

The Relationship Between Enteral and Parenteral Nutrition on Body Weight, Incidence of NEC, Sepsis and Length of Care for Preterm Infant in Dr. Soetomo General Hospital Surabaya

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ABSTRACT

The incidence of preterm birth in Indonesia still accounts for the highest mortality rate. Failure to provide adequate nutrition will have an impact on growth failure, risk of infection and longer duration of care for preterm infant. This study aims to analyzing the relationship between enteral and parenteral nutrition on body weight, the incidence of NEC, the incidence of sepsis and the length of care at Dr. Soetomo Hospital Surabaya. A total 106 subjects were enrolled, 78 infants were LBW, 19 infants were VLBW. Gestational age between 32-<37 weeks as many as 96 subjects. 68 infants were female. A total of 49 patients (46.2%) received parenteral nutrition. There is a relationship between enteral nutrition and the incidence of sepsis ($p=0.03$), parenteral nutrition and body weight ($p=0.005$), parenteral nutrition and the incidence of sepsis ($p=0.001$), and parenteral nutrition and the length of care for preterm infants ($p=0.001$). There is a relationship between enteral nutrition with the incidence of sepsis and parenteral nutrition with body weight, incidence of sepsis and length of care in preterm infants.

Key words: Preterm infant, Enteral, Parenteral nutrition, Neonatal sepsis, Hospitalization.

INTRODUCTION

According to the World Health Organization (WHO), preterm infant before 37 completed weeks of gestation accounts for 24% of neonatal death.¹ Judging from the number of babies born prematurely, Indonesia is the fifth country with the highest number of preterm babies in the world, amounting to 675,700 babies. The incidence of preterm birth in Indonesia still contributes to the highest mortality rate and is the second cause of death after pneumonia in children aged less than five years. Preterm infants are particularly vulnerable to complications due to impaired respiration, difficulty in feeding, poor body temperature regulation and high risk of infection. With the increasing contribution of neonatal deaths to overall child mortality, it is critical to address the determinants of poor outcomes related to preterm birth to achieve further reductions in child mortality.²

It remains well-recognized that adequate growth is one of the critical problem for every preterm infant. Inappropriate nutritional intake in preterm infants may be responsible for postnatal growth restriction (PGR) and adverse long-term outcomes and it remains a challenge for neonatologists. Early administration of optimal nutrition to preterm birth survivors lowers the risk of adverse health outcomes and improves cognition in adulthood.^{3,4}

During periods of critical illness, provision of enteral nutrition, which necessitates the use of parenteral nutrition, is unachievable. Parenteral nutrition is usually indicated in infants for whom enteral nutrition is contraindicated or delivers less than 75% of total protein and energy requirements.⁵

Enteral feeding is preferred to parenteral feeding, as the latter may be associated with catheter-related complications, infections, and sepsis, among others. However, institution of early parenteral nutrition can sometimes be critical and a necessary adjunct to enteral therapy.³

Various studies related to enteral and parenteral nutrition on the outcome of premature babies have been carried out, but have different final results. Previous studies have estimated that enteral nutrition has a strong association with the incidence of NEC in about 90-95% of cases of NEC occurring in infants with initiation/reinitiation of enteral nutrition or gradual increase in nutritional volume. In contrast to the results of a study conducted by Biswas *et al.* (2017) which compared the provision of nutrition in the two groups of early feeding versus late feeding on the risk of NEC, the results showed that the incidence of NEC was not significantly different between groups ($p=1.000$ vs $p=0.719$). In this study, the average weight of the patients in the two groups was also not significantly different (1196.3 ± 135.9 grams vs. 1172.3 ± 136.4 grams; $p=0.288$).⁶

The aim of this study is to analyze the relationship between enteral and parenteral nutrition on body weight, incidence of NEC, sepsis and length of care in preterm infants at Dr Soetomo General Hospital.

