



## Original Research

# The Effect of Intermittent and Continuous Feeding on Growth and Discharge Time in Very Low Birth Weight Preterm Infants

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### Abstract

**Objectives:** The aim of this study was to determine the effect of intermittent bolus feeding and continuous feeding models on early growth and discharge time in very low birth weight infants.

**Methods:** The study was designed as a prospective, randomized, and controlled study. Infants born in our hospital with birth weight below 1500 g within a 1 year period were included in the study. The number of samples was determined by power analysis. Babies were randomized according to birth weight and fed with intermittent bolus feeding and continuous feeding models. Demographic characteristics, clinical findings, diagnosis, nutritional status, and length of hospital stay were compared.

**Results:** The study was conducted with 80 preterm infants, which consisted of continuous feeding (n=41) and intermittent bolus feeding (n=39). There was no significant difference in gender, gestational week, birth weight, height, and head circumference distribution of the babies between groups. The difference between the reach time to birth weight and maximum weight loss rates, parenteral feeding time, transition time to full enteral feeding, transition time to oral feeding, development of feeding intolerance, mechanical ventilation time, and hospitalization time in intensive care unit were not statistically significant. Necrotizing enterocolitis (NEC) Stage I and II developed in 34.1% of babies fed with continuous feeding model and 28.2% of babies fed intermittently; NEC was detected to start in 4.5±2.8 days in the continuous feeding group and in 2.8±5.2 days in the intermittent group. These differences were found to be insignificant between the two groups (p=0.634 and p=0.266, respectively).

**Conclusion:** There was no difference between growth parameters and discharge time of preterm babies who were applied continuous and intermittent bolus feeding model. Although there was no statistically significant difference on the development of NEC, it was determined that NEC developed earlier in the intermittent bolus feeding model.

**Keywords:** Continuous feeding; intermittent feeding; very low birth weight preterm baby

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Prematurity is among the most important causes of neonatal mortality and morbidity in developing countries.

According to Turkey Demographic and Health Survey 2013

data, 47% of deaths in the 1<sup>st</sup> year of life in our country takes place in the neonatal period.<sup>[1]</sup>

The nutritional requirement of the prenatal fetus is met

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by the mother through the umbilical vein, but this nutrient transfer ends with the birth. The main goal of preterm infant nutrition is to maintain the appropriate nutrient transfer that can provide growth and development as in the womb. Therefore, parenteral and enteral nutrition should be initiated as soon as possible after birth in preterm babies. For the premature baby to be fed effectively and safely orally, coordination of sucking, swallowing, and breathing is required.<sup>[2]</sup> Therefore, the feeding of premature infants born before 34 weeks should be done by gavage method (nasogastric/orogastric), which is a safe way initially.<sup>[3]</sup> It is important to start with proven data in planning the nutrition of very low birth weight (VLBW) preterm babies in the risky group. It has been reported that intermittent feeding in preterm babies cyclically increases the secretion of intestinal hormones compared to continuous feeding and increases the secretion of serum gastrin, insulin, and gastric inhibitory peptide, as seen in healthy term babies.<sup>[4]</sup> Continuous feeding model in preterm babies has been shown to cause biliary stasis, gallbladder enlargement, and non-contraction.<sup>[5]</sup> There is no consensus on the effects of feeding preterm babies with a continuous feeding model or intermittent feeding model on growth parameters (weight, height, and head circumference), parenteral feeding time, transition time to complete enteral feeding, and the development of necrotizing enterocolitis (NEC).<sup>[6]</sup> It has been shown in neonatal animal studies that intermittent feeding increases skeletal muscle protein synthesis by increasing the amount of amino acids and insulin in the circulation.<sup>[7]</sup> It has been reported in studies performed with near-infrared spectroscopy in preterm babies that continuous feeding decreases the need for splanchnic oxygenation and should be preferred in case of hypoxic-ischemic intestinal injury.<sup>[8]</sup> The aim of this study is to evaluate the effect of intermittent and continuous feeding on early growth parameters, early morbidity findings, and discharge time in VLBW preterm infants.

## Methods

The study has a cross-sectional, randomized, and controlled design. The study was carried out in Şişli Hamidiye Etfal Training and Research Hospital, Neonatal Intensive Care Unit between February 2016 and February 2017 (1 year). The differences between the two different feeding models in preterm babies in terms of their effectiveness in tolerance, as well as the detected complications were compared.

