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Original Article

The effect of feeding with own mother's milk on bronchopulmonary dysplasia in very low birth weight infants

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Abstract

Aim: This study aimed to evaluate the effect of feeding with own mother's milk on the incidence of bronchopulmonary dysplasia (BPD) and other preterm morbidities in very low birth weight (VLBW) infants.

Materials and Methods: VLBW infants followed in our unit were divided into three groups according to their predominantly feeding type such as own mother's milk group (MM), preterm formula group (PF) and mix fed group (MxF) in the first postnatal month. Groups were compared regarding demographic and clinical features including BDP.

Results: The mean birth week of 117 VLBW infants was 29.3 ± 2.1 weeks and the mean birth weight was 1115 ± 265 g. Seventy seven infants were in the MM group, 17 infants were in the PF group and 23 infants were in the MxF group. There was a significant decrease in BPD incidence in the MM group compared to infants in the PM group (p=0.03). The frequency of necrotizing enterocolitis, late-onset sepsis and severe intraventricular hemorrhage (IVH) were found to decrease in the MM group when compared with other infants.

Conclusion: The incidence of BPD decreases in VLBW infants fed with their own mother's milk compared to VLBW infants fed with formula. Also besides feeding with mother's milk may contribute to a decrease in the frequency of severe IVH.

Keywords: Breastfeeding; bronchopulmonary dysplasia; intracranial hemorrhages; mother's milk; newborn.

INTRODUCTION

Bronchopulmonary dysplasia (BPD) is one of the most common morbidities in premature infants (1). BPD may cause prolonged hospitalization, neurodevelopmental problems and re-hospitalization (2,3). Besides exposure of immature lungs to oxidative stress, volutrauma, barotrauma, the role of undernutrition in the pathogenesis of bronchopulmonary dysplasia is important (4,5).

Today, breast milk feeding is known to reduce morbidities such as necrotizing enterocolitis (NEC), late-onset sepsis (LOS) and retinopathy of prematurity (ROP) (6-8). Breast milk can reduce the incidence and severity of BPD in premature infants with its anti-inflammatory properties (9) and anti-oxidant properties (10).

To date, few studies have been conducted researching the effect of breastfeeding on the development of BPD. In these studies, the effects of feeding with own mother's milk, feeding with donor mother's milk and feeding with the preterm formula on BPD development were investigated (7,11,12). In many countries, including our country, donor mother's milk and human-based human milk fortifiers are not used. This may limit the generalization of the current research results. In this study, we aimed to determine the effect of feeding with own mother's milk on the incidence of BPD in very low birth weight (VLBW) infants compared to preterm formula feeding. Secondly, the effect of feeding with own mother's milk on other common premature morbidities such as NEC, LOS, ROP and intraventricular haemorrhage (IVH) was evaluated.

MATERIAL and METHODS

In this study, VLBW (birth weight <1500 g) infants whose birth week is less than 32 weeks and born in our hospital between January 2018 and March 2019 were included.

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Infants with a major congenital anomaly or chromosomal anomaly, infants who were found to have severe metabolic acidosis (Base excess <–16 mmol/L) at birth and those who died before discharge or who were transferred to another center were not included in the study.

The study was approved by the Scientific Research and Publication Ethics Committee of our university. Hospital records of all infants included in the study and follow-up forms of intensive care within the first 30 days of the postnatal period were examined retrospectively. Gestational age, birth weight, delivery methods, gender, multiple pregnancies, antenatal steroid, small for gestational age (SGA), maternal preeclampsia, premature preterm rupture of membranes (PPROM), chorioamnionitis, Apgar score at 1st and 5th min, SNAP-PE score, patent ductus arteriosus (echocardiographic documentation with medical and/or surgical treatment), neonatal sepsis (proven or suspected), surfactant requirement, intubation requirement and total enteral feeding (120 ml/kg/day) time of the patients were recorded. Intensive care follow-up forms within the first 30 days of the postnatal period were examined and through which type and how much the infant was fed were recorded for each day. The patients were divided into three groups according to how much of the total amount of enteral nutrition taken by the infant was mother's milk or formula during the first month. Infants receiving mother's milk at 70% or more of the total enteral feeding volume were called predominantly the own mother's milk (MM) group, infants receiving preterm formula at 70% or more of the total enteral feeding volume were called predominantly preterm formula (PF) group and the remaining infants were called mixed-fed (MxF) group. Predominantly receiving own mother's milk infants were compared with other infants in terms of BPD and other morbidities.