METHODS

The study is an analytic observational with a cross sectional design study using retrospective data. The data were collected from the medical record of neonates who mothers gave birth in Dr. Soetomo General Hospital from January 1 to

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April 30, 2020. Technical sampling was simple random sampling. Newborns delivered at less than 37 completed weeks of gestation, receive enteral and/or parenteral nutrition during hospitalized were included in the study. Infants who died before discharge, presented with any congenital malformation and incomplete medical records were excluded. Gestational age was calculated based on LNMP or Ballard Score clinical examination. Newborn weight was measured within 60 minutes of childbirth where calibration was considered for each neonate. The independent variable were premature infants who receive enteral nutrition in the form of breast milk, formula or only formula milk and receive parenteral nutrition. The dependent variable was body weight, incidence of sepsis, incidence of NEC and length of care. Body weight describes as body mass. Increase body weight when it reaches the target of growth velocity 10-15 g/kg/day. We reviewed data of all neonates and collected the data of sample characteristic such as sex, gestational age, birth weight, body weight on discharge, mode of delivery, and outcome. The collected data were edited, coded, and entered in distribution tabulation and were analyzed using computer assisted statistical package (SPSS version 21). Chi square and logistic regression analysis were used to analyze the data. Independent and dependent variables with a p-value of less than 0.05 level of significance were considered significantly significant. Ethical approval was obtained from the Health Research Ethics Committee (KEPK) located at Dr. Soetomo General Hospital Surabaya with the issuance of the statement of ethical clearance No. 1971/KEPK/IV/2020.

RESULTS

In this study, 106 participants were collected according to the inclusion and exclusion criteria. The collected data from January 1 to April 30, 2020 have been reviewed from all of medical record of the neonates that admitted in NICU ED Dr Soetomo hospital. The characteristics of the subjects of this study are all listed in table 1. The subjects in this study were mostly female (64.2%). Infants with very low birth weight were found in 78 subjects (73.6%) and the highest gestational age based on Ballard Score was >32 weeks (90.6%). Table 1 shows that of the 106 subjects, 49 patients (46.2%) received parenteral nutrition. Administration of enteral and parenteral nutrition showed weight gain at discharge according to the target as many as 30 patients (28.3%), 3 patients had incidence of NEC (2.8%), 10 patients had proven sepsis based on blood culture result (9.4%), and the length of care is about 14 days. There were statistically significant association between the administration of enteral nutrition and the incidence of sepsis, between parenteral nutrition and the body weight, parenteral nutrition and the incidence of sepsis, and parenteral nutrition and the length of care in preterm infants ($p=0.03$, $p=0.005$, $p=0.001$, and $p=0.001$ respectively).

DISCUSSIONS

Based on the results of the bivariate analysis between enteral nutrition and the incidence of sepsis in preterm infants using the chi-square test, a p-value of 0.03 was obtained. The p-value < 0.05 so it can be said that there is a relationship between enteral nutrition and the incidence of sepsis. The result can be clinical sepsis characterized by signs and symptoms of sepsis but not accompanied by positive blood culture results. These results are in line with research conducted by Flider, *et al.* (2004) related early enteral feeding with the incidence of nosocomial sepsis in LBW infants in a multivariate analysis, including significant variables in univariate analysis showing that age at start of enteral feeding, RDS, and birth weight were the most significant predictors of the risk of sepsis. nosocomial ($p = 0.0005$, $p = 0.024$, $p = 0.011$).⁷

Research by Okascharoen, *et al.* (2007) said that all neonates admitted to the tertiary NICU and all cases of sepsis were nosocomial infections. They diagnosed the infection at the first sepsis evaluation, to avoid positive results associated with previous septic episodes, and to avoid

Table 1: Characteristics of Neonates that admitted in Dr. Soetomo hospital from January-April 2020.

