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Original Article

Importance of Milk Expression for Preterm Infants

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Mothers of preterm infants may find it difficult to express breast milk. There is a low breast milk rate among preterm infants at discharge at our hospital, and here we tested the hypothesis that milk expression factors were the cause of the low rate. The study subjects were born before 33 gestational weeks at our hospital between March 2005 and June 2014. Nutritional evaluation was performed at discharge and noted whether breast milk, infant formula, or a mix of the 2 was being given. We compared the group given breast milk or the mix versus the group given formula. Of the 337 infants, 40 cases were excluded. Data from 297 infants were analyzed. The mean (SD) gestational age and birth weight were 29.5 (2.4) weeks and 1,230 (391) g, respectively. At discharge, 26 (8.8%), 102 (33.3%), and 174 (57.9%) infants were given breast milk, formula, and the mix, respectively. A multivariate logistic regression analysis showed that the first milk expression (h) was the risk factor for the formula group: adjusted odds ratio (95% confidence interval) 1.06 (1.02-1.09) and $p = 0.002$. Delayed first milk expression could affect the low breast milk rate at discharge. Improvement of milk expression should be achieved to promote breastfeeding.

Key words: breast milk, breastfeeding, formula, milk expression, preterm

Breast milk is beneficial for preterm infants, not only nutritionally, but also to prevent necrotizing enterocolitis (NEC), obesity, and for improved neurodevelopment [1-5]. For the mothers of preterm infants, it can be difficult to express breast milk [6]. Reports of the proportion of preterm infants given breast milk upon discharge from the NICU have varied widely from 60-68% [7, 8] to 6-29% [9]. Risk factors for the need for infant formula were reported: delayed start of milk expression, infrequent milk expression, young mother, an unmarried mother, smoking, early gestational age (GA) and low educational background [6, 7, 10-12].

According to an unpublished report in our hospital, the breast milk rate at the discharge of the preterm infants (born before 33 gestational weeks) was very low at 8.8%, and insufficient maternal support for milk expression was identified. In the present study, we tested the hypothesis that milk expression factors were the cause of the low breast milk rate among preterm infants at discharge at our hospital.

Materials and Methods

For this retrospective analysis, we obtained the medical records data on all surviving infants born before 33 gestational weeks between March 2005 and June 2014 at the study hospital, Kochi Health Sciences Center in Kochi, Japan. Exclusion criteria included maternal factors (inability to express milk due to disease or a postpartum condition, lack of milk expres-

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sion data) and infant factors (chromosomal abnormalities, multiple anomalies, congenital infection, inability to be discharged home).

Outcomes. The primary outcome was the breastfeeding status at the time of NICU discharge, *i.e.*, breast milk, formula, or a mix of the two. We defined breast milk in accord with the definition set by the World Health Organization: "no supplemental liquids or solid foods other than medications or vitamins." 'Formula' indicated that an infant was receiving only formula at the time of discharge. 'Mix' indicated that both breast milk and formula were being used. Furman *et al.* analyzed their data at the corrected age of 40 weeks in order to reduce the discrepancy in discharge days [10]. If infants were discharged after the corrected 40 weeks/0 days point, the data from the corrected 40 weeks/0 days point were used to determine the breastfeeding status at discharge.

Confounding factors. We adjusted for the confounding factors of maternal age, marital status, smoking status, primiparity, pregnancy-induced hypertension, diabetes mellitus, first milk expression time, interval between milk expressions, singleton, GA, sex, Apgar scores (1 and 5 min), birth weight, birth height, birth head circumference (HC), mode of delivery, respiratory distress syndrome (RDS), chronic lung disease (CLD), intraventricular hemorrhage (IVH), and NEC [13-16]. The best estimate for GA was determined according to an early prenatal ultrasound examination, the last menstrual period, and the physical examination of the infant at birth. Milk expression was performed by midwives and the mothers. In this retrospective study, we could not distinguish the ways that milk was expressed, *i.e.*, manually or mechanically.

