Annals of Neonatology Journal

OPEN ACCESS
ISSN: 2636-3596

Original Article

Clinical Outcomes of Rapid Versus Slow Enteral Feeding Advancements in Preterm Infants

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DOI: 10.21608/ANJ.2021.78433.1028
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Abstract

Background: Adequate nutrition is important for optimum growth and neurological outcome. **Aim of work:** To evaluate the effect of rapid versus slow enteral feeding advancements on the clinical outcomes of preterm infants. **Patients and methods:** This is a prospective randomized controlled study over a period of six months. It included all preterm neonates with gestational age less than 37 weeks and haemodynamically stable from September, 2017 to March, 2018. Neonates (<37 weeks) were divided into two groups by simple randomization: Group I with slow advancement and group II with rapid advancement. All included neonates in this study underwent the followings: Full history taking, examination and Investigations. **Results:** The study included 100 preterm infants who were divided into two groups: 50 slow cases (I) and 50 rapid cases (II). There was a statistically significant variation as regards the duration of hospital stay (mean 19.37±10.36 and 17.89±9.58 days in groups I and II, respectively), as well as the time it took to reach full enteral feeding (mean 14.89±3.89 and 9.18±3.58 days in the slow and rapid feeding groups, respectively). In group I, there were 18 (36.0 %) deaths compared to 7 (14.0 %) deaths in group II. **Conclusions:** Rapid advancement of enteral feeding is associated with shorter duration of hospital stay, shorter duration to achieve full enteral feeding, and decreased mortality in comparison to slow advancement group.

Key words: Preterm infants**;** rapid enteral feeding; slow enteral feeding, nutrition.

Introduction

About 15 millions of preterm infants are born annually worldwide. Preterm birth is a major cause of neonatal mortality and the second cause of deaths in children under the age of five years. [1] Adequate growth is an extremely an important issue for preterm infants especially those <1500gm. Adequate nutrition is important for optimum growth and neurological outcome.[2] Defective nutrition practice due to deficient calorie and protein supplement can occur with suboptimum parenteral nutrition, delayed advancement in enteral feeding and delayed fortification of breast milk. This is not only affecting growth but also can cause cholestasis, chronic lung disease and osteopenia.[3] The sufficient nutritional practice is a matter of challenge in managing preterm infants especially those from 33-37 weeks which represents the majority of preterm infants. The American Academy of Pediatrics (AAP) 1977 stated that the growth of preterm infants should be similar to that of the intrauterine fetus. This is usually not attained in the clinical practice and most of the preterm infants assessed at the age of 40weeks are growth restricted.[4] Most of neonatologists, nutritionists and pediatrician recommend using human milk as a best source of nutrition for preterm infants. Enteral feeding is a safe and more preferred method than parenteral nutrition. Parenteral nutrition can be used as adjunct therapy in critical cases.[1] The cause of delayed feeding in preterm infants is mostly due to fear of immaturity of gastro-intestinal tract, respiratory distress syndrome, mechanical ventilation and necrotizing enterocolitis.[5] Early enteral feeding should start in the first 24 hours after birth. It can help to develop the intestinal villi, activate the enzymes and develop the microbiota. So it can prevent the infection and the occurrence of necrotizing enterocolitis.[6] Growth failure in preterm infants is an interaction of several factors as diseases that increase the catabolic state, endocrinal disorders, incoordination of suckling and swallowing, CNS damage and drugs that affect the metabolism. The most important cause is inadequate nutrient intake in the first few days after birth.[7] Delayed enteral feeding in preterm infants with prolonged parenteral nutrition is associated with increased risk of sepsis. [8] Early aggressive feeding of preterm infants by supplying increased amounts of IV amino acids immediately after birth with minimal enteral feeding and rapid achievement of full enteral feeding will reverse the catabolic state, start anabolism, increase linear growth and improve the long term neurologic outcome and cognitive function. [9]

The aim of this work: Was to evaluate and compare the effect of rapid versus slow enteral feeding advancements on the clinical outcomes of preterm infants

Methods

Study setting & type: A prospective randomized, controlled, single–center study conducted in the Neonatal Intensive Care Unit (NICU) of Assiut University Children Hospital. Preterm babies were randomly assigned to either slow enteral feeding or rapid enteral feeding group through simple randomization and allocation was concealed by sealed envelopes, which were equal in number for each group. Study investigations were not blinded to the interventions. It was done over a period of six months.

