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ORAL CARE PREVENTS LATE-ONSET SEPSIS IN RISK PRETERM INFANTS

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Abstract

The incidence of infections in preterm infants is still quite high. In this study, oral care with human breast milk was implemented in risk preterm infants as a precaution. The study was conducted using a quasi-experimental method with a non- equivalent control group and posttest only design in 40 risk preterm infants. The participants were divided into two groups of 20. The data were analyzed using independent t-test and a Wilcoxon test. The results show that this intervention has an effect on the incidence of late-onset sepsis in preterm infants. The effect is based on symptoms: body temperature instability (p= 0.021), C-reactive protein (p= 0.006), and leukocytes (p= 0.020) all indicated differences between the two groups. It is recommended that this practice be adopted as a routine therapy program in perinatology.

Keywords: exclusive breastfeeding, late-onset sepsis, oral care, risk preterm infants, sepsis

Abstrak

Perawatan Mulut Mencegah Sepsis Neonatorum Awitan Lambat pada Bayi Prematur Risiko Tinggi. *Angka kejadian infeksi setelah lahir pada bayi prematur masih cukup tinggi. Pelaksanaan intervensi pemberian oral care menggunakan air susu ibu pada bayi prematur risiko tinggi telah dilakukan sebagai pencegahan. Penelitian dilakukan menggunakan metode kuasi eksperimen dengan desain post-test only, kelompok kontrol non ekuivalen, pada 40 bayi prematur risiko tinggi sebagai sampel. Responden dibagi menjadi dua kelompok, masing-masing kelompok 20 responden. Data dianalisis menggunakan uji t independen dan wilcoxon. Hasil Intervensi ini terbukti memiliki manfaat terhadap dalam menurunkan kejadian sepsis neonatorum awitan lambat pada bayi prematur berdasarkan tanda klinis seperti ketidakstabilan suhu tubuh (p= 0,021), hasil pemeriksaan C-Reaktif Protein (p= 0,006) dan leukosit (p= 0,020) yang menunjukkan adanya perbedaan yang bermakna antara kelompok kontrol dan kelompok intervensi. Intervensi ini diharapkan dapat dilanjutkan menjadi program terapi rutin yang akan dilakukan di ruang rawat perinatologi.*

Kata Kunci: *ASI eksklusif, bayi prematur, oral care, sepsis, sepsis neonatorum awitan lambat*

Introduction

Neonatal sepsis contributes to neonatal morbidity and mortality (Qazi & Stoll, 2009). Neonatal sepsis that occurs 72 hours after birth is known as late-onset neonatal sepsis and is caused by the contamination of the infants' environment (Hammoud, Al-Taiar, Thalib, Al-Sweih, Pathan, & Isaacs, 2012).

The incidence of late-onset neonatal sepsis increases with the survival of preterm infants, especially in those with a very low birth weight (Kinney, Lawn, Howson, & Belizan, 2012). As a result of the immaturity of organs, preterm infants with low or very low birth weight often experience some problems in the period immediately after birth. This condition is a high-risk factor for the incidence of late-onset neonatal sepsis because it is related to invasive action, long-term use of medical equipment (including central venous access and mechanical ventilation), and failure of early enteral feeding using breast milk. It can also affect the duration of parenteral nutrition and length of treatment (Troger et al., 2014).

Bekhof, Reitsma, Kok, and Van Straaten (2013) revealed that early diagnosis of late-onset neonatal sepsis is quite tricky, especially in preterm infants who often have non-specific signs. However, the most common symptoms are the reduction of spontaneous activity, the lack of sucking, periods of respiratory arrest (apnea), pulse rate of less than 100 per minute (bradycardia), pulse rate of over 180 per minute (tachycardia), and instability of body temperature (hypothermia).

Some researchers rely on the results of laboratory tests, such as leukocytes, C-reactive protein (CRP), procalcitonin (PCT), and blood cultures to diagnose sepsis (Stemberger & Tesovic, 2012). However, blood culture examinations often produce negative results due to the limited amount of blood obtained (Bekhof et al., 2013). According to Downey, Smith, and Benjamin (2010), infection control in preterm infants remains a foundation in the prevention of late-onset neonatal sepsis.