Subject characteristics	Total (N = 106)
Birth Weight (gram)	
≥ 2500	9 (8.5)
< 2500	78 (73.6)
<1500	19 (17.9)
Gender	
Male	68 (64.2)
Female	38 (35.8)
Mode of Delivery	
Spontaneous	15 (14.2)
Caesarian section	90 (84.9)
Forceps	1 (0.9)
Gestational Age (New Ballard Score)	
32- <37 weeks	96 (90.6)
28- < 32 weeks	10 (9.4)
Apgar Score	
>7	89 (84)
4-6	37 (16)
Parenteral Nutrition	
Yes	49 (46.2)
No	57 (53.8)
Enteral Nutrition Type	
Human milk + Formula milk	59 (55.7)
Formula milk	47 (44.3)
Using Ventilator	
Yes	6 (5.7)
No	100 (94.3)
NEC	
Yes	3 (2.8)
No	103 (97.2)
Sepsis	
Yes	10 (9.4)
Clinical sepsis	18 (17)
No	78 (73.6)
Length Of care (days). median(min-max)	14 (4-46)
Blood culture	
Yes	96 (90.6)
No	10 (9.4)
Type Of Bacteria	
Klebsiella pneumonia ESBL	4 (3.8)
Klebsiella pneumonia	1 (0.9)
Acinetobacter baumannii	4 (3.8)
Staphylococcus capitis	1 (0.9)
Body Weight On Discharge	
Weight gain at good velocity	30 (28.3)
Weight gain at bad velocity	30 (28.3)
No weight gain/loss	3 (2.8)
Weight loss	43 (40.6)

Table 2: The association between enteral nutrition and the incidence of sepsis in preterm infants.

Sepsis	Enteral Nutrition		p-value
	Human Milk + Preterm Formula Milk	Preterm Formula Milk	
Proven Sepsis	5	12	0.03*
Clinical Sepsis	22	13	
No Sepsis	73	75	

Data is displayed in N (%). Chi-square test was used in the analysis of Table 2.

*p value <0.05 which means the variable is statistically significant.

repeated readings from the same neonates. This is necessary so that the positive culture criteria really detect late-onset sepsis. Infection based on positive blood culture results alone will underestimate the incidence of late onset sepsis. However, suspicion of clinically late onset sepsis as the reference standard, which relies on subjective judgments, is likely to result in an overestimate of laboratory results.⁸

Table 3: The association between parenteral nutrition and the weight in preterm infants.

Body weight	Parenteral Nutrition	r	p-value
Weight Gain at Good Velocity	38	0.27	0.005*
Weight Gain at Bad Velocity	32		
Weight loss	26		
No weight gain/loss	4		

Data is displayed in N (%). Chi-square test was used in the analysis of Table 3.

*p value <0.05 which means the variable is statistically significant.

. r = rho.

Table 4: The association between parenteral nutrition and sepsis in preterm infants.

Sepsis	Parenteral Nutrition		p-value
	Yes	No	
Proven Sepsis	19	0	0.001*
Clinical Sepsis	22	10	
No Sepsis	59	90	

Data is displayed in N (%). Chi-square test was used in the analysis of Table 4.

*p value <0.05 which means the variable is statistically significant.

Table 5: The association between parenteral nutrition and the length of care in preterm infants.

Length of care	Parenteral Nutrition (N%)	r	p-value
	100	0.45	0.001*

Data is displayed in N (%). Chi-square test was used in the analysis of Table 5.

*p value <0.05 which means the variable is statistically significant.

r = rho.

Enteral nutrition should be started as soon as possible after birth, using maternal colostrum and milk as the first options. Enteral nutrition promotes gastrointestinal development functions, even when administered in small, "trophic" or large intestinal quantities. The growth and development of the gastrointestinal mucosa depends on enteral, not parenteral, nutrition. Enteral nutrition increases capacity to increase feeding tolerance and growth, reduces need for phototherapy (by increasing stools), decreases cholestasis, decreases osteopenia (more calcium and phosphorus in enteral than IV feeding), increases gastrointestinal trophic hormone surges, increases gastrointestinal motility. Breastfeeding is not only reduces the incidence of late-onset sepsis and NEC but also improves neurodevelopmental outcomes in premature infants.⁹