Aim: To evaluate the effect of rapid versus slow enteral feeding advancements on the clinical outcomes of preterm infants.

Patients: The study included all the Respiratory Distress Syndrome (RDS) preterm neonates admitted to NICU with gestational age less than 37 weeks and haemo-dynamically stable from September, 2017 to March, 2018. All newborns with gastrointestinal tract anomalies, haemo-dynamically unstable, gestational age equal or more than (37 weeks), who developed NEC and preterm on mechanical ventilation, were excluded.

Methods: Sample size in our study was calculated by EPI at power 80%, with confidence 95.0%, Alpha 0.5 equal 100 patients. Open EPI is free and open source software for epidemiologic statistics program. In descriptive and analytic research, Open EPI includes statistics for counts and measurements, stratified analysis with accurate confidence limits, matched pair and person-time analysis, sample size and power calculations, random numbers, sensitivity, specificity, and other assessment statistics. Simple randomization was used to separate neonates (<37 weeks) into two groups. Group 1"Slow progression: Feeding began on first day of feeding with 20mL/kg of expressed human milk per day. (EHM) or standard formula (in the absence of EHM) and increased by 20 ml/kg/day till maximal enteral feeds of 180 ml/kg/day obtained. "Rapid advancement" is the second group. Feeding was started with 20 mL/kg/day of expressed human milk (EHM) or normal formula (where EHM was not available) on the first day of feeding and increased by 30 mL/kg/day till maximal enteral feeds of 180 mL/kg/day were reached. The following procedures were performed on all newborns in this study: Full history taking (Gestational age, birth weight, mode of delivery, PROM, chorioamnionitis, abdominal distension, vomiting, consanguinity, maternal illnesses), age and weight determination at the time of initiating enteral feeding. Meticulous examination (Vital signs, daily abdominal circumference, daily weight recording, and an assessment of the system) was done. Investigations as serum electrolytes (Na, K, Ca, and glucose), CRP, and abdominal ultrasonography were all performed.

Research outcome measures: To compare effects of rapid versus slow enteral feeding advancements on preterm infants' clinical outcomes, as length of hospital stay, total days of TPN intake, time to establish full enteral feeding, and necrotizing enterocolitis rates, feeding intolerance and number of days took to regain birth weight. The collecting of cases took six months, and there was no follow-up after discharge. During admission, feeding outcome was recorded.

Ethical considerations

Ethical approval: An approval for the study was obtained from the ethical committee in the Faculty of Medicine, Assuit University. IRB: 17100036

Informed written consents were taken from the patients' parents.

Confidentiality: Patients' data was kept confidential.

Statistical analysis

We used SPSS/version 24 (Statistical Package for Social Sciences software Chicago, USA) for statistical analysis. Per-protocol population was analyzed and descriptive values were expressed as mean±SD or number (%). Independent Student's t test was used for comparison between normally distributed data, in the two groups, Mann-Whitney test was used for comparison when data was not normally distributed and Chi-squared test to compare proportions between both groups. P value was considered significant if < 0.05.

Results

This was a six-month prospective study undertaken at Children's Hospital Neonatal Intensive Care Unit (NICU), with 100 neonates divided into two groups: slow group I and rapid group II. There were 45 females and 55 males in the studied groups. In groups I and II, the mean weight at admission was 1.25±0.414 and 1.28±0.45, respectively. In groups I and II, the mean gestational age at admission was 30.80±2.80 and 32.14±2.22, respectively. As indicated in table (1) fig. (1,2) there were no significant differences between the slow and rapid groups in terms of age at the start of feeding, weight, gestational age, gender, and mode of delivery (P>0.05) . As regarding feeding intolerance, abdominal distention, increase gastric aspirate (>50 %), feeding interruption and NEC between slow & rapid groups, there were non-statistically significant differences as shown in table (2).

