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Comparison of feeding intolerance between very preterm and moderate preterm neonates – a prospective cohort study

Abstract

Background: Premature babies are prone to develop many complications. One of the common complications is Feeding Intolerance (FI).Though FI is a common problem, literature contains little information about the influence of prematurity on feeding intolerance. There is also scarcity of information regarding the prevalence of feeding intolerance among preterm babies.

Objective: To compare the incidence of feeding intolerance and the association of co-morbid conditions with feeding intolerance between two groups of preterm (28-32wks and >32-36wks).

Methods: This study was an observational cohort study. All apparently stable preterm babies (28 to 36 weeks) admitted to SCABU (Special Care Baby Unit) was included in the study. The babies were stratified on enrolment into two groups according to gestational age of 28 to 32 weeks (group-1) and >32 to 36 weeks (group-2). Then feeding intolerance and other outcome variables were observed and compared between two groups

Results: Total percentage of feeding intolerance among the study population was 36.7%. Feeding intolerance in group-1 and group-2 were 40.0% and 34.3% respectively. But the difference was not statistically significant. Mean days to reach full feeding of two groups were 19.8 days (group-1) and 11.5 days (group-2) respectively and the difference was significant (p=0.0001). Suspected sepsis had significant association with feeding intolerance (p=0.0003)

Conclusion: Our study concluded that feeding intolerance was common in preterm infants and it is 36%. But very preterm babies had not significantly higher rate of feeding intolerance than moderate preterm. Among the co-morbid conditions only suspected sepsis had significant association with feeding intolerance.

Keywords: preterm, feeding intolerance, co-morbid conditions

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Forrukh Ahammad,[1] Tahmina Begum,[2] JesminAkter,[3] Evana Nasrin[4]

[1]Assistant Professor, Neonatology, Khulna Medical College, Bangladesh

[2]Professor of Pediatrics, BIRDEM Academy and Hospital, Banladesh

[3]Assistnat Professor Neonatology, Sir Salimullah Medical College, Banglsdesh

[4]Junior Consultant Paediatrics, UHC, Bangladesh

Correspondence: Forrukh Ahammad, Assistant Professor (Neonatology), Khulna Medical College, Khulna, Bangladesh, Email forrukh13@yahoo.com

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Introduction

Neonatal death is high in our country and it comprises 60% of total Under-5 mortality.[1] So to achieve MDG-4 we have to reduce neonatal death. The Lancet series on neonatal health reported that preterm birth directly causes 28% of neonatal deaths.[2] Prematurity and its complication is the major cause of neonatal death in our country and shares around 45% of neonatal death. Premature babies are prone to develop many complications. One of the common complications is Feeding Intolerance (FI). Feeding intolerance can be attributed to the immaturity of gastrointestinal motility,[3, 4] as small intestinal motility and phase-3 activity of the migrating motor complex (MMC) are more immature in preterm infants, especially those with a gestational age of less than 32 weeks.[3,5] Gastrointestinal motility is influenced by motilin, a 22 amino-acid peptide produced by the enterochromaffin cells of the duodenal and jejunal mucosa.[6] Gastric emptying, in particular, is dependent on co-ordination between the motor activities of the gastric antrum and duodenum. Preterm infants often have difficulty in tolerating oral feeds due to immaturity of mechanical and hormonal control of their gastrointestinal system.[3] Feed tolerance requires co-ordinated caudal intestinal transit of food. The clusters of phase 3 migrating motor complexes (MMC) that propagate food are associated with a two- to fourfold increase in plasma motilin levels.[7] But the association between motilin, MMCs and feed tolerance, however, is unclear in preterm infants. Even though the numbers of MMCs are reduced in preterm infants of less than 32 wk gestation[8] fetuses by week 20 of gestation, demonstrate intestinal distribution of motilin similar to that in adults. Motilin levels of fasting preterm infants are also similar to those of term infants, who rarely exhibit the degrees of feeding intolerance characteristic of premature infants.[5] It is also noted that fetal intestine is structurally mature by 25 weeks of gestation and capable of digesting and absorbing milk feeds, motor activity develops more slowly and may limit the tolerance to enteral feeds.[9] FI often needs prolong parenteral nutrition which predisposes nosocomial infections, hepatic dysfunction and prolong hospitalization.[10,11] Though FI is a common problem, literature contain little information about the influence of prematurity on feeding intolerance. There is also scarcity of information regarding the prevalence of feeding intolerance among preterm babiesand whereas the more preterm babies develop more frequent feeding intolerance yet to be determined.

Objectives

1. To find out the incidence of feeding intolerance among preterm neonates.
2. To compare the incidence of feeding intolerance between two groups of preterm (28-32wks and>32 - 36wks).
3. To compare the time taken for full enteral feeding between the two groups.