BPD was defined as oxygen requirement >21% or continuous positive airway pressure or mechanical ventilation at 36 weeks postmenstrual age (13). Other neonatal morbidities included grade 3–4 IVH (using the Papile classification system) (14), NEC (modified Bell's stage ≥2) (15), LOS (sepsis, a positive blood culture after the day of life 3 with antibiotic treatment ≥5 days), ROP requiring laser treatment.

Preterm infant feeding protocol

In our unit, premature infants with the hemodynamically stable and normal abdominal examination are started on the first postnatal day with minimal enteral nutrition (10–15 mL/kg/day) and parenteral nutrition (3–3.5 g/kg/day protein and 1 g/kg/day lipid). Minimal enteral feeding is started at 10 mL/kg daily in infants with birth weight ≤1000 g and 10–15 mL/kg daily (with an orogastric catheter) in infants with birth weight >1000 g. If tolerated, the feeding volume is increased by 10–15 mL/kg daily. In the feeding of infants, feeding with own mother's milk is preferred first. If the mother's milk is not sufficient or if there is a definite contraindication that requires non-use of mother's milk, the preterm formula Aptamil Prematil® liquid (Nutricia) is used. When the daily enteral feeding volume reaches 100 mL/kg, a scale of human milk fortifier Eoprotin® (Nutricia) is added to each 25 mL of breast milk. When the enteral feeding volume reaches 100–120 mL/kg/day, parenteral nutrition is terminated.

RESULTS

Total 152 VLBW infants were born during the study period. Three infants with major congenital or chromosomal abnormalities and 32 infants with significant metabolic acidosis at birth or who died within the first month were excluded. No patient was transferred to an external center. The remaining 117 infants had a mean birth week of 29.3±2.1 weeks and a mean birth weight of 1115±265 g (Table 1). Moderate to severe BPD was found to develop in 30 (25.6%) of these infants. When the patients were grouped according to the type of nutrition in the postnatal first 30 days; 77 infants were in the predominantly own mother's milk (MM) group, 17 infants were in the predominantly preterm formula (PF) group and 23 infants were in the mixed-fed (MxF) group.

Demographic and clinical characteristics of MM and PF groups were similar. The frequency of BPD in the MM group was found that decreased significantly compared to the PF group (20.7% vs 47%, p=0.03). No significant difference was found in terms of the incidence of NEC, ROP, grade 3–4 IVH between MM and PM groups (Table 1).

When the MM group were compared with other infants (PF + MxF), the groups were found to have similar demographic and basic clinical characteristics. The incidence of NEC, LOS and grade 3–4 IVH was significantly lower in the MM group compared to other infants (p values of 0.003, 0.027, and 0.047, respectively, Table 1).

DISCUSSION

In our study we investigated the relationship between feeding type and BPD, the incidence of BPD was found lower in the MM group when compared to the PF group (p=0.03). Also besides unlike previous studies, it was observed that the incidence of grade 3–4 IVH was decreased in feeding with own mother's milk VLBW infants (p=0.047).

BPD is one of the most common morbidities of premature infants. In our study, the incidence of BPD in VLBW infants was 25.6%. In previous studies, the incidence of BPD in VLBW infants has been reported to be between 18.4–30.4% (7, 11, 12). Today, an intensive effort is being made to reduce the incidence and severity of BPD. For this purpose, treatments such as volume-targeted ventilation, pre and postnatal steroids, vitamin A and caffeine are widely used (4, 16, 17). In recent years, studies investigating the effect of human milk on the development of BPD have been reported. Spiegler et al. reported that the incidence of BPD decreased (from 20.8% to 11.2%) in human milk-fed VLBW infants compared to preterm infants fed with the formula (11). Similarly, in our study, the incidence of BPD in the MM group was found to decrease by more than 50% compared to the PF group (Table 1).