We could not find an appropriate definition of the interval between milk expressions, and we therefore defined this interval by using the following equation: (time of 10th milk expression − time of first milk expression)/9. RDS was defined as the diagnosis of RDS based on clinical and radiographic findings. CLD was defined as the oxygen requirement at corrected 36 weeks. The grade of IVH was diagnosed by cranial echography using the Papile classification system, whereby grades III and IV correspond to severe IVH [17]. NEC was defined as stage II or higher on the Bell classification system [18].

Statistical analysis. We performed a univariate logistic regression analysis to compare the groups given breast milk and mix with the formula group, because of the very low rate of breast milk being provided at discharge. The mean differences, risk ratios, and 95% confidence intervals (95%CIs) were calculated using a simple descriptive analysis. We conducted multivariate logistic regression analyses to adjust for confounding factors, including maternal age, marital status, smoking status, primiparity, first milk expression time, interval between milk expressions and GA. Adjusted odds ratios (AORs) and their 95%CIs were also calculated.

The shortest number of days and the mean (SD) number of days until discharge were 22 and 65.3 (21.8) days, respectively. We took note of whether or not a certain day (from day 4 to day 21) after birth might predict the breastfeeding status at discharge.

Our hospital prioritizes breastfeeding over formula feedings in infants. The increase rate of feeding was 10-20 mL/kg/day. Human milk from donors was not used. During this research period, there was no specific program for breastfeeding for preterm infants.

Statistical analyses were performed using JMP 10.0.2 (SAS Institute, Cary, NC, USA). The present study protocol was approved by the Ethics Review Committee of Kochi Health Sciences Center (141023).

Results

Of the 337 infants born during the specified period, the cases of 40 were excluded, and the data from the remaining 297 infants were subjected to the analyses. The reasons for the excluded cases were as follows. Maternal factors: tumor 2, systemic lupus erythematosus 1, stroke 1, sepsis 1, lack of milk data 3. Neonatal factors: death 20, transfer 5, malformation 3, cytomegalovirus infection 2, short bowel syndrome 1, milk allergy 1. The means (SD) of the GA and BW values were 29.5 (2.4) weeks and 1,230 (391) g, respectively. The means (SD) of the first milk expression time and the interval between milk expressions were 6.5 (8.5) h and 5.3 (1.7) h, respectively. The numbers of infants in the breast milk, formula, and mix groups at discharge were 26 (8.8%), 99 (33.3%), and 172 (57.9%), respectively.

The univariate logistic regression analysis for the formula group revealed that the risk factors were young mother, unmarried, smoking, multiparity, delayed first milk expression, early GA and small HC (number of cases lacking data, 83) (Table 1). The first milk expression times of the breast milk and mix groups versus the formula group were 5.7 ± 7.1 and 8.1 ± 10.5 h, respectively.

The multivariate logistic regression analysis for the formula group showed that the risk factors were young mother, unmarried, smoking, multiparity and delayed first milk expression (Table 2). The AOR (95%CI, *p*-value) of first milk expression was 1.06 (1.02–1.09, 0.002). The rates of breast milk and mix classified by maternal age were 1/5 (20.0%), 54/95 (56.8%), 127/177 (71.8%) and 16/20 (80.0%) for < 20 years, 20–30 years, 30–40 years and ≥ 40 years old, respectively.

