. Early introduction of enteral feeding in preterm infants is associated with improved growth, better nitrogen balance, and maintenance of the intestinal barrier.[1–3] Hylander et al, demonstrated a protective effect of human milk feedings against infection and sepsis/meningitis for VLBW infants during NICU hospitalization and further underscore the potential immunologic benefit of providing maternally expressed human milk to hospitalized VLBW infants[7]

The burden of neonatal sepsis is huge in India. Hospital-based studies suggest an incidence of 30 per 1000 live births,[4] whereas community-based studies indicate an incidence of 2.7–17% of all live births.[4,5] Nearly, one-fifth of neonates with sepsis die in the hospital; the figure rises to up to 50% for those with culture proven sepsis (Delhi Neonatal Infection Study Group; personal communication). They stay longer in hospital, consume more resources, and are also at high risk of developing major neurodevelopmental disabilities at later stage.[6]

In this study , we evaluate the impact of feed introduction and feed advancement on the rate of sepsis and duration of NICU stay and survival outcome

MATERIALS AND METHODS

A one year prospective, hospital based, observational study in Neonatal intensive care unit at a tertiary referral hospital during the period from June 1st 2017 to May 31st 2018.

Those babies for whom enteral feeding were started within 72 hours are included in early feeding group and after 72 hours were included in late feeding group. IV fluids/TPN were given for the second group till the enteral feeds are initiated. Trophic feeding started as 10-15 ml/kg/day is divided into equal aliquots and administered by gavage feeding at 2 hourly feeding schedule. Baby is monitored for any evidence of feed intolerance .

Naso/Orogastric tube feeding given depending on gestational age and clinical status of the infants for initiation of enteral feeds. In any baby who develops clinical signs of sepsis or sepsis screen is positive, blood will be sent for culture and sensitivity.

Inclusion criteria

1. Gestational age less than or equal to 32 completed weeks (32 weeks +6days) (by antenatal USG or clinical); and
2. Birth weight less than or equal to 1500 grams

Exclusion Criteria

1. Major congenital anomalies.
2. Surgical conditions where feeding is contraindicated like tracheo-esophageal fistula, congenital diaphragmatic hernia, intestinal atresia, malrotation etc.

Prior to the commencement, ethical clearance was obtained for the study from Institutional Ethics Committee

RESULTS

A total of 102 preterm babies were included in the study. There were 67 preterms(65.7%) in early feeding group and 35 preterms(34.3%) in late feeding group. There were 50 males in and 52 female babies in the study population

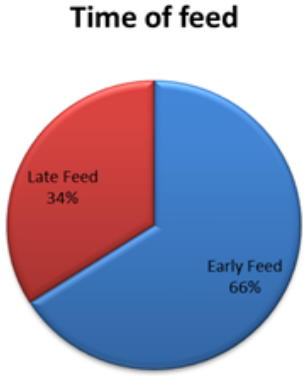

Fig 1: Distribution according to Time of feed

In the early feeding group, 36 babies were females (53.7%) as compared to 31 males (46.2%). In the late feeding group , 16 babies were females (45.7%) as compared to 19 males (54.2%)

Gestational age of newborns included in the study was < = 32 completed weeks (32+6 days). Most of the neonates were with gestational age between 30 to 32 weeks , n =55 (53.9 %) followed by 28 - 30 weeks , n= 34 (33.3%) and few cases were less than 28 weeks , n = 13 (12.7%).

