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ORIGINAL RESEARCH

Tolerance of Early Enteral Nutrition In Relation To Meconium Passage in Preterm Neonates, A Hospital Based Prospective Observational Study

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ABSTRACT

Background: Enteral nutrition has significant role in gastro intestinal system maturation. At some centres enteral nutrition among preterm neonates is getting delayed to initiate with concern that initiation of feeding before passing of meconium may not be tolerated well and may increase the risk of necrotizing enterocolitis.

Material and Methods: Preterm neonates got either enteral or parenteral nutrition as per their nutritional methods as advised by neonatologist, were analysed as 2 groups. Group -1 with preterm neonates in whom feeding was initiated before passage of meconium and Group -2 with preterm neonates in whom feeding initiated after passage of meconium. Incidence of NEC, time taken to achieve full feeds and duration of hospital stay were analysed among two groups.

Results: Incidence of NEC, among neonates in whom feeding was started before passage of meconium was 10.5%, in comparison to 9.5% in whom feeding was started after passage of meconium (RR 95% CI 0.4250 to 2.9137). There is no statistically significant increase in risk of NEC with initiation of enteral nutrition before passage of meconium. Preterm neonates in whom feeding initiated before passage of meconium had earlier achievement of full feeds (95% CI 0.1258 to 3.2182) and shorter duration of hospital stay(95% CI 0.0605 to 3.9875) in comparison with preterm neonates in whom feeding initiated after passage of meconium.

Conclusion: Initiation of feeding before passage of meconium in a hemodynamically stable preterm neonates does not increase the risk of NEC. Preterm neonates in whom feeding initiated before passage of meconium had earlier achievement of full feeds and shorter duration of hospital stay in comparison with preterm neonates in whom feeding initiated after passage of meconium.

Keywords: Enteral nutrition, necrotising enterocolitis, time taken achieve full feeds, total duration of hospital stay.

INTRODUCTION

Gut formation and its rotation back into abdominal cavity completes by 10 weeks of gestation. By 16 weeks the foetus can swallow amniotic fluid. By term gestation, foetus swallows about 150cc/kg/day of amniotic fluid which has carbohydrates, proteins, fat, electrolytes, immunoglobulin and several growth factors which plays an important role in maturation of gastro intestinal system.[1,2] Preterm birth interrupts this development.[3] Even if nutrients are provided parenterally, lack of enteric intake leads to diminished functional adaptation of immature gastro intestinal system and increased susceptibility to infection due

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to impaired barrier function by intestinal epithelium, lack of colonization by normal commensal flora and colonization by pathogenic organisms.[4]

There are studies on early enteral nutrition in preterm neonates. In a meta analysis[5] of 9 trials done by Bombel, Morgan, Mc Guire at el. In which a total of 754 very preterm or very low birth weight neonates were included in study. These trials did not provide any evidence that early trophic feeding affected feed tolerance or growth rates. Meta-analysis did not detect a statistically significant effect on the incidence of necrotising enterocolitis, typical risk ratio = 1.07 [95% CI : 0.67 to 1.70]; risk difference = 0.01 [95% CI : 0.03 to 0.05]. In a study done by Alison leaf, Jon Dorling, Stephen Kempley et al.[6] on preterm growth restricted infants, 404 preterm neonates were studied. Full sustained enteral feeding was achieved at an earlier age in the early group, median age was 18 days compared with 21 days (hazard ratio = 1.36 [95% CI : 1.11-1.67]). There was no evidence of a difference in the incidence of NEC- 18% in the early group and 15% in late group (relative risk = 1.2 [95%CI : 0.77-1.87]). In studies done by Mosqueda 2008[7] and Van Elburg 2004[8] – no difference in feed tolerance and incidence of NEC between early feeding group and delayed feeding group.

In a study done by Akram Sallakh, Fazileh Bashar-Hashemi et al. during 2007-2008, a total of 170 preterm neonates consisting of 125 who received trophic feeding within 48hours of birth and 45 fed enterally after 72 hr. Feeding intolerance, possibility of NEC, episodes of sepsis, body weight, length of NICU stay and duration of parenteral nutrition were assessed serially. In this study, time to gain weight (13.75 ± 5.21 versus 20.53 ± 6.31 (P< 0.001)), duration of parenteral nutrition (9.26 ± 4.572 days versus 14.11 ± 6.415 days (P <0.001)), hospital stay (12.14 ± 8.612 versus 21.11 ± 1.156(P <0.001)) were significantly shorter in early feeding group compared to late feeding group. In 2005 Tyson and Kennedy[9] reviewed 11 studies of minimal enteral feeding. In 10 studies that compared minimal enteral feeding versus enteral fasting, they noted that the minimal feeding group took fewer days to reach full enteral feeds (weighted mean difference = 2.6 days). In a study done by Khayata S, Gutcher G in 1987 (10), comparing early versus late feeding in LBW infants, the time to gain birth weight (13.75 ± 5.321 versus 20.53 ± 6.31 (P<0.001)), duration of parenteral nutrition (9.26 ± 4.572 days versus 14.11 ± 6.415 days(P<0.001)), hospital stay (12.14 ± 8.612 versus 21.11 ± 1.156 (P<0.001)) were significantly shorter in early compared to late feeding group.