Table 3 displays the results of our analysis of predicted breastfeeding status at discharge based on the infant status on days 4–21 after birth. The AOR (95%CI, *p*-value) of day 5 was 2.17 (1.15–4.22, 0.017). After day 5, the AORs were significantly

Table 1 Characteristics of infants receiving breast milk or mix versus only formula at the time of NICU discharge

	Breast milk and mix (n = 198)	Formula (n = 99)	MD or RR (95%CI)	*p*-value
Maternal age (year)	32.7 ± 5.1	29.9 ± 6.1	2.7 (1.4–4.0)	<.0001
Unmarried	11 (5.6%)	15 (15.2%)	0.37 (0.17–0.77)	0.006
Smoking	3 (1.5%)	12 (12.1%)	0.13 (0.04–0.43)	0.0002
Primiparity	116 (58.6%)	33 (33.3%)	1.76 (1.30–2.38)	<.0001
PIH	37 (18.7%)	14 (14.1%)	1.32 (0.75–2.33)	0.328
DM	5 (2.5%)	0 (0%)	–	0.173
First milk expression (h)	5.7 ± 7.1	8.1 ± 10.5	−2.4 (−4.4–−0.35)	0.022
Interval between milk expressions (h)	5.5 ± 1.6	5.3 ± 1.5	0.16 (−0.22–0.53)	0.420
Singleton	146 (73.7%)	72 (72.7%)	1.01 (0.88–1.17)	0.853
GA (wks)	29.7 ± 2.3	29.1 ± 2.4	0.70 (0.13–1.26)	0.016
Male	104 (52.5%)	48 (48.5%)	1.08 (0.85–1.38)	0.511
AS 1 min	6.2 ± 2.1	6.0 ± 2.1	0.23 (−0.28–0.74)	0.369
AS 5 min	7.9 ± 1.6	7.6 ± 1.4	0.23 (−0.14–0.60)	0.221
BW (g)	1,253 ± 389	1,183 ± 394	69 (−25–164)	0.149
Height (cm)*	36.5 ± 4.8	35.9 ± 3.4	0.64 (−0.60–1.87)	0.312
HC (cm)*	26.4 ± 2.4	25.5 ± 2.9	0.94 (0.20–1.68)	0.013
CS	165 (83.3%)	83 (83.8%)	0.99 (0.89–1.11)	0.912
RDS	137 (69.2%)	73 (73.7%)	0.94 (0.81–1.09)	0.417
CLD	5 (2.5%)	7 (7.1%)	0.36 (0.12–1.10)	0.061
IVH 3–4	1 (0.5%)	1 (1.0%)	0.50 (0.03–7.91)	1.000
NEC	0 (0%)	1 (1.0%)	–	0.333

AS, Apgar score; BW, birth weight; CI, confidence interval; CLD, chronic lung disease; CS, caesarean section; GA, gestational age; DM, diabetes mellitus; HC, head circumference; IVH, intraventricular hemorrhage; MD, mean difference; NEC, necrotizing enterocolitis; PIH, pregnancy-induced hypertension; RDS, respiratory distress syndrome; RR, risk ratio.
*Lack of data; Height 71, HC 83.

Table 2 Multivariate logistic regression analysis for the formula group

	AOR	95%CI	*p*-value
Maternal age (yrs)	0.90	0.86–0.95	<0.0001
Unmarried	2.74	1.06–7.23	0.038
Smoking	8.74	2.26–44.40	0.001
Primiparity	0.31	0.17–0.54	<0.0001
First milk expression (h)	1.06	1.02–1.09	0.002
Interval between milk expressions (h)	0.85	0.70–1.02	0.085
GA (wks)	0.99	0.97–1.004	0.156

AOR, adjusted odds ratio; CI, confidence interval; GA, gestational age.