Table 1. Characteristics and outcome of study infants

	All patient n=117	MM group n=77	PM group n=17	PF or MxF group n=40	MM group versus PM group p	MM group versus PF or MxF group p
Gestational age, mean±SD, weeks	29.3±2.1	29.1±2.2	29.0±2.1	28.7±2.0	0.63	0.15
Birth weight, mean±SD, g	1115±265	1136±266	1108±258	1075±261	0.29	0.12
Caesarean delivery, n (%)	112 (94.9)	74 (96.1)	17 (100)	37 (92.5)	0.54	0.33
Male gender, n (%)	57 (48.7)	41 (53.2)	8 (47.0)	16 (40)	0.39	0.07
Multiple pregnancies, n (%)	26 (22%)	19 (24.6)	2 (11.7)	7 (17.5)	0.20	0.26
Antenatal steroids, n (%)	67 (56.8)	44(57.1%)	10 (58.8)	22 (55)	0.56	0.48
Small for gestational age, n (%)	30 (25.4%)	21 (27.2)	4 (23.5)	9 (22.5%)	0.50	0.37
Maternal preeclampsia, n (%)	38 (32.2%)	23 (29.8)	6 (35.2)	15 (37.5)	0.43	0.26
PPROM, n (%)	21 (17.8%)	12 (15.5)	4 (23.5)	9 (22.5)	0.31	0.24
Chorioamnionitis, n (%)	9 (7.7%)	5 (6.5)	2 (11.7)	4 (10)	0.37	0.36
Apgar score at 1 min, median (min-max)	6 (2-8)	6 (2-8)	6 (4-8)	6 (4-8)	0.49	0.89
Apgar score at 5 min, median (min-max)	7 (3-9)	7 (3-9)	7 (7-9)	8 (7-9)	0.26	0.76
SNAP-PE, mean±SD	14.2±13.3	12.9±13.3	17.2±11.5	16.7±13.2	0.066	0.08
Late-onset sepsis, n (%)	15 (12.8%)	6 (7.8)	4 (23.5)	9 (22.5)	0.07	0.027
Patent ductus arteriosus that required treatment, n (%)	24 (20.5%)	13 (16.8)	4 (23.5)	11 (27.5%)	0.37	0.14
Need for surfactant, n (%)	45 (38.4%)	26 (33.7)	9 (52.9)	19 (47.5)	0.11	0.10
Need for intubation, n (%)	43 (36.7)	27 (35)	8 (47)	16 (40)	0.25	0.37
Age achieved feeding of >120 mL/kg/d, days	10.6 ± 3.9	10.1±3.6	11.9±5.8	11.4±4.3	0.42	0.12
Necrotizing enterocolitis, n (%)	14 (11.9)	4 (5.1)	3 (17.6)	10 (25%)	0.10	0.003
Grade 3–4 intraventricular haemorrhage, n (%)	6 (5.1%)	1 (1.3)	2 (11.7)	4 (10%)	0.08	0.047
Retinopathy of prematurity that required laser treatment, n (%)	9 (7.6%)	7 (9%)	2 (11.7%)	2 (5%)	0.51	0.34
Bronchopulmonary dysplasia, n (%)	30 (25.4)	16 (20.7%)	8 (47%)	14 (35%)	0.03	0.075

MM, predominantly fed own mother's milk; MxF, mixed fed; PM, predominantly fed preterm formula; PPROM, premature preterm rupture of membranes; SNAP-PE, Score for Neonatal Acute Physiology II; VLBW, very low birth weight

The role of oxidative stress, inflammation and inadequate nutrition in the pathogenesis of BPD is important (4, 5). Inadequate nutrition can lead to an inability to resist oxidative stress, barotrauma, and infectious complications (18). The incidence of BPD can be reduced by providing adequate protein and calorie support starting from the first postnatal day. However, the protein and mineral content of mother milk is low compared to preterm formulas. As a result, in most of the premature infants fed with mother milk (even if fortified), weighing is slower than in formula-fed infants (11, 29). However, mother's milk can reduce the risk of BPD with its balanced amino acid structure and bioactive ingredients.