## Sample Analysis of the Research

The universe of the study consisted of babies with a birth weight m babies in terms of their effectiveness in toler-

ance, as well as the detected complications were compared of Şişli Hamidiye Etfal Training and Research Hospital for 1 year. The sample size of the study was determined by power analysis. When the significance level was determined as 0.05, the confidence interval as 0.95, and the strength level as 0.95; 36 preterm babies for each group, and a total of 72 preterm babies constituted the sample. Considering that 10% of patients may be lost during the study, the total number of patients was determined as 40 for each group.

## Exclusion Criteria from the Study

Babies with congenital anomalies affecting enteral feeding (esophageal atresia, duodenal atresia, anal atresia, etc.), babies with intrauterine infection or early sepsis, babies lost during the study, and small for gestational age babies were excluded from the sample.

## Collection of Data

To evaluate the functionality and adequacy of the prepared forms, pre-application was performed with four premature babies who were followed up in the neonatal intensive care unit. Data collection and follow-up form were revised and finalized as a result of pre-application.

First of all, the purpose of the study was explained verbally to the parents of the babies included in the study and their written consent was obtained with the "Informed Consent Form." Preterm babies meeting the criteria of the research were randomized as one continuous and one intermittent feeding by enumeration in computer environment. Total parenteral nutrition (TPN) was started in the first 24 h of life as a standard in all babies according to the clinical application protocol. In our standard clinical practice, TPN containing 2 g/kg/day protein and 2 g/kg/day lipid is started on the 1st day of life in babies with a birth weight below 1500 g, and when clinically stable, with a daily increase of 1 g/kg/day, protein is increased to 3.5 g/kg/day and lipid to 4 g/kg/day. The research data were recorded in the form prepared for the research from 09:00 in the morning until 09:00 in the next day. The gestational week, birth weight, gender, and multiple pregnancy status of the babies included in the study were recorded in the follow-up form. The hospitalization periods of the babies, the diagnoses they received during their hospitalization and during their follow-up were recorded. Growth parameters of the babies, weight, height, head circumference measurements, maximum weight loss rate, weight intake, and final diagnosis during discharge were recorded. Final growth data were obtained by taking height, weight, and head circumference measurements during discharge.

## Nutrition Model

With parenteral nutrition, minimal enteral feeding was initiated in all babies within the first 48 h. The babies included in the study were preferred to receive breast milk primarily, but in cases, where breast milk was not sufficient, pre-term formula, which is considered the closest alternative to breast milk, was used. If more than 75% of the feeding amount of preterm babies were provided with breast milk, they were accepted to be fed with breast milk model. Breast milk enrichment (Euprotein® Nutricia GmbH Werk Fulda in the form of 4 scales/100 ml) was added for those whose enteral feeding was 100 ml/kg/day with breast milk. TPN was discontinued in preterm babies who received more than half of their nutritional requirements enterally or whose enteral feeding was 120 kcal/kg/day. In preterm babies who received the whole amount of food enterally, the transition to oral feeding was applied as a complementary bottle-feeding method. The transition of babies who could take the entire amount of breast milk in 15–20 min with a bottle and did not encounter any problems with their vital signs was considered successful and the breast-feeding process was started in these babies.

## Intermittent Nutrition Group

The babies in this group were fed every 2–3 h intermittently. An orogastric tube was inserted every day at 09:00 in the morning and residue control was performed. The amount of nutrition put into the syringe was kept 10 cm above the baby and the fluidity was obtained by gravity through the orogastric tube. The baby was placed in a prone or right lateral position to accelerate gastric emptying after feeding.

## Continuous Nutrition Group

Babies in this group were fed continuously. An orogastric tube was inserted to perform standard measurements every day at 09:00 in the morning. Continuous feeding was performed for 24 h, in 3 h of period (2.5 h feeding infusion and 0.5 h gastric drainage). Before feeding, breast milk/formula was heated to 37 °C. The heated milk was drawn into the syringe and passed through the infusion set. The syringe was placed in the infusion pump and its speed was adjusted to last in 2.5 h. The infusion pump and infusion set were placed in the incubator to minimize heat loss. After the infusion, open abdominal drainage was used for ½ h. In case, babies could not tolerate feeding, no switch was made between the two feeding models.

Ethical consent (Decision number: 288, 28.01.2014) was obtained from Şişli Hamidiye Etfal Training and Research Hospital before data collection. Parents of premature babies included in the study groups were informed verbally and in writing, and consent was obtained.