Table 3 Prediction of breastfeeding status (breast milk and mix) at discharge

		OR (95%CI)	*P*-value	AOR (95%CI)	*P*-value
Breast milk at day:	4	0.93 (0.56–1.56)	0.792	1.65 (0.89–3.15)	0.115
	5	1.16 (0.70–1.92)	0.553	2.17 (1.15–4.22)	0.017
	6	1.38 (0.84–2.28)	0.208	2.29 (1.22–4.44)	0.010
	7	1.12 (0.67–1.86)	0.667	1.78 (0.93–3.46)	0.080
	8	1.14 (0.69–1.90)	0.607	2.33 (1.20–4.65)	0.012
	9	1.05 (0.62–1.77)	0.859	2.07 (1.06–4.15)	0.033
	10	0.88 (0.53–1.45)	0.604	1.56 (0.84–2.97)	0.165
	11	1.32 (0.80–2.17)	0.276	2.56 (1.35–5.02)	0.004
	12	1.57 (0.95–2.59)	0.079	2.37 (1.30–4.45)	0.005
	13	1.52 (0.93–2.49)	0.098	2.38 (1.30–4.47)	0.005
	14	1.56 (0.94–2.57)	0.080	2.48 (1.34–4.72)	0.004
	15	2.06 (1.26–3.40)	0.004	3.35 (1.81–6.42)	<0.0001
	16	2.35 (1.42–3.89)	0.0008	3.72 (1.98–7.22)	<0.0001
	17	2.00 (1.21–3.30)	0.006	3.41 (1.83–6.60)	<0.0001
	18	2.51 (1.52–4.17)	0.0003	3.86 (2.09–7.37)	<0.0001
	19	3.04 (1.81–5.11)	<0.0001	4.66 (2.46–9.21)	<0.0001
	20	3.07 (1.82–5.18)	<0.0001	3.55 (1.93–6.73)	<0.0001
	21	2.73 (1.63–4.56)	0.0001	2.97 (1.64–5.55)	0.0003

elevated except for days 7 and 10.

Discussion

In this study, delayed first milk expression was the risk factor for the formula group at discharge. Furman *et al.* showed that the start of milk expression within 6h was the significant factor [10]. Our findings of 5.7 ± 7.1 h and 8.1 ± 10.5 h for the start of milk expression in the breast milk group and mix group versus the formula group are compatible with the Furman *et al.* result.

Success for breastfeeding preterm infants has been reported to include "maternal education, early and frequent milk expression, and continuous support" [19]. As is the case for mothers of infants delivered at term, preterm mothers also need to achieve early and frequent milk expression [20]. Ideal first milk expression and the interval between milk expressions are within 1h after birth and at least 2–3h, respectively [21]. Here, the mean (SD) of the first milk expression was 6.5 (8.5) h, with 5.3 (1.7)-h intervals. Clearly, there is much room for improvement.

Young mother, unmarried, and smoking were also risk factors for formula use in this study, and this is compatible with previous reports [6, 10–12]. Multiparity was a risk factor in this study, although Furman *et al.* observed no difference between primiparity and multiparity in this regard [10]. The reason for our result might be that it was difficult to continue milk expression because the multiparous mothers had to take care of their older children after their discharge.

Our results showed that the breastfeeding status on day 5 and after day 5 would be better for predicting formula use, except for days 7 and 10 (Table 3). Previous studies showed that the amount of expressed milk on day 4 [22] and day 7 [23] could predict the breastfeeding status at week 6. Delayed milk expression would lead to the delay of the establishment of breastfeeding, which would affect the nutritional status at discharge. In the present study, the mothers stayed at the hospital for approx. 1 week after delivery. It may be useful to target successful milk expression during this week.

There are some limitations of the present study. First, we were unable to analyze sociological data such as parental income and education level, which could affect the breastfeeding status at the time of discharge [24]. Although further studies should be conducted to corroborate our data, we propose perinatal education as one method that could help lessen the disadvantages caused by sociological factors [25, 26]. Second, we did not have maternal factors such as skin-to-skin contact at birth, breast massage, and frequency of maternal visits to the NICU. These factors should be analyzed as clinical data for future research.

Other risk factors such as maternal age and marital status, which we could not easily intervene, were statistically significant. On the other hand, we are able to support milk expression at our hospital. The active involvement of post-natal healthcare personnel is beneficial. In addition to early-initiated and frequent milk expression, the amount of breast milk expressed should be investigated in the near future. We should also help mothers to continue milk expression on their own.

In conclusion, we found that delayed first milk expression was the risk factor for the formula group at discharge. Improvement of milk expression should be achieved in order to promote breastfeeding.

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