Mean gestational age in the study population was 29.9 weeks with SD = 2.02

Table 1 : Association between time of feeding and Gestational age

Gestational Age	Time of Feeding		Total
	Early Feed	Late Feed	
<28 weeks	4	9	13
28-30 weeks	23	11	34
30-32 weeks	40	15	55
Total	67	35	102

Chi-square = 8.590; df=2; p=0.014

It was noted that mean gestational age was higher in the early feeding group as compared to late feeding group. Of the 13 babies who were born <28 weeks of GA , only 4 babies were in early feeding group (31%) as compared to 23 out 34 babies(67%) between 28- 30 weeks GA and 40 out of 55 babies (72.7%) in the 30 – 32 weeks GA. This difference was statistically significant

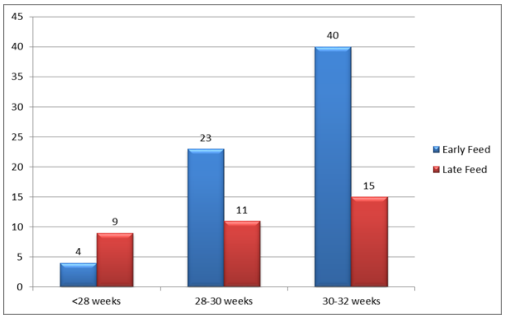

Fig 2 : Distribution of feed initiation with gestational age

Babies with birth weights < 1500g were included in the study. 56% of the babies were between 1200 - 1500 gms , 25% were between 1000 – 1200 gms and 19% were below 1000 gms. Mean birth weight in the study population was 1220.75 gms with a SD of 241.09.

Table 2 : Association between time of feeding and birth weight

Birth weight	Time of Feeding		Total
	Early Feed	Late Feed	
<1000	9	10	19
1000 - 1200	15	11	26
1200 - 1500	43	14	57
Total	67	35	102

Chi-square = 5.362; df=2; p=0.069

On analysing the primary outcome, among the 102 preterm neonates in our study 37 developed sepsis(36.27%). Sepsis included probable sepsis and culture proven sepsis. Culture proven sepsis was 14.7 % and probable sepsis was 21.57 %.

Late feeding group showed 64.5% of sepsis whereas early feeding group had only 22%. Out of 15 culture proven cases 9 were in late feeding group and 6 in early feeding group. Organisms isolated mainly included Klebsiella , pseudomonas, acinetobacter and staphylococcus. It was also noted that 8 cases of fungal sepsis were identified (Candida Sp.) . P value is significant (<0.001)

Table 3: Association between time of feeding and development of sepsis

	Time of Feeding		Total
	Early Feed	Late Feed	
No Sepsis	52	13	65
Sepsis with Negative Culture	9	13	22
Sepsis with Positive culture	6	9	15
Total	67	35	102

Chi-square = 16.968; df=2; p<0.001

There were a total of 15 culture proven sepsis. 9 of them were late feeders and 6 of them were early feeders. In late feeding group , 3 babies had Acinetobacter sepsis, 2 babies had Klebsiella and fungal sepsis, 2 babies had fungal sepsis alone, 2 babies had Staphylococcus aureus sepsis. In the early feeding group, 1 baby had Klebsiella and fungal sepsis, 1 baby had Klebsiella sepsis alone, 3 babies had fungal sepsis alone and 1 baby had Pseudomonas sepsis.

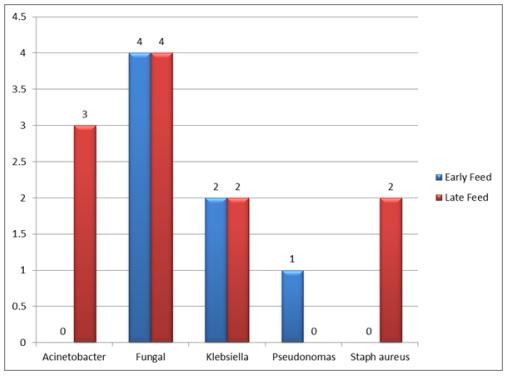

Fig 3 : Culture result

On analysing secondary outcomes, early feeding group attained full enteral feeds with mean 16.77 days (S.D 9.1) where as late feeding group attained full enteral feeds with mean 23.94 days (S.D 17.39). Early feeding resulted in earlier attainment of full enteral feeds with statistically significant p value of <0.008. Similarly, mean duration of hospital stay in early feeding and late feeding infants were 34.15 (SD 18.9) and 50.56 (SD 29.4) respectively . The mean number of days of hospital stay was significantly lower in Early feed group with a statistically significant P value of 0.001 On analysing the mortality , among the early feeders 1 baby did not survive among a total number of 67 , (1.5%) as compared to 5 out of 35 babies died in late feeders. (14.3%). This is statistically significant with a p value of 0.009. It should be noted that none of the late feeding babies had haemodynamic instability at the time of feed initiation in our study group.