There are studies established the safety aspects of early enteral nutrition but the time to initiate the enteral nutrition is still on debate, they have not given any recommendation on time of initiation of enteral nutrition in relation to meconium passage. This study focus mainly over tolerance of early enteral nutrition in relation to meconium passage.

Research Question

Whether early initiation of feeding before passage of meconium compared with late initiation of feeding after meconium passage, improves feed tolerance without increasing the risk of NEC in preterm neonates-?

Aim

To establish safety aspects of early enteral nutrition in relation to meconium passage in preterm neonates.

Objectives

a. Primary Objectives:

1. To compare the incidence of NEC in preterm neonates in whom feeding was started before passage of meconium with incidence of NEC in preterm neonates in whom feeding was started after passage of meconium.

2. To compare ‘time taken to achieve full feeds’ and ‘duration of hospital stay’ in preterm neonates in whom feeding was started before passage of meconium with incidence of NEC in preterm neonates in whom feeding was started after passage of meconium.

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MATERIAL & METHODS

It was a prospective observational study was conducted at Neonatal Intensive Care Unit a Pragna children hospital, Hyderabad between 2015-2017. Study population was preterm neonates (born before completion of 37 weeks) satisfying inclusion criteria.

Sample size:

As it is primarily a qualitative data, to estimate sample size following formula was used:

$N = 4PQ / r^2$

P = Prevalance from older study (5) = 8.1

Q = 100-P = 91.9

r = Permissible error, taken as 5%

Sample size = $4 \times 8.1 \times 91.9/5^2$

$= 2977.56/25$

$= 119.1$

And owing to the possibility of drop outs, calculated sample size was increased by 25% and the total sample size is taken as 150.

A] Inclusion criteria :

1. Preterm neonates who were born before completion of 37 weeks of gestation.
2. Neonates, whose parents gave consent to participate in study.
3. Clinically stable with respect to cardio-respiratory and enteric System.

B] Exclusion criteria :

1. Neonates born at term or Post term
2. Neonates having risk of developing NEC like birth asphyxia, sepsis, shock.
3. Neonates having predisposing conditions for failure to pass meconium like anal agenesis.
4. Neonates with syndrome presentation.
5. Neonates diagnosed as Failure to pass meconium due to pathological causes like meconium ileus, bowel obstruction.
6. Neonates who are withdrawn or referred or posted for surgeries during study.

Methodology:

The preterm neonates satisfying inclusion criteria were taken into study. Preterm neonates got either enteral or parenteral nutrition as per their nutritional methods as advised by neonatologist They were analysed as 2 groups during their regular treatment or care as

Group -1: Preterm neonates in whom feeding was initiated before passage of meconium and

Group -2: Preterm neonates in whom feeding initiated after passage of meconium.

Enteral nutrition was given as per preterm feeding guidelines. During the study period without interrupting regular treatment, the nutritional practices and the pattern of feed tolerance of two groups were observed and recorded.

Measurement of outcomes: incidence of NEC measured by clinical and laboratory findings.

1. Clinical characteristics.

a. Systemic signs: Respiratory distress, apnea and/or bradycardia, lethargy, temperature instability, irritability, poor feeding, hypotension (shock), decreased peripheral perfusion, acidosis, oliguria, bleeding diathesis.

b. Abdominal (enteric) signs: Abdominal distension or tenderness, gastric aspirates (feeding residuals), vomiting (of bile, blood, or both), ileus (decreased or absent bowel sounds), hematochezia (grossly bloody stools), abdominal wall erythema or induration, persistent localized abdominal mass, or ascites.