The bioactive content including lactoferrin, oligosaccharides, polyunsaturated fatty acids, nucleotides and immunoglobulins is highest in fresh mother milk (especially colostrum) compared to donor mother milk and frozen mother milk (20). Therefore, it is important to give premature infants their own mother's milk (especially colostrum) as fresh. The content of preterm mother milk and term mother milk is also different. The protein, electrolyte and anti-inflammatory content of preterm mother milk are higher than both donor mother milk and term mother milk (21-23). Donor mother milk is not used in our unit. Therefore, all infants were fed with own mother's milk. This situation, unlike other studies, contributed to a more homogenous mother milk group.

Patel et al. showed that increased human milk use correlated with a decrease in the incidence of BPD (12). In our study, BPD rate was lowest (20.7%) in the group with the highest mother's milk use and BPD rate was highest (47%) in the group with the highest formula use. When these results are evaluated together with the study of Patel et al., the importance of feeding with predominantly mother's milk in preterm infants is revealed.

Although it causes slower growth, mother milk feeding is known to reduce the incidence of NEC, ROP and LOS (6-8). In our study, it was seen that the incidence of NEC, LOS and grade 3–4 IVH was decreased in VLBW infants fed with mother's milk. This protective effect is thought to be related to anti-inflammatory agents such as immunoglobulins, lactobacillus spp, oligosaccharides, lysozyme and lactoferrin, which are contained in mother milk (24). Mother milk reducing morbidities such as NEC and LOS may indirectly contribute to the reduction of BPD risk.

The positive effect of mother milk on neurodevelopmental outcomes of premature infants is well known (25, 26). Furthermore, the impact of mothermilk on IVH and periventricular leukomalacia is not well investigated to date. Mother milk is rich in growth factors and neurotrophins (such as brain-derived neurotrophic factor, nerve growth factor, insulin-like growth factor-1) (27). It is also known that breast milk contains pluripotent stem cells (28). In some of the studies comparing feeding with mother milk or preterm formula in preterm infants, the incidence of grade 3–4 IVH was also evaluated. In these studies, although a decrease in the incidence of grade 3–4 IVH was seen in preterms fed with mother milk, this decrease was not statistically significant (11,29). In our study, a significant decrease in the incidence of stage 3–4 IVH was observed in preterm infants fed with predominantly mother's milk compared to infants fed with a formula (p= 0.047). This result may not be random. In Keller et al.'s study, nasopharyngeal mother's milk (0.1 ml breast milk 3-8 times a day) was given to patients who developed grade 3–4 IVH (30). In their study, porencephalic defects (21% vs. 58%) and progressive ventricular dilatation (71% vs. 91%) showed a tendency to decrease in patients who received nasal drops of fresh breast milk (30). This protective feature of mother milk can stop the progression of early-stage (grade 1-2) IVH to hydrocephalus in preterm infants. Colostrum containing pluripotent stem cells and inhibiting pro-inflammatory cytokines secretion is also important in this regard.

The present study has limitations such as the fact that this study was conducted from a single center, the number of patients was not sufficient to evaluate some secondary outcomes, and the feeding type after the first postnatal month was not evaluated. However, in our study, all infants fed with mother milk were fed with their own mother's milk. In this way, a more homogenous mother's milk group was formed and contributed to the limited literature on this subject.

CONCLUSION

Mother milk feeding in the first postnatal month decreases the incidence of BPD in premature infants. In addition, mother milk feeding in premature infants may also contribute to the reduction of the incidence of grade 3–4 IVH. Therefore, especially in premature infants, starting from the first postnatal day, the highest level of fresh mother's milk use should be targeted. We think that the effects of mother milk on BPD and IVH should be investigated in multicenter studies including infants with extremely low birth weight (birth weight <1000 g) who are much more sensitive to the negative effects of oxidative stress and inflammation.

Competing interests: The authors declare that they have no competing interest.

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