Pre-term newborns need treatment that can prevent sepsis after birth. Rodriguez, Vento, Claud, Wang, and Caplan (2015) reveal a strategy in the form of oral care using breast milk/colostrum as soon as the infant is born. According to Pammi and Abrams (2011), the lactoferrin in breast milk is an important component in defense against infection. Breast milk also contains bioactive substances (immune and trophic) that provide antimicrobial, anti-inflammatory, antioxidant, and immunomodulatory functions, thereby increasing intestinal microbiota and accelerating intestinal maturation. These bioactive substances are mostly found in breast milk from mothers who give birth to preterm infants. Under normal conditions, during the womb, the fetus will obtain bioactive materials from the amniotic fluid until 40 weeks' gestation. If the infant is born in insufficient months or prematurely, then the bioactive material will be produced through breast milk (Rodriguez & Caplan, 2015).

According to a preliminary study conducted on the number of occurrences of infection in the perinatology room of a hospital in Jakarta in 2016, the incidence of diseases is high at around 16.7% to 18.9% due to the installation of central venous access or peripherally inserted central venous catheter (PICC) and associated pneumonia (VAP) ventilator. The incidence of this infection is most common in infants weighing <1499 grams. Once observed, the intervention of oral care with ASI/colostrum can be applied to newborns. This intervention is expected to provide a significant reduction in the incidence of infection so that premature newborns are not affected by sepsis. This is achieved by monitoring the hemodynamic and laboratory indicators, such as oxygen saturation, respiration, pulse, thermoregulation, perfusion, CRP, PCT, Immature to Total neutrophil ratio (IT ratio), and baby leukocytes in the Hospital Perinatology room in the Jakarta area.

Methods

The implementation of evidence-based nursing (EBN) through the provision of oral care was carried out using a quasi-experimental research method with a non-equivalent control group, post-test only design (Sugiyono, 2015). The sampling technique was consecutive sampling. The sample in this study consisted of 40 high-risk preterm infants. The sample was divided into two groups: 20 infants in the intervention group and 20 infants in the control group. The inclusion criteria for the infants who are the respondents in this study are high-risk preterm infants with a gestational age of fewer than 37 weeks, while the exclusion criteria include infants born with congenital abnormalities, born to mothers infected to the Human Immunodeficiency Virus (HIV), drug abuse, and chorioamnionitis pregnancy.

This study was conducted in a general hospital in Jakarta and had been approved administratively and carried out by applying the principles of research ethics. The implementation of EBN involved nurses who worked in the care room, especially the special care nursery (SCN) room four, a high-risk newborn transition space.

Every preterm newborn included in the inclusion criteria was immediately given oral care using breast milk (0.2 mL) eight times a day (every 3 hours).

The variables measured to determine the success of this intervention included gestational age and birth weight identified through the patient's medical record data. Each infant's condition was also assessed from several sepsis indicators, including hemodynamic status and laboratory examination result.

The hemodynamic status was assessed using the oxygen saturation (normal: more than 88%), as measured by oximetry (calibrated). The frequency of breath was calculated in one minute (normal: 40–60 times/minute) by looking at the movements of the infants' chest and abdomen during inspiration, followed by the expiration process (normal pulse or heart rate: 100–140 times/minute) as measured using a stethoscope. Peripheral perfusion was measured by calculating the capillary refill time (CRT, normal: less than 2 seconds) and infants' body temperature (normal: 36.5^{o}C–37.5^{o}C) using a thermometer (calibrated). The laboratory results assessed include leukocytes (normal: 6–14 × 103/µL), CRP (normal: <5.0 mg/L), IT ratio (normal: 0.00–0.20), and PCT (normal: <0.05). The laboratory normal value guidelines were adjusted to the reference values of the hospital laboratory.

Oral care was performed using a 1 mL syringe by dripping it slowly on the right and left sides of the infant's buccal mucosa and paying attention to the infant's response. Dropping the breast milk in the infant's buccal mucosa can prevent the colonization of pathogenic bacteria, which can cause sepsis in infants, especially in the infant observed to have nothing per oral (NPO) status and has not drunk the breast milk orally. Breast milk given during oral care is preferably derived from the colostrum of the infant's mother. However, if breast milk is not available yet, then donor breast milk can be used as an alternative. The control group in the implementation of EBN consisted of infants who were not given oral care via breast milk since the first 24–48 hours after birth.