2. Laboratory features.

a. Imaging studies. The abdominal radiograph will often reveal an abnormal gas pattern consistent with ileus. These films may reveal bowel wall edema, a fixed-position loop on serial studies, the appearance of a mass, pneumatosis intestinalis (the radiologic hallmark

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used to confirm the diagnosis), gasless abdomen indicating ascites, portal or hepatic venous air, pneumobilia, or pneumoperitoneum with the appearance of gas under the diaphragm.
b. Blood and serum studies. Thrombocytopenia, persistent metabolic acidosis, and severe refractory hyponatremia constitute the most common triad of signs and help to confirm the diagnosis. Serial measurements of C-reactive protein (CRP).
c. Analysis of stool for blood.
Incidence and staging of NEC was done by modified Bell's criteria.
1. Stage I (suspect) includes clinical signs and symptoms, including abdominal signs and non diagnostic radiographs.
2. Stage II (definite) includes clinical and laboratory signs and pneumatosis intestinalis and/or portal venous gas on radiographs.
a. Mildly ill. b. Moderately ill with systemic toxicity
3. Stage III (advanced) includes more severe clinical signs and laboratory abnormalities, pneumatosis intestinalis, and/or portal venous gas on radiographs.
a. Critically ill (e.g., disseminated intravascular coagulation [DIC], shock) and impending intestinal perforation.
b. Critically ill as in stage 3 a but with pneumoperitoneum
Data collection methods: Neonatal identification data with IP. no. instead of original names, antenatal history, birth history and neonatal examination findings were collected from case records. Meconium passage time was recorded. Nutritional information like content of feed and time taken to achieve full feeds, duration of hospital stay and other relevant information was recorded on 'Data collection form' during study, was taken for

Statistical Analysis

Statistical analysis: Data was entered in Microsoft excel sheet. Odds ratio, relative risk, risk ratio and risk difference were calculated with respective 95% confidence intervals. Statistical analysis was done using medcalc, socscistatistics software and significance between proportions will be tested with Chi – Square test and comparison between two means will be done by t- test. P value < 0.05 was considered as statistically significant.

RESULTS

A total of 150 neonates of study population were analysed as 2 groups as per the nutritional method as advised by neonatologist.
Group -1: Preterm neonates in whom feeding was initiated before passage of meconium and
Group -2: Preterm neonates in whom feeding initiated after passage of meconium.

Comparison between Group 1 and Group 2 in terms of incidence of NEC

Table 1: Incidence of NEC among two groups

Group	Total no.	Feeds tolerated by	NEC developed in	Percentage
Group -1	76	68	8	10.526%
Group -2	74	67	7	9.459%

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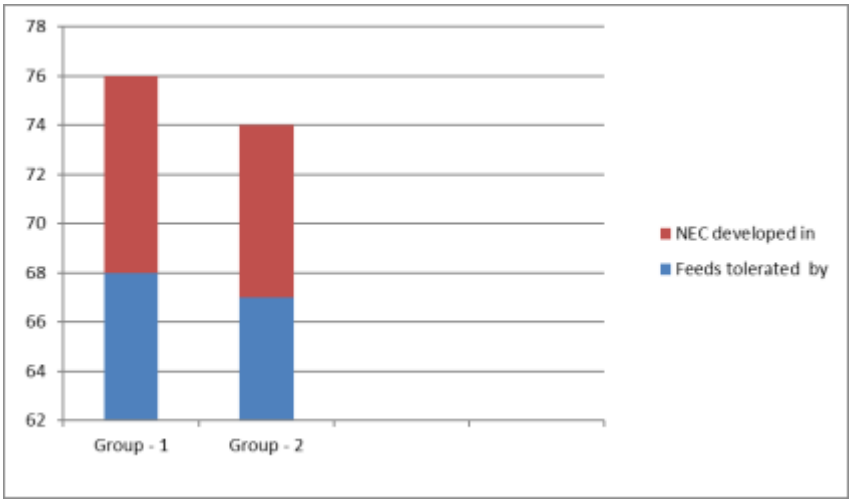

Fig No 1: Bar chart showing incidence of NEC among two groups

Comparison between Group 1 and Group 2 in terms of incidence of NEC., Odds ratio 1.1261. Relative risk 1.1128, 95% CI 0.4250 to 2.9137, Significance level P = 0.8277.

Chi square test:

	Results		
	No. babies tolerated feeds	No. babies had NEC	**Row Totals**
Group – 1	68 (68.40) [0.00]	8 (7.60) [0.02]	76
Group – 2	67 (66.60) [0.00]	7 (7.40) [0.02]	74
Column Totals	135	15	**150 (Grand Total)**

The chi-square statistic is 0.0474. The p-value is .827623. The result is not significant at p <.05.