## Definition

### NEC

Modified Bell's Criteria were used for staging. Feeding of babies with Stage Ia and Ib was interrupted for 3 days. Feeding of babies with stage  $\geq$  was interrupted for 7–10 days. Due to the small number of the patient group, when comparing the NEC status between the groups, the evaluation was made as NEC was present or NEC was absent at all stages.

### Nutritional intolerance

In addition to clinical conditions such as abdominal distension, it was accepted as the requirement to have a residual of 30% or more of the previous feeding amount in feeding, or to have a residue of 50% and more once in the 3 h feeding period, and the need for at least 24 h of break from feeding.<sup>[9,10]</sup>

### Statistical Analysis

The frequency and percentage distributions related to the data were given. The relationship between variables measured at a categorical level was evaluated using the Chi-square test. Whether the data showed normal distribution were examined with the Kolmogorov–Smirnov test, and independent t-test was used for the data showing normal distribution. Significance level was accepted as  $p < 0.05$ .

## Results

The distribution of independent variables according to the feeding model groups of preterm babies is presented in Table 1. The mean gestational period in the continuously fed group was  $29.3 \pm 1.8$  weeks, while it was  $29.4 \pm 1.9$  weeks in the intermittently fed group. The difference between the groups according to the gestational period was statistically insignificant and it was observed that the groups were distributed homogeneously. When the growth parameters were evaluated, no statistically significant difference was found between the continuous feeding model and the intermittent feeding model, it was determined that both models had no significant effect on short-term growth (Table 1). In both groups, no statistically significant difference was found in terms of maximum weight loss time and maximum weight loss amount (Table 1). The comparison of variables related to nutritional characteristics of preterm babies according to the feeding model is given in Table 2. The difference between the mean days of TPN feeding of the groups and the mean days of transition to full enteral feeding was statistically insignificant. There was no statistically significant difference between the mean successful transition days to oral nutrition and the number of nutritional intolerance development between the groups (Table 2).

**Table 1.** Distribution of demographic characteristics of preterm babies included in the study according to feeding model groups

	Feeding model		$\chi^2$	P
	Continuous feeding (n=41)	Intermittent feeding (n=39)		
Gender, n (%)				
Female	15 (36.5)	18 (44.7)	0.385	0.496
Male	26 (63.5)	21 (55.3)		
	<b>Mean±Standard deviation</b>			
Gestation period, weeks	29.3±1.8	29.4±1.9		0.758*
Birth weight (g)	1331±266	1339±319	-0.131	0.896
Discharge weight (g)	2391±406	2507±519	-1.109	0.271
Birth height (cm)	38.8±3.0	38.11±3.4	0.896	0.373
Discharge height (cm)	44±2.3	44.5±2.3	-0.878	0.382
Birth head circumference (cm)	27.4±2.3	27.9±2.4	-1.144	0.256
Discharge head circumference (cm)	31.8±1.9	32.3±1.4	-1.488	0.198
Time to reach birth weight, days	9.7±3.0	9.9±4.4	-0.255	0.800
Maximum weight loss rate, percent	9.2±3.9	9.5±4.2	-0.396	0.693

\*t: Independent t-test.

**Table 2.** The effect of feeding models of preterm babies on enteral and parenteral nutrition parameters

	Feeding model		$\chi^2$	P	
	Continuous feeding (n=41)	Intermittent feeding (n=39)			
Enteral feeding model, n (%)					
Only breast milk	13 (31.7)	13 (33.3)	4.768	0.09	
Breast milk+formula	18 (43.9)	17 (43.6)			
Only formula	10 (24.4)	9 (23.1)			
	<b>Mean±Standard deviation</b>		<b>t</b>	<b>P</b>	
TPN time, days	16.1±9.3	16.4±10.7	-0.118	0.592	
Transition time to complete enteral nutrition, days		19.1±11.1	17.5±11.2	0.635	0.288
Transition time to oral feeding, days	29.3±14.7		29.6±16.3	-0.071	0.943
The frequency of developing nutritional intolerance, n		1.1±1.3	1.2±1.9	-0.092	0.927

NEC development status of premature babies according to the feeding model is presented in Table 3. The number of days to develop NEC was determined as 4.5±2.8 days in babies fed with the continuous feeding model and as 2.8±5.2 days in the group fed intermittently. Although the difference in the time to develop NEC between the groups

was statistically insignificant, it was determined that NEC developed earlier in intermittent feeding model group (Table 3). The demographic data of both groups obtained at discharge are presented in Table 3. The mechanical ventilation time was 4.5±6.9 days in the continuous feeding group and 8.1±11.6 days in the intermittent feeding group, with