Results

Respondents' Characteristics. The characteristics of each variable in this study consisted of gestational age and birth weight, which are described in Table 1.

The results in Table 1 showed that the mean gestation time of the most severe preterm infants in the perinatology room of a hospital was 31.95–32.75 weeks with a standard deviation of 2.438 and 2.268. The youngest respondent was 26 weeks, and the oldest respondent was 36 weeks. The results of processing Table 5.1 also show that the mean weight of the premature babies was 1528.75–1764.75 grams with a standard deviation of 339.093–500.732. The lowest pre-term birth weight was 800 grams, and the highest pre-term birth weight was 3080 grams.

Table 1. Respondents' Characteristics Based on the Infants' Gestational Age and Birth Weight in the Intervention and Control Groups (n1= 20, n2= 20)

Variable	Mean	Standard Deviation (SD)	Range (Min-Max)	p
Gestational Age (Weeks)				
Intervention	31.9	2.44	26–36	0.289
Control	327	2.27	29–36	
Birth Weight (Gram)				
Intervention	1528.7	339.09	800–1955	0.089
Control	1764.7	500.73	1100–3080	

Information: *Independent t-test* result using *Levene's Test*
$p < 0.05$, there is a significant difference

Table 2. Comparison of Infants' Oxygen Saturation, Breath Frequency, Pulse Frequency, CRP Value, and IT Ratio in the Intervention and Control Groups (n1= 20, n2= 20)

Variable	Mean	Standard Deviation (SD)	Range (Min-Max)	p
Oxygen Saturation (%)				
Intervention	95.53	0.993	94–98	0.010
Control	94.15	1.981	90–97	
Breath (times/minute)				
Intervention	49.95	2.212	45–54	0.099
Control	51.4	3.136	45–58	
Pulse (times/minute)				
Intervention	143.75	12.590	104–164	0.833
Control	144.5	9.545	127–163	
CRP (mg/L)				
Intervention	0.315	0.232	0.1–0.9	0.006
Control	4.482	5.975	0.1–18.2	
IT Ratio				
Intervention	0.098	0.056	0.02–0.2	1
Control	0.098	0.050	0.02–0.2	

Information: *Independent t-test* result using *Levene's Test*
$p < 0.05$, there is a significant difference

As shown in the results in Table 2, the data were normally distributed, and the difference in comparison was based on oxygen saturation, respiration, perfusion, pulse, CRP value, and IT ratio by using an unpaired independent t-test that first looks at the data variants using Levene's test. The results of the difference in the ratio of preterm infant oxygen saturation showed that the mean oxygen saturation of pre-term infants in the intervention group was 95.53% higher than the mean oxygen saturation in the control group, which was 94.15% with p= 0.010. These results indicate that there are significant differences between the two groups.

In the perfusion variable, the data obtained from the patients were constant, and there was no variation in every preterm infant. In comparison, in the respiratory variable, the average respiratory frequencies of the respondents in the intervention and control groups were 49.95 and 51.40 times per minute, respectively, with p= 0.099. These results indicated that there were no significant differences between the two groups.

As shown in Table 2, the average pulse frequency in the preterm infants in the intervention group was 143.75, while that in the control group was 144.50 times per minute with p= 0.833. These results indicated that there were no significant differences between the two groups. For CRP values, based on the results in Table 2, the mean CRP of preterm infants in the intervention group was 0.315 lower than that of preterm infants in the control group 4.481 mg/L with p= 0.006. These results indicated that there were significant differences between the two groups. Meanwhile, the mean IT Ratio value of preterm infants in the intervention group and the control group was 0.098 with p= 1. These results indicated that there were no significant differences between the two groups.