There were statistically significant variations in IV fluid duration (mean 9.30±2.33 and 6.56±1.12 days in groups I and II, respectively), hospital stay (mean 19.37±10.36 and17.89±9.58 days in groups I and II respectively) , time to regain birth weight (mean 15.46±4.8 and 12.43±5.32 days in groups I and II respectively), and time to reach full enteral feeding (mean 14.89±3.89 and 9.18±3.58 days in groups I and II, respectively), as shown in table (3). As shown in table (4) and fig.(3), there were statistically significant differences between the slow and rapid groups in terms of weight at discharge, with mean values of 2040±42.71 and 2200±34.8 gm in group I and II, respectively, and mortality, with 18 (36.0 percent) deaths in group I versus 7 (14.0 percent) deaths in group II.

Discussion

Every year, around 15 million preterm babies are born around the world. Preterm birth is commonest reason of neonatal death and the second most common cause of death in children under the age of five. [1] For preterm infants, especially those weighing less than 1500 grams, adequate growth is critical. Appropriate nourishment is essential for optimal growth and neurological outcomes. [2] The current study evaluated the slow and rapid progression of feeds in preterm neonates, and the outcome was measured in terms of hospital stay, time to regain birth weight, I.V fluid usage, and time to reach the full enteral feed. In the current study, there was insignificant variation between slow and rapid groups (P >0.05) as regards, age at the start of the feed, gestational age, sex, and weight at admission. There was also insignificant difference in delivery mode between the two groups (P>0.05). This was in line with Saha et al, who found that the gestational age, admission weight, admission age, and gender were comparable in both the slow and rapid enteral feeding groups.[10]

In our research, IV fluids administration period was shorter (9.30) versus (6.56) days between two groups I and II respectively with a statistical significance difference (P<0.001). This was in line with Krishnamurthy et al., who found that the rapid enteral feeding group required a shorter period of IV fluid versus slow enteral feeding group (6.66 versus 9.33 days and 5.75 versus 10.00 days, respectively, p-value >0.05) for both birth weight < 1500 gm and the birth weight (1500 gm - <2500 gm) study populations. [11] This research found that rapid enteral feeding took less time to reach full enteral feeding (9.18 days) than slow enteral feeding (14.89 days), with a highly significant difference (P<0.000). This was consistent with Karagol et al, who found that infants in intervention group reached full volume feedings faster (9.33 versus 14.66 days) than those in the slow enteral feeding group, with a p-value < 0.05. [12] This was also in line with the findings of Oddie et al, who discovered that slow advancement of feeding was linked with a longer time to complete full enteral feeding and a higher rate of invasive infection.[13] This was consistent with the findings of Modi et al, who discovered that rapid advancement of feeding led to shorter IV fluid duration and earlier acquisition of full enteral feeding. [14] Also, a study done by Nangia et al discovered that full feeding was achieved earlier in rapid group . [15]

In current study, rapid enteral feeding group required substantially fewer days to gain weight versus slow enteral feeding group (p<0.05). Same findings were found by Kadam et al, who found that the rapid feeding group took less time to gain birth weight. [16] In this study, the rapid group had a significantly shorter hospital stay (17.89 days) than the slow group (19.37 days), with a significant variation (P< 0.05). In a randomized controlled trial comparing slow and rapid enteral feeding in preterm neonates, Karagol et al found that rapid feeding enhancement group achieved earlier full enteral feeding, required fewer days of parenteral nutrition, took less time to regain birth weight, and spent less time in the hospital. [12] A study conducted by Nangia et al. discovered that the early total enteral feeding group had a shorter hospital stay. [15] Among our results, the rapid enteral feeding group had a higher rate of feeding problems, such as abdominal distention, feeding intolerance, and increased gastric residual, than the slow enteral feeding group, although there was no statistical difference between the two groups. In slow enteral feeding, vomiting frequency was more common than rapid enteral feeding, although there was insignificant difference between two groups. This was in line with findings by Sallakh-Niknezhad et al. [17]

This was also observed by Nangia et al, who found that feeding was interrupted in both the rapid and slow enteral feeding groups, with insignificant difference in feeding intolerance between two groups. [15]