4. Association of feeding intolerance with other conditions. (e.g. Suspected sepsis, Phototherapy etc.)

Methods

a. Type of study: Prospective, observational and analytical.

b. Place of study: Special Care Baby Unit (SCABU), BIRDEM.

c. Period of study: September 2012–August 2013

d. Sample size: Total study subject- 60.

Cases were taken by consecutive sampling. 25 Preterm in Group-1, (28-32wks) and35 preterm in Group-2(>32-36 wks)

Inclusion criteria

a. Feeding not started OR,

b. Feeding started but not more than 30% of daily requirement was reached.

Exclusion criteria

a) Structural anomalies of GIT

b) Respiratory failure with mechanical ventilation

c) Severe asphyxia

d) Congenital cyanotic heart disease

e) If feeding started and >30% of daily requirement was reached at enrolment.

f) NEC stage II/III vii) Proven sepsis

g) IUGR

Procedure

All apparently stable preterm babies (28 to 36 wks) admitted to SCABU was included in the study. Gestational age was assessed from history of last menstrual period or first trimester ultrasonography. If those two information were unavailable only then New Ballard Score was performed. The babies were stratified on enrollment into group-1 (28 to 32 weeks) and group-2 (>32 to 36 weeks). Then they were followed up for up to the age of full feeding and final outcome. Feeding started in both groups of infants when they were clinically stable and feeds were given as intermittent boluses every 2 hourly.The neonates in both groups were received expressed breast milk (mother's milk or other mother milk). Feeds were usually started at 10–20ml/kg/day. Feeding increased by 10–20ml/kg every 24 hourly until a maximum of 150ml/ kg/day was achieved. Parenteral nutrition was started from the first day of admission and discontinued when the infant received 120ml/kg of milk per day.Gastric residuals were measured every 6 hours before the feed. Full enteral feeding was defined as receiving milk as much as 150ml/kg/day. Feeding was withheld if FI was found. Feeding was resumed 6 to 24 hours after the problem resolved. The number of episodes of vomiting, gastric residuals of >50% of the previous 6 h feeds, and of the number of occurrence of abdominal dissention was recorded.

Case definitions

Feeding intolerance - Some studies have used specific parameters such as GRV (Gastric Residual Volume) more than 30% of the previous 6 hours of feeding[12] or GRV that was equal to or more than previous feeding.[13,14] The majority of the researchers, however, defined feeding intolerance as the presence of GRV more than 50% of previous feeding.[15-19] We considered FI as;

a) GRV > 50% of previous 6 hrs feed OR

b) Vomiting more than once in 24 hours period OR

c) Abdominal distention (clinically) with or without visible bowel loops

N jaundice was considered when preterm babies developed jaundice requiring phototherapy according to AAP (American Academy of Pediatrics) guideline. *Suspected sepsis* defined as clinical sign-lethargy, poor feeding, hypo or hyperthermia, less activity, abdominal distension AND Laboratory finding- Leucopenia/leucocytosis, Thrombocytopenia OR Positive CRP/ Procalcitonin>500iu. *IDM* (Infant of Diabetic Mother)-when mother required insulin to control blood glucose.

Then FI and other outcome variables were observed and compared between two groups. Outcome variables were:

1. Frequency of feeding intolerance among study subjects
2. The duration required by the infant to achieve full enteral feeding.
3. Co-morbid conditions and feeding intolerance.

Statistical analysis: Comparisons for continuous variables were made by Student's t-test and for categorical data, χ^2 test and Fisher's exact test was used wherever applicable. Level of significance was set at $p<0.05$.The computer program SPSS; Release 12.0 (SPSS Inc., Chicago, IL, USA) and Epi info version 3.5.4 was used for statistical analysis.

Results

(Tables 1–5)

Table 2 showed the distribution of co morbid conditions among the groups. The difference of occurrence of those conditions among the groups was not statistically significant.

Table 3 showed the frequency of feeding intolerance in two groups. Occurrence of feeding intolerance was not significantly more in very preterm babies than moderate preterm.

Table 4 showed the association of feeding intolerance with RDS, Suspected sepsis, N. Jaundice and IDM. Chi square test was done for each condition and only suspected sepsis was significantly associated with feeding intolerance (p 0.0003).

Table 5 showed that Group-1 babies reached full feeding at 19.8 days (mean) but group-2 reached full feeding much earlier 11.5 days (mean). Difference of means was tested by t-test and it was significant (p=0.0001).

Table 1 Mean gestational age and birth weight of two groups

Group	Gestational age Mean± SD	Birth wt Mean±SD
Group-1 (n=25)	30.96 wk± 1.42	1470 gm±0.33
Group-2 (n=35)	33.94 wk±0.72	2160 gm±0.61

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Table 2 Frequency of Co-morbid conditions in two groups

	Group-1	Group-2	Total	*p value*
RDS N (%)	11 (50.0)	11 (50.4)	22 (100.0)	0.16
Suspected sepsis N (%)	10 (47.6)	11 (52.4)	21 (100.0)	0.25
Jaundice N (%)	24 (46.2)	28 (53.8)	52 (100.0)	0.07
IDM N (%)	13 (37.1)	22 (62.9)	35 (100.0)	0.2

Tables 3 Feeding intolerance of two groups.