The results of the analysis in Table 3 using the Wilcoxon test showed that the mean thermoregulation of preterm infants treated in the perinatology room of the hospital was 16 (80%) in the intervention group and 8 (40%) in the control group with p= 0.021. These results indicated

Table 3. Comparison of the Thermoregulation Status, Perfusion, and Leukocyte Value in the Intervention and Control Groups (n1= 20, n2= 20)

Variable		Intervention		Control		p
		n	%	n	%	
Thermoregulation (^{0}C)	Stable	16	80	9	40	0.021
	Unstable	4	20	12	60	
	Total	20	100	20	100	
Perfusion	Lengthen	0	0	4	20	0.157
	Does not lengthen	20	100	16	80	
	Total	20	100	20	100	
Leukocyte	Normal	16	80	9	45	0.020
	Leukopenia/ Leukocytosis	4	20	11	55	
	Total	20	100	20	100	

Information: *Wilcoxon Test* result
p< 0.05, there is a significant difference

that there were significant differences between the two groups. Likewise, the number of leukocyte levels in the intervention group showed that 16 (80%) had normal levels of leukocytes, in contrast to the results obtained in the control group, only 8 (40%) with p= 0.020. Thus, it can be concluded that there were also significant differences between the two groups.

Discussion

Respondents' Characteristics. The result shows that infants in this research are preterm infants with the gestational age ranging between 26 and 36 weeks. Most infants in this research have a birth weight ranging from 1100–1955 grams.

Pre-term infants with low birth weight have a risk of experiencing late-onset neonatal sepsis. This is due to their immature immune system, which facilitates the translocation of pathogenic bacteria to the barrier epithelium of the intestinal mucosa (Gephart & Weller, 2014).

Late-onset neonatal sepsis in preterm infants is also caused by a large number of invasive procedures performed during the infant's treatment, including the installation of invasive catheters, such as the central venous access, which can provide access to the entry of blood vessel pathogens and cause late-onset neonatal sepsis in preterm newborns (Rodriguez et al., 2015).

Kinney, Lawn, Howson, and Belizan (2012) reveal that a preterm infant with low birth weight are susceptible to infection as soon as the infant is born. The condition of infants born with immature organ function due to fewer months of birth causes the infants to receive several invasive procedures of treatments to support their body condition compared to infants who are born with appropriate gestational age who received fewer procedures.

Pre-term infants are not exposed to bioactive substances that act as immunostimulant contained in the amniotic fluid. The bioactive material is produced until 40 weeks of gestation (Rodriguez & Caplan, 2015). Infants born to an earlier gestational age cannot perform anoral intake properly because the coordination of reflex sucking and swallowing is not yet perfect. This condition causes the infants to be directly attached to the orogastric tube, which prevents the normal flora of the infants' oropharyngeal canal from developing. This results in the colonization of pathogenic bacteria in the oropharyngeal canal, which can increase late-onset neonatal sepsis (Rodriguez & Caplan, 2015).

The incidence of late-onset neonatal sepsis, which tends to occur in preterm infants at high risk due to invasive procedures received after birth, can be prevented by applying evidence-based interventions. Such intervention can come in the form of giving oral care using breast milk, which is dripped on the infant's buccal mucosa as soon as the infant is born. The provision of oral care using breast milk can be a complement to trophic feeding in preterm infants (Morgan, Bombell, & McGuire, 2013).

On the basis of the preliminary study conducted by Rodriguez et al. (2010), Rodriguez et al. (2015), and Sohn, Kalanetra, Mills, and Underwood (2015), this intervention (i.e., giving the mother's breast milk/ colostrum through the buccal mucosa to the oropharynx as soon as the infant is born) is considered safe and feasible when applied to preterm newborns. Early breastfeeding is protective against infection. The lactoferrin and glycoprotein contents of breast milk have antimicrobial characteristics, thus protecting the infant from the risk of infection (Downey et al., 2010; Pammi & Abrams, 2011).

Comparison of Sepsis Incidence Based on Oxygen Saturation, Respiratory, Pulse Rate, Perfusion, Thermoregulation, Leukocyte, CRP, PCT, and IT Ratio Indicators in the Intervention and Control Groups. The results of this study indicate a significant difference between oxygen saturation in the intervention group and the control group. However, when it is viewed from the oxygen saturation values of both groups (ranging from 90% to 98%), these indicate that the infants' oxygen saturation rates in both groups are in the healthy category and are not indicators of sepsis (Lee et al., 2015).