**Table 3.** The effects of feeding models on the development of NEC, ventilator use, and hospital stay

	Feeding model		P
	Continuous feeding (n=41)	Intermittent feeding (n=39)	
NEC (Stage I+II), n (%)	14 (34.1)	11 (28.2)	0.634
NEC development time, days	4.5±2.8	2.8±5.2	0.266
Duration of stay on the ventilator, days	4.5±6.9	8.1±11.6	0.09
Duration of hospital stay, days	47.4±19.8	47.4±20.7	0.986
Gestation period during discharge, weeks	35.9±2.1	36.6±2.1	0.198

no statistically significant difference between the groups ( $p>0.05$ ). No statistically significant difference was found between the two groups in terms of length of hospitalization and gestation time at discharge (Table 3).

## Discussion

The importance of nutrition in the 1<sup>st</sup> weeks of life, which is the most critical period after birth for VLBW premature babies, is an undeniable fact. Careful determination of the nutritional preferences of premature babies according to the current situation is an important variable that can affect the baby's calorie intake, growth scale, and hospital stay.<sup>[11]</sup> Especially in preventing the problems that may develop in the long-term follow-up of VLBW infants and increasing the quality of life, the treatment they receive in the neonatal intensive care units, as well as the maintenance of nutrition, which is a team work, is among the top issues emphasized. The main purpose of preterm infant feeding is to provide the necessary nutritional support to maintain growth and development close to intrauterine levels.<sup>[12,13]</sup> Nutrition is predicted to continue in the extrauterine period without interruption and will be provided with aggressive parenteral nutrition and early enteral nutrition models in the early period.<sup>[14]</sup> Due to problems such as respiratory distress syndrome and gastrointestinal system immaturity seen in the 1<sup>st</sup> days of life in VLBW preterm babies, enteral nutrition may not be adequately provided. On the other hand, for premature infants whose enteral feeding decision is made, intermittent or continuous feeding preferences are still a matter of debate.

When the gender and gestation weeks of the preterm babies included in the study were examined, it was seen that both groups were homogeneously distributed. It was determined that the weight, height, and head circumference values of the premature babies included in our study and weight, height, and head circumference measurements at discharge showed no significant difference in both groups. As a result of the study performed by Silvestre et al. with VLBW infants, it was reported that the group fed continuously and intermittently had homogeneous characteristics and there was no difference between discharge growth parameters when the protocols were terminated.<sup>[15]</sup> In a study comparing intermittent and continuous feeding in 245 babies with a birth weight of <1750 g, it was reported that there was no difference in reaching birth weight again.<sup>[16]</sup>

It is seen that different results have been obtained in comparative studies on the feeding model in VLBW preterm infants. In addition to studies supporting that intermittent feeding is more physiological and increases protein synthesis in skeletal muscle,<sup>[7]</sup> and intermittent feeding in-

creases gastric emptying rate and increases weight gain,<sup>[17]</sup> especially in VLBW preterm babies, the continuous feeding model is more effective in transition to full enteral nutrition and in reducing the risk of hypoxic ischemic intestinal injury.<sup>[18]</sup> In our study, no difference was found between babies in the continuous and intermittent feeding groups between the time to reach birth weight and the mean maximum weight loss. The rapid reach to birth weights of newborns in both enteral feeding models can be explained by the early initiation of parenteral feeding.

## TPN

It is accepted that early parenteral nutrition has positive effects on early growth without increasing the frequency of mortality and morbidity.<sup>[19]</sup> In our study, no statistically significant difference was found between the days of TPN and the time of transition to full enteral feeding in babies in the continuous and intermittent feeding group. Similar to the results of our study, it is reported that the enteral feeding model does not affect the TPN duration.<sup>[17]</sup> However, there are studies reporting that the duration of TPN administration is longer in preterm babies who receive intermittent feeding.<sup>[20]</sup> In the meta-analysis on the subject, it was accepted that intermittent and continuous feeding models have no effect on TPN duration.<sup>[6]</sup>

## Complete Enteral Nutrition

The results regarding the effect of the feeding model on the transition to full enteral nutrition show differences in studies. It is hypothesized that intermittent feeding has a positive effect on the gastrointestinal physiological development process and provides the stimulation necessary for development in a more physiological way. In studies evaluating the effect of feeding models on full enteral nutrition in preterm babies, while it has been reported that the transition period is longer in the continuous feeding model, on the contrary, there are studies reporting that the transition period is reduced in the continuous feeding model.<sup>[17,20]</sup> However, in two different studies comparing continuous and intermittent feeding models, it was found that there was no difference between transition times to full enteral nutrition.<sup>[15,16]</sup> In our study, no difference was found between the intermittent feeding model and the continuous feeding models in terms of transition times to full enteral feeding.