Feeding intolerance	Group-1 n=25(%)	Group-2 n=35(%)	Total N=60(%)	*p value*
Present	10(40)	12(34.3)	22(36.7)	
Absent	15(60)	23(65.7)	38(63.3)	0.33

Table 4 Association of feeding intolerance (FI) with RDS, Sepsis, Phototherapy and IDM

	Feeding intolerance	No feeding intolerance	Total	*p value*
RDS n (%)	10 (45.5)	12 (54.5)	22 (100.0)	0.15
Susp.sepsis n (%)	14 (66.7)	7 (33.3)	21 (100.0)	0.0003
N. Jaundice n (%)	20 (38.5)	32 (61.5)	52 (100.0)	
IDM n (%)	13 (37.1)	22 (62.9)	35 (100.0)	0.46

*Fisher's exact test

Table 5 Difference in postnatal age at full feeding between two groups

Group	Mean days ± SD	
Group-1 (n=25)	19.8, 9.5	***p value*=0.0001**
Group-2 (n=35)	11.5, 4.5	

Discussion

In our study we categorized the babies into two groups, group-1 babies were > 28-32 weeks gestational age and group-2 babies were >32-36 weeks. In a recent paper WHO classified the preterm babies into three categories, extreme preterm (<28wks), very preterm (>28-32 weeks) and moderate preterm (>32-37weeks).[20] Many other studies done on feeding intolerance on different population group. SR Jadcherla stratified their study population into three groups that was <28 weeks, 28-32 weeks and >32-35 weeks.[21] Aly et al.,[22] categorized their study subjects into two groups of preterm, ≤32 weeks and >32weeks.22 We did not include the patients of <28 weeks because their number was less and they used to suffer from some other type of serious conditions. It was also expected that they have more frequent feeding intolerance. Our intension was to see the difference of feeding intolerance among the two preterm groups (very preterm and moderate preterm) who were reasonably stable. Though a lot of study done on feeding intolerance in preterm babies but the methodology they followed was so diverse that we faced difficulties to compare our study with others. A good number of studies done to see the effect of pro kinetic agents on feeding intolerance. Some researchers took their study subjects on the basis of birth weight not the prematurity. Another problem was lacking of a universal definition of feeding into lerance. In a recent Cochrane review of the use of erythromycin in the improvement and/or prevention of feeding intolerance, the authors reported that a meta-analysis was not performed because the diverse definitions of feeding intolerance made this type of analysis unfeasible.[4] In this study feeding intolerance was observed between two groups of preterm babies (Table 4) Forty percent of very preterm babies had feeding intolerance and 34% of moderate preterm had feeding intolerance. But the difference was not statistically significant. Jadcherla SR conducted a study on impact of prematurity and co-morbidities on feeding milestones in neonates. He found infants >28 weeks GA (i.e. group-2 and group-3) attained successful feeding milestones by similar PMA which was consistent with our study. Table 4 showed the association of feeding intolerance with co-morbid conditions.

We have analysed co-morbidities like RDS, suspected sepsis, phototherapy and infant of diabetic mother. Only suspected sepsis had significant association with feeding intolerance (p=0.0003). Other conditions failed to show any significant association with feeding intolerance. This finding was consistent with the study of SR Jadcherla .[21] In this study we found the mean age to reach full feeding of group-1 and group-2 were 19.8 days and 11.5 days respectively (Table 5) and the difference was statistically significant (p=0.0001). SB De Mauro and co-workers.[22, 23] have done a study on the impact of feeding interval on feeding outcomes in very low birth-weight infants. They found that the preterm babies reach full feeding at 16 days of life. He considered full feeding as 120ml/kg/day and the mean gestational age of their study subjects were 28.3 weeks. A randomized trial on feeding tolerance in preterm infant showed time to reach full feeding was 13days.[24] Mean gestational age was of study subjects of that study was 26.8 weeks and they consider 160ml/kg/day as full feeding. Another randomized controlled study on feeding intolerance in preterm infants found the age at full feeding were achieved at 52 days.[25]Their study subjects' mean gestational age at enrolment was 27.5 weeks and full feed regarded as 130ml/kg/day. So there were wide variations in the age at full feeding due to variation in the study subjects gestational age and differences in the definition of full feeding as well as presence of co-morbid conditions.

Limitation

The study was conducted at only one centre with small sample size. Only severe asphyxia was excluded, moderate asphyxia may had some influence on FI. Adverse maternal conditions were not considered. Ultra sonographic gestational age assessment was done by different sonologist.

Disclosure

The paper has been read and approved by all authors and has not been published totally or partially in any other journal and it will not be published in other periodicals.

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None.

Competing interests

The author declares no conflicts of interest regarding publication of this paper.

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