In another study, Jain et al. showed that early and rapid advancement with enteral feeding did not result in an increased incidence of food intolerance in stable preterm babies. [18] In this study, the rapid group had lower incidence of NEC versus slow group, but the difference was non-significant. This was in line with Kadam et al. and Morgan et al., who reported that the rapid feeding group had no more episodes of feed intolerance or NEC versus slow feeding group. [16&19] This was also consistent with Corpeleijn et al., who found a higher incidence of NEC when the feeding group progressed slowly. [20]

In the current study, mortality was (36.00 percent vs. 14.00 percent; p-value was <0.05) in the slow and rapid feeding groups respectively, which was a statistically significant difference in agreement with Saha et al., [10] In addition, Kadam et al. reported that the rapid feeding group did not have a higher rate of mortality or sepsis than the slow feeding group. [16] This was in line with Morgan et al., who found that while there was no increase in mortality in the rapid group, there was a higher rate of sepsis in the slow group. [19] This contradicts Krishnamurthy et al's findings, who found low mortality attributed to both NEC and sepsis; these occurrences of NEC and sepsis were similar for both groups but without statistically significant differences. [11] This contradicts the findings of Modi et al, who reported that rapid feeding was not correlated with a reduction in the causes of mortality, sepsis, or serious morbidities during hospitalization. [14]

Limitation of the study: The limitations of the study were the small sample size and it was not a multicenter study.

Conclusions

In preterm infants aged 37 weeks or less, rapid enteral feeding advancement reduces the time to reach full enteral feeding and removes the requirement for PN administration. Furthermore, quick advances in enteral feed improved these high-risk newborns' short-term outcomes. Our findings also suggest that birth weight is regained faster. Despite the initiation of full feeds, NEC incidence reduced dramatically, as did hospital stay length, minimizing parental stress and financial burden.

Improved early postnatal growth, a decrease rate of catheter-related infections, and reduced newborn care costs are all advantages of rapid enteral feeding increments.

Lists of abbreviations:

CBC: Complete blood count

CNS: Central nervous system

CRP: C-reactive protein

EHM: Expressed human milk

IV: intravenous

NEC: Necrotizing enterocolitis

NICU: Neonatal intensive care unit

EPI: epidemiologic statistics program

Author's contributions

All of authors shared equally in this work and have seen and approved the submitted version of the manuscript.

Conflict of interest

The authors have no conflict of interests to declare.

Funding

This study received no special funding and was totally funded by the authors.

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Date received: 18th May 2021, accepted 19th June 2021

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Table (1) Demographic data of studied groups

Characteristics	Slow group "n=50"	Rapid group "n=50	p-value
Age at beginning of feeding (days)	4.50±2.87	4.64±3.24	0.820
Sex:			
Male	26(52.0%)	29(58.0%)	0.344
Female	24(48.0%)	21(42.0%)	
Weight on admission "kg"	1.25±0.414	1.28±0.45	0.371
Gestational age "weeks."	30.80±2.80	32.14±2.22	0.372
Mode of delivery			
Vaginal delivery	16(32.0%)	21(42.0%)	0.285
Cesarean section	34(68.0%)	29(58.0%)	
No of infants fed with:			
Exclusive breast milk	17(34.0%)	14(28.0%)	
Breast milk +formula	23(56.0%)	27(54.0%)	0.276
Formula only	10(20.0%)	9(18.0%)	

Table (2) Feeding outcome of studied groups

Feeding characteristic	Slow group "n=50"	Rapid group "n=50"	p-value
Feeding intolerance	12(24.0%)	14(28.0%)	0.342
Abd. Distension	10(20.0%)	13(26.0%)	0.271
Vomiting	14(28.0%)	11(22.0%)	0.378
Increase gastric aspirate (>50%)	13(26.0%)	16(34.0%)	0.481
Feeding interruption	12(24.0%)	15(30.0%)	0.348
Necrotizing enterocolitis (NEC)	11(22.0%)	7(14.0%)	0.228