DISCUSSION

Adequate nutrition is essential for the optimal growth and health of premature infants. Enteral nutrition is preferred to total parenteral nutrition (TPN) because the former avoids complications related to vascular catheterization, sepsis, adverse effects of TPN, and fasting. Early parenteral nutrition in these babies remains critical and should be used as an adjunct to enteral nutrition. The need of the hour is to reassess the feeding practices in preterm infants with a goal to reach full enteral feeding in the shortest time, while maintaining optimal growth and nutrition and avoiding the adverse consequences of rapid advancement of feeding.

Cochrane meta-analysis on studies evaluating the clinical effects of early trophic feeding done by Tyson et al[8] , has showed that among infants given trophic feedings, there was an overall reduction in mean days to full feeding (weighted mean difference [WMD] = -2.6 days), number of days that feeding was withheld (WMD = -3.1 days) and total hospital stay (WMD = -11.4 days) compared to infants given no enteral nutrient intake. There was no significant increase in the risk of necrotizing enterocolitis (relative risk = 1.16 [0.75, 1.79]).

McClure et al[9] have shown a reduction in episodes of culture confirmed sepsis and faster weight gain in babies receiving minimal enteral nutrition.

However , there are instances where feeding may be delayed because of non availability of breast milk or concerns of developing NEC. In a systematic review (nine trials, 754 VLBWI) by Morgan et al[10], it was shown that early introduction of trophic feeds compared to fasting had a non-significant trend towards reaching full feeds earlier (mean difference − 1.05 days (95% CI −2.61, 0.51)) and no difference in NEC There are only limited number of studies comparing the sepsis risk for early versus late feeding . A randomised controlled trial was done by Mc Clure et al[9] in 2000. Results from the study has shown a reduction in both culture confirmed sepsis and a marker of sepsis following trophic feeding. Nosocomial infections result in higher infant mortality and morbidity, prolonged inpatient stay and increased costs. Sepsis may have been reduced secondary to the decreased need for parenteral nutrition. The large difference in episodes of coagulase negative staphylococci in the above study seem to suggest this. Parenteral nutrition predisposes to sepsis because of both its interference with the immune system and the potential portal of infection via intravenous cannula. Alternatively, translocation of

enteric pathogenic micro-organisms into the circulation may have been reduced either because of improved gastrointestinal mucosal barrier function or beneficial alteration of the enteric flora.

In the present study significant difference observed in development of sepsis in late feeding infants compared to early feeding group. It has also shown that there is a statistically significant difference in hospital stay among early versus late feeders which ultimately reflects on the hospital costs and utilisation of resources. It also confirms the fact that there is no increased mortality in eary feeders as compared to late feeders .In the context of limited evidence from available randomized control trials, to base decisions regarding feeding policy in preterm neonates , the present study yielded comparable results favouring early introduction of enteral feeds.

However, the study has its limitations being a single centre study with low sample size. Standardization of enteral feeding could not be done as there was no breast milk banking facility.

CONCLUSION

With an improved outcome of preterm neonatal survival , clinicians are facing new challenges with nutrition , growth and control of sepsis in this vulnerable group. Studies have shown that early enteral feeding in very low birth weight (VLBW) infants is associated with reduced incidence of sepsis, improved milk tolerance, postnatal growth, and shorter hospital stay.[11,12] In our current single centre observational study , we noticed that,the incidence of sepsis was much higher in the late feeding goup (62.8%) as compared to the early feeding group (22.38%). There was no increased mortality in the early feeding group. The babies who received early feeding attained full feeds much earlier than the late feeding group. Average hospital stay , and hence hospital costs, were much low in the early feeding group

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