Comparison between Group -1 and Group – 2 in terms of time to achieve full feeds and duration of hospital stay

Table 2: Time taken to achieve full feeds and duration of hospital stay among two groups

Parameter	**Group – 1 (Mean+ SD)**	**Group -2 (Mean+ SD)**
Time taken to achieve full feeds	10.30 ± 4.988	11.972 ± 4.580
Duration of hospital stay	14.421 ± 6.310	16.445 ± 5.843

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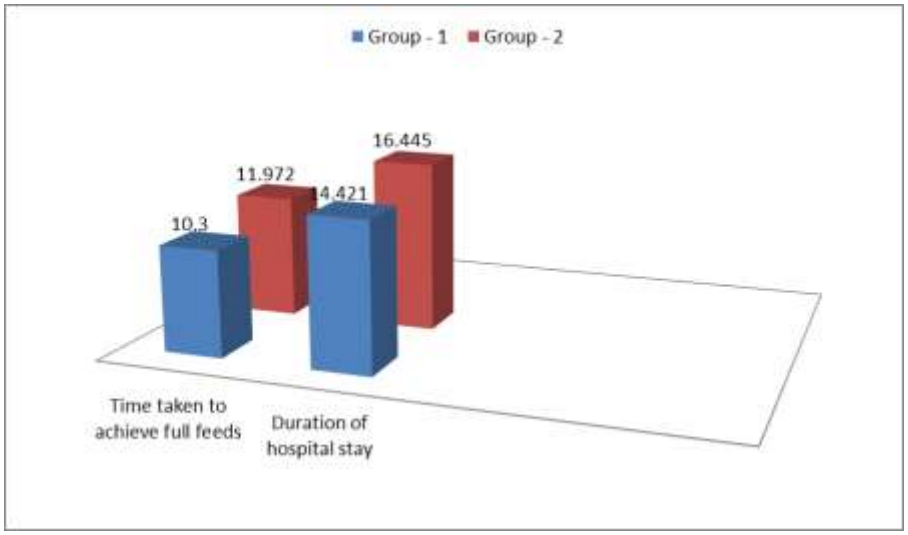

Fig. no. : 2 Bar chart showing comparisons of time taken to achieve full feeds and duration of hospital stay between two groups

Comparison between Group -1 and Group – 2 in terms of time to achieve full feeds	
Difference	1.672
Standard error	0.782
95% CI	0.1258 to 3.2182
t-statistic	2.137
DF	148
Significance level	P = 0.0343

Comparison between Group -1 and Group – 2 in terms of duration of hospital stay	
Difference	**2.024**
Standard error	**0.994**
95% CI	**0.0605 to 3.9875**
t-statistic	**2.037**
DF	**148**
Significance level	**P = 0.0434**

DISCUSSION

Comparison between Group 1 and Group 2 in terms of incidence of NEC., Odds ratio 1.1261. Relative risk 1.1128, 95% CI 0.4250 to 2.9137, Significance level P = 0.8277. The chi-square statistic is 0.0474 and the p-value is .827623, the result is not significant at $p < .05$ in this study. There is no increase in incidence of NEC with starting of enteral nutrition before passage of meconium. The study result is comparable to previous studies - metanalysis of 9 trials done by Bombel, McGuire et al. and trials done by Mosqueda, Van elburg ; Alison leaf, Jon Dorling, Stephen kempley et al.

In comparison between the two groups in terms of time taken to achieve full feeds, in the present study, full feeds achieved in Group- 1, is 10.30 ± 4.988 and full feeds achieved in Group – 2, is 11.972 ± 4.580, mean difference = 1.672 days with standard error = 0.782 , 95% confidence interval 0.1258 to 3.2182 and significance level P = 0.0343 which is less than 0.05. t-static (t-test) = 2.137. These results was comparable to studies done by A Leaf et al. (2012), Kyayata S, Gutcher G and Akram Sallah et al.

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In comparison between the two groups in terms of duration of hospital stay, the present study showed duration of hospital stay in Group - 1 is 14.421 ± 6.310 and duration of hospital stay in Group- 2 is 16.445 ± 5.843, mean difference : 2.024 days with standard error : 0.994 , 95% confidence interval 0.0605 to 3.9875 and significance level P = 0.0434. t-static(t- test) = 2.037. This result was comparable to study done by Khayata S, Gutcher G.

CONCLUSION

Conclusions from the study were 1. Initiation of feeding before passage of meconium in a hemodynamically stable preterm does not increase the risk of NEC. 2. Preterm neonates in whom feeding initiated before passage of meconium had earlier achievement of full feeds and shorter duration of hospital stay in comparison with preterm neonates in whom feeding initiated after passage of meconium.

Limitations

The study only included children presenting to our hospital, a tertiary care centre which caters to a particular group of people and sample size was small. Hence, the results may not representative of the general population. Outcomes of early enteral nutrition over parenteral in terms of time taken to achieve birth weight, incidence of sepsis and mortality are not included in the study.

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