Table (3): Clinical outcome of studied groups

Outcome	**Slow group**	**Rapid group**	**P -value**
duration of IV fluid "days"	9.30±2.33	6.56±1.12	0.001**
-Time taken to reach full enteral feed "days"	14.89±3.89	9.18±3.58	0.0.000***
-Duration of hospital stay "day"	19.37±10.36	17.89±9.58	0.02*
- Regain birth weight "days"	15.46±4.8	12.43±5.32	0.04*

* Significant, ** highly significant

Table (4): Discharge status of studied groups

Item	**Slow group**	**Rapid group**	**P- value**
Discharge weight "gm" Mean ± SD	2040±42.71	2200±34.8	0.02*
Discharge status: **Died**	18(36.0%)	7(14.0%)	0.01*
Alive	32(64.0%)	43(86.0%)	

* Significant

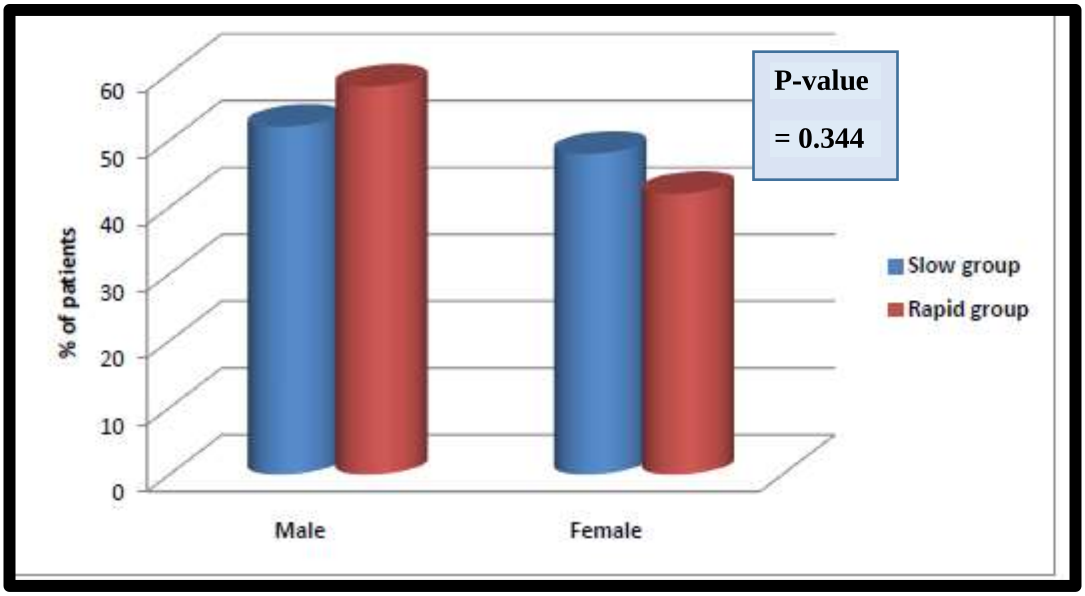

Fig. (1) Gender distribution of the studied groups

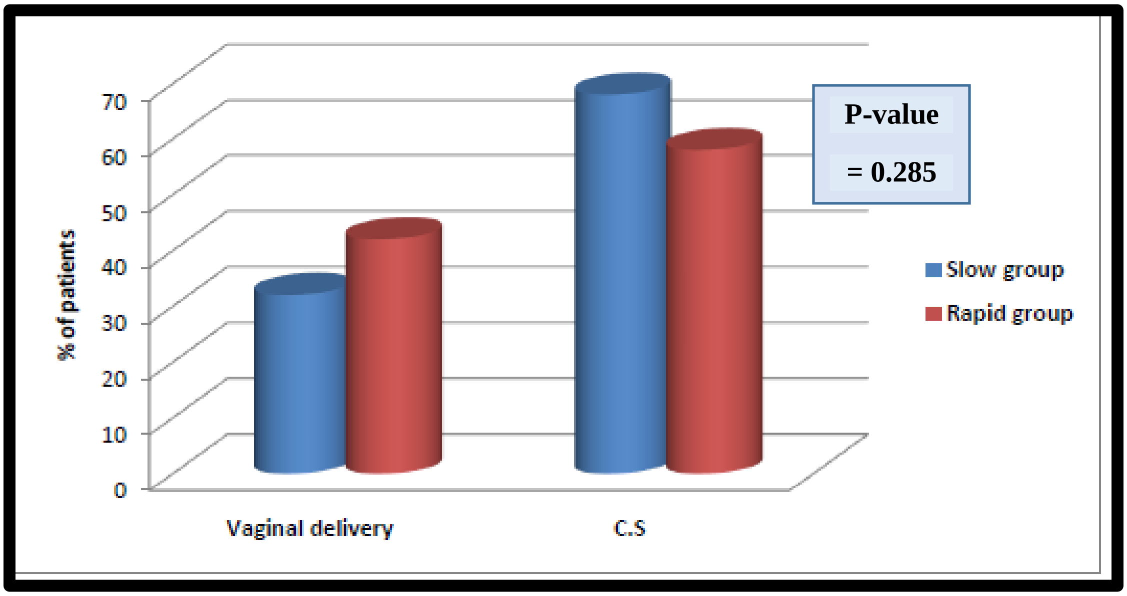

Fig. (2) Mode of delivery of the studied groups

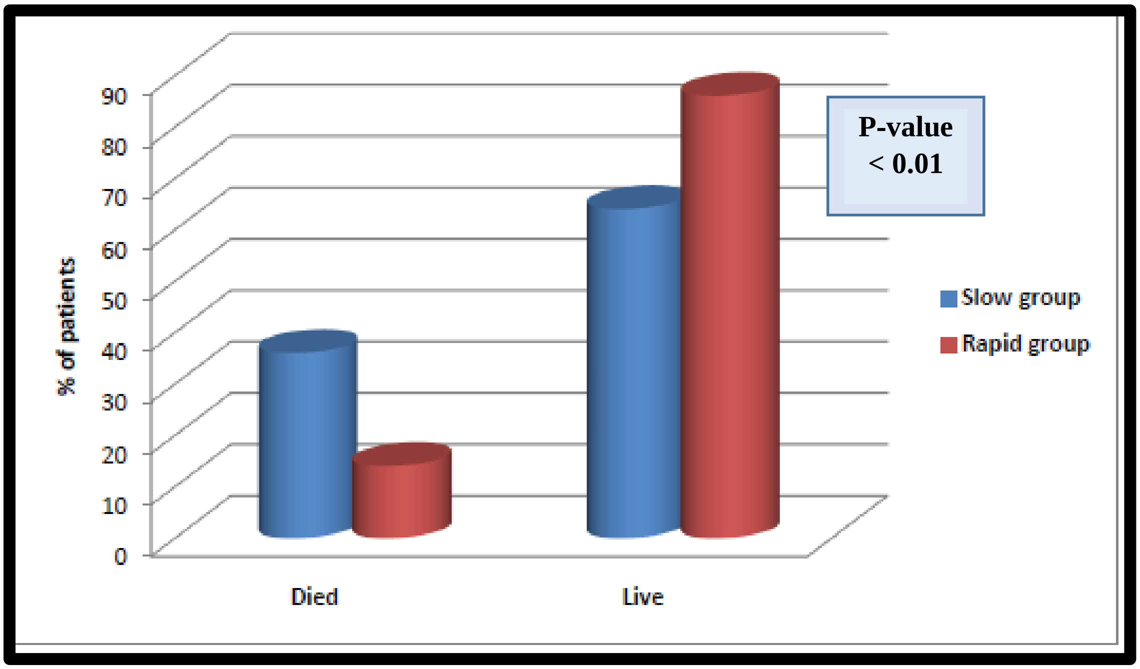

Fig. (3) The outcome of the studied groups

Citation: Safwat M. Abdel-Aziz; Amany M. Riad Garas; Mohamed M. Sayed; Amira M. Shalaby. "Clinical Outcomes of Rapid Versus Slow Enteral Feeding Advancements in Preterm infants". Annals of Neonatology Journal 2021; 3(2): 128-144 doi: 10.21608/anj.2021.78433.1028