The results of this study also show the leukocyte, CRP, and thermoregulation values that have significant differences in both groups. The CRP values in the two groups range from 0.1–18.2 mg/L, indicating the presence of infants who experienced sepsis. If it is viewed in more detail, the control group shows CRP values of 0.1–18.2 mg/L, which are far above the value in the intervention group ranging from 0.1–0.9 mg/L. This is an essential finding in the implementation of this EBN, which indicates that the provision of oral care using breast milk can have an impact on the low CRP value in the intervention group. The average amount of CRP is fewer than 5 mg/L. This is consistent with the opinion of Rodriguez and Caplan (2015) and Lee et al. (2015) who stated that clinical instability (e.g., the instability of body temperature, desaturation, and perfusion) and an increase in infection markers (e.g., CRP, leukocyte, and IT ratio) can be indicators of sepsis. To overcome this, biochemical and immunology research have been conducted showing that oral care using breast milk, especially colostrum, can provide the highest level of protection against nosocomial infections in infants.

Gomella, Cunningham, and Eyal (2013) revealed that body temperature instability, such as hypothermia, is a clinical sign of sepsis in preterm infants, while hyperthermia is more common in term infants after the first 24 hours of life. Moreover, perfusion problems, cyanosis, and respiratory problems, such as tachypnea and apnea occurring in the early 24 hours after birth or after one week of age can also be used as a marker of sepsis (Dong & Speer, 2015). However, this problem is not observed in the implementation carried out in the current work.

Bekhof et al. (2013) added that the first enforcement of a late-onset neonatal sepsis diagnosis in neonates is quite tricky, especially in preterm infants who often show symptoms that are difficult to recognize. Common symptoms commonly found in infants who experience sepsis are reduced infant activity, weak muscle tone, a period of persistent breathing stops, decreased or increased pulse rate, and body temperature instability (Downey et al., 2010).

According to Rodriguez et al. (2011), if during the procedure of giving oral care the infant shows signs of agitation, has desaturation with <88% saturation, or shows changes in vital signs, then the procedure must be stopped because it could

indicate that the infant experiences worsened conditions and the intervention does not provide any benefit to improve his/her condition.

The result of this evidence-based implementation also aligns with the research conducted by Thibeau and Boudreaux (2013), Lee et al. (2015), and Rodriguez et al. (2015) who reported that infants given oral care did not experience decreased oxygen saturation, bradycardia, cyanosis, hypotension, thermoregulation instability, or other side effects. All infants who received oral care showed a sucking response to the orogastric tube during oral care.

Rodriguez et al. (2010) added that the implementation of oral care is safe and can be easily performed because it does not endanger the infants' condition. Moreover, the provision of oral is an alternative for infants who have an NPO status. This means that, for the time being, the infant does not receive fluid intake orally for specific reasons, and this oral care is applied as a complement to trophic feeding in the first-day infant's life (Morgan et al., 2013).

The Comparison of Late-Onset Neonatal Sepsis Events Based on Laboratory Results between the Intervention and Control Groups. Some indicators that are used as markers of sepsis are in accordance with the study of Lee et al. (2015) who categorized the clinical signs of sepsis into three groups: (a) general signs (fever, apnea/tachypnea, respiratory disorder, and fluid imbalance), (b) laboratory results (leukopenia/leukocytosis and increased CRP), and (c) hemodynamic changes (hypotension, tachycardia, perfusion changes, and decreased urine output).

To prove the occurrence of sepsis, some researchers relied on the results of laboratory tests, such as leukocytes, CRP, PCT, and blood cultures (Stemberger & Tesovic, 2012). However, some of the results of blood culture examination are not accurate due to the limited amount of blood obtained during the blood collection (Bekhof et al., 2013; Stemberger & Tesovic, 2012).

Intestinal atrophy in infants can also prevent enteral feeding in the first days of the infant's life due, which increases the risk of enteral eating intolerance and necrotic enterocolitis (NEC) (Rodriguez & Caplan, 2015).

Providing oral care has a good impact on enteral drinking tolerance in preterm newborns. Infants who are routinely given oral care tend to drink faster and do not experience NEC compared to infants who are not given oral care (Pammi & Abrams, 2011). This is consistent with previous studies, which reported that giving colostrum or breast milk to preterm infants immediately after birth can cause systemic immunostimulatory effects (Gephart & Weller, 2014).