## Nutritional Intolerance

The effect of intermittent and continuous feeding models on feeding intolerance in preterm babies is not fully known. Since the definition of nutritional intolerance differs in studies, its frequency and the effect of nutritional

models on nutritional intolerance are not fully known.<sup>[6]</sup> In general, in studies, the effect of increasing the amount of food given on nutritional intolerance has been examined. In the comparison of the slow feeding model (20 ml/kg daily increase) and the fast feeding model (30 ml/kg daily increase) in preterm babies with a birth weight between 1000 and 1499 g, it was reported that the frequency of the development of nutritional intolerance showed no difference.<sup>[21]</sup> In the last multicentric study, which included 2804 babies with daily increases of 30 ml/kg and 18 ml/kg, and 24-month follow-up, no difference was reported between late-onset sepsis, NEC, and mortality rates with two feeding increase models.<sup>[22]</sup> In studies comparing continuous and intermittent feeding models, it was reported that there was no difference between the development of nutritional intolerance and the interruption of nutrition.<sup>[16,20]</sup> In our study, in which intermittent and continuous feeding models were applied, no difference was found between the frequency of the development of feeding intolerance in VLBW premature babies, supporting the literature.

## NEC

Undoubtedly, the most important factor in comparing the results of feeding models in preterm babies is the effect of the feeding model on NEC development. No difference was detected between the development of suspected NEC and the frequency of proven NEC in preterm babies who were applied intermittent feeding model and continuous feeding model with intragastric catheter.<sup>[6,16,23]</sup> In 185 preterm babies in which the effect of the amount of nutrition on the development of NEC was evaluated, NEC developed at a frequency of 13% in the slow feeding (15 ml/kg/day) model and of 9% in the fast feeding (35 ml/kg/day) model, and the incidence of NEC stage >2 in preterm babies did not change statistically.<sup>[24]</sup> The findings we obtained in our study support the knowledge that intermittent and continuous feeding models have no effect on the development of NEC in preterm babies. In our study, although statistically insignificant, it was determined that the time to develop NEC in VLBW babies who were fed continuously was later than the time of NEC development in VLBW babies fed intermittently. Differently, it has been reported that in the continuous feeding model in 70 preterm babies, the incidence of NEC (Bell Stage I) was lower and continuous feeding is better in terms of gastrointestinal tolerance.<sup>[20]</sup>

## Mechanical Ventilation Support

In our study, it was found that continuous and intermittent feeding models did not affect the duration of stay on mechanical ventilation in VLBW babies. Similar to the results of our study, Dsilna et al. reported no difference in their study

on VLBW babies between the feeding models applied to babies and the mechanical ventilation support.<sup>[20]</sup>

It was found that the hospitalization periods of babies of continuous feeding and intermittent feeding models were similar, and the feeding model did not affect the length of stay. It was reported that there was no difference between the mean length of hospital stay of preterm babies who were applied different feeding models.<sup>[15,24]</sup> On the other hand, it has been shown that the duration of hospital stay was significantly reduced in the nutritional model with a high daily increase in the amount of nutrition (30 ml/kg daily increase).<sup>[21]</sup> The discharge time, mean week of gestation, and growth parameters were found similar in the groups fed continuously and intermittently in our study. It has been reported that intermittent and continuous feeding models do not affect the growth parameters at discharge and discharge time of preterm babies.<sup>[6,15]</sup>

As a result, it was found that there was no difference between growth parameters and discharge time of preterm babies who were applied continuous and intermittent feeding models. Although there was no statistical significance on the development of NEC, it was determined that NEC developed earlier in the intermittent feeding model. It was concluded that both feeding models can be used safely in VLBW preterm babies. The research was conducted in a hospital's neonatal intensive care unit. It may be suggested to conduct similar studies with larger and different sample groups.

## Disclosures

**Ethics Committee Approval:** Ethical consent (Decision number: 288, 28.01.2014) was obtained from Şişli Hamidiye Etfal Training and Research Hospital before data collection. Parents of premature babies included in the study groups were informed verbally and in writing, and consent was obtained.

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**Conflict of Interest:** None declared.

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