In this study, the body weight have the significant relationship to parenteral nutrition in preterm infants. Research by Wang, *et al.* (2021) showed that 23.9% of infants were small for gestational age at birth. Poor weight gain outcome after parenteral nutrition was observed in 62% of infants. More than half of preterm infants experience poor weight gain during parenteral nutrition. Although avoiding excessive early growth rates may play a role in the prevention of cardiovascular disease, there are no data showing the overall benefit of limiting nutrient intake, or limiting growth in premature infants. Meanwhile, strong data suggest that inadequate nutrition and growth can permanently affect brain outcomes.¹⁰ Growth failure has been reported among up to 90% of premature newborns on discharge from the neonatal intensive care unit (NICU) and may persist in the first years of life. Postnatal growth retardation remains a challenge for neonatologists. Adequate nutritional support immediately after birth is essential for premature newborns to limit growth retardation. Over the past decade, early "aggressive" nutrition has become the benchmark in the NICU to achieve neonatal growth as close to the fetus as possible at the same gestational age.¹¹

This study showed that parenteral nutrition have significant effect on the incidence of sepsis in premature infants. Many studies related to parenteral nutrition related to blood infections (BSI). Nosocomial BSI due to parenteral nutrition is a potentially fatal complication with an attributable mortality rate of 11% in neonates. The high mortality, high incidence rate of late-onset sepsis and central line-associated blood infections (CLABSIs), necessitates efforts to reduce these risks as much as possible. Reasons for parenteral nutrition were identified as a risk factor by a number of studies including infusion contamination; However, catheters can be infected at any time during catheterization due to handling, which is exemplified by the fact that coagulase-negative Streptococci (CoNS) are the most common pathogen identified in neonatal CLABSI.¹²

However, there are other factors that can influence the incidence of sepsis in neonates besides parenteral and enteral nutrition which can come from the mother and neonate. Maternal risk factors are premature rupture of membranes, maternal infection and fever during delivery, foul-smelling amniotic fluid, cloudy and meconal amniotic fluid, and multiple pregnancy; Neonatal risk factors were prematurity, low birth weight, asphyxia, resuscitation during labor, invasive procedures, congenital abnormalities, length of care in the neonatal intensive care unit. Other risk factors are more often found in males than females, in black neonates, and low socioeconomic neonates.^{13,14}

Based on the results of the bivariate analysis between parenteral nutrition and the length of care in premature infants using the chi-square test, the p-value of 0.001 was obtained. The p-value < 0.05 so it can be said that there is a relationship between parenteral nutrition and the length of care. Length of care can be considered as an indicator of severity for preterm infants. A study by Lima, *et al* in Oliveira, *et al* (2020) showed that an increase of one day in length of care for very low birth weight infants increased the incidence of stunted growth of head circumference and weight at discharge (z score 2 by age). corrected), by 3% and 2%, respectively. The period of hospitalization was lower in the study by Abranches, *et al.* on Oliveira, *et al.* (2020) when studying preterm infants <32 weeks' gestation for gestational age (39.7 ± 13.8 days).¹⁵

The strength of this study are the research subjects with large case sample data. The limitations of this study include a cross-sectional design that only assessed the dependent and independent variables at one time so that it did not analyze other factors that could affect the outcome of body weight, incidence of NEC, incidence of sepsis and duration of care for premature infants. Retrieval using medical record data will be highly risk if it is not recorded properly, so research designs such as cohorts are recommended to avoid data bias. Further research needs to be done with different study designs and uniform patient conditions.

CONCLUSION

It is necessary to consider the assessment of other variables that may affect the outcome of body weight, incidence of NEC, sepsis and length of care in preterm infants (e.g use of ventilator, CPAP, HFN, central intravenous access, etc) and further studies with prospective research methods to determine whether outcomes of body weight, incidence of NEC, sepsis and duration of treatment were only affected by enteral and parenteral nutrition.

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