This evidence-based implementation aims to reduce the incidence of late onset neonatal sepsis in preterm newborns basically using maternal colostrum or mother's breast milk. However, due to the limitation of child nursing residents who are unable to properly collect maternal colostrum immediately after birth, and coordination problems with the parties concerned, the provision of oral care is modified using donor breast milk for infants who do not get breast milk from their mothers (Møller, Fink, Sangild, & Frøkiær, 2011).

The American Academy Association of Pediatrics (2012) has submitted a policy related and recommends that all preterm infants should receive breast milk. Pasteurized donor breast milk can be an alternative if the mother cannot produce enough milk instead of giving formula milk to the infant. This recommendation is based on several proven benefits of breastfeeding, including a decrease in the incidence of late-onset neonatal sepsis, NEC, retinopathy of prematurity, shorter days of care, and improvement of neural development compared with preterm infants receiving formula milk (Underwood, 2013).

Previous studies related to the provision of breast milk derived from donors in preterm newborns have revealed that there is a low incidence of sepsis, enteral eating intolerance, NEC, and acceleration of intestinal maturation compared to the use of formula milk (Gibbins, Wong, Unger, & O'Connor, 2013).

The previous studies that reported the benefits of breast milk in preterm infants compared giving breast milk to giving formula. The women who provided breast milk were not just biological mothers but also donors. Donor breast milk contributed to an increase in body weight and reduced the incidence of NEC in preterm infants compared to formula milk feeding, which is known to provide increased growth in infants in the short term, but also increases the rate of NEC in preterm infants (Bertinov et al., 2013).

According to Gibbins et al. (2013), the provision of donor breast milk for preterm infants, whose mothers cannot produce breast milk, also has several challenges, such as nutritional composition, safety, supply, and immune protection. Most donor breast milk supplies are obtained from mothers who gave birth to mature babies and who have already weaned their babies but still pump their milk and then donate. Such breast milk usually has a lower protein and fat content and many bioactive molecules compared with the breast milk of mothers in the first weeks of giving birth to their preterm infants.

The process of sending a breast milk donor can minimize the potential contamination of breast milk with infectious agents. Therefore, milk banks have rigid standards for the early detection of donor breast milk and carry out the pasteurization process before distributing the breast milk supplies. This is because pasteurization is very useful in reducing the risk of transmission of HIV, CMV, Hepatitis B, and Hepatitis C. However, this pasteurization process also harms the milk by reducing the amounts of oligosaccharides and lactoferrin found in breast milk (Underwood, 2013).

Nevertheless, donor breastfeeding is a good alternative because it also provides benefits in stimulating biofactor substances in the mucous membrane compared to giving formula milk or fasted babies (NPO), which can trigger the colonization of pathogenic bacteria in the oral cavity (Underwood, 2013).

The implementation of oral care using breast milk may face several obstacles. Some limitations include the difficulty in coordinating to provide maternal colostrum immediately after childbirth, the problem in collaborating with doctors in charge of the room, and problems with the providers of donor breast milk. The small number of samples and research time, which is too short, may have also affected the results of this study, which are not significantly different from those of the control group.

Conclusions

There are significant differences in oxygen saturation, CRP, thermoregulation, and leukocytes in the intervention and control groups after the provision of 8 × 0.2 mL of oral care using breast milk. Oxygen saturation rates in both groups were in the normal range, indicating that oral care has an impact on maintaining oxygen saturation in preterm infants. The CRP value in the intervention group is lower than that in the control group, showing that oral care using milk provided the infants' bodies some line of defense against infection. The provision of oral care using breast milk has also been proven to maintain the stability of body temperature in the intervention group. This finding shows that the leukocyte values in the normal range can be maintained by performing oral care using breast milk.

In the implementation of the EBN of oral care in pre-term infants, child nursing residencies encountered several obstacles. However, overall, the results of the EBN implementation provided benefits to the preterm infants in the prevention of late-onset neonatal sepsis. Hence, the nurses in the perinatology room can provide

oral care for the preterm newborns, especially with maternal colostrum. If the maternal colostrum is not available, it can be safely replaced by oral care using donor breast milk.

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