

Introduction

Use of human milk fortifier (HMF)

- Breastmilk alone cannot supply adequate nutrients and electrolytes to meet preterm infants' growth requirements.
- So, HMF is typically added to support growth for preterm infants.

Association of HMF and feeding intolerance (FI)

- Empirically known that HMF can cause feeding intolerance symptoms as osmolarity increases.
- However, few studies have conducted quantitative analysis.

Therefore, this study aims to identify risk factors in vulnerable patients for adverse reactions to HMF based on clinical data.

Methods

Retrospective cohort study

- Single center (Neonatal intensive care unit at Seoul National University Children's Hospital)
- 2019.01 – 2020.12

Inclusion criteria

- Gestational age of less than 32 weeks
- Birth weight of less than 1500 grams
- Administered HMF

Feeding intolerance after fortification (FIF)

- Symptom : Clinically significant symptoms such as vomiting, regurgitation, abdominal distension or increased frequency of apnea which cannot be explained by other medical conditions.
- Timing : within 7 days of HMF administration

Results

Table 1. Characteristics comparison between patients with and without feeding intolerance and without FIF

	Feeding intolerance (-) N=129 (90.8%)	Feeding intolerance (+) N=13 (9.2%)	p-value
Gestational age (weeks)	29.3±2.78	29.3±3.01	0.959
Body weight at birth (gram)	1155.7±324.5	1046.2±288.05	0.244
1 minute Apgar score	4.9±1.96	4.8±2.23	0.863
5 minute Apgar score	7.3±1.76	7.2±1.63	0.912
Small for gestational age	23 (17.8)	4 (30.8)	0.257
Male sex	74 (57.4)	9 (69.2)	0.408
Cesarean section	64 (49.6)	6 (46.2)	0.812
Multiple gestation	97 (75.2)	6 (46.2)	0.025
Prenatal factor			
Maternal hypertension	15 (11.6)	1 (7.7)	0.669
Chorioamnionitis	67 (51.9)	7 (53.8)	0.896
Oligohydramnios	18 (14.0)	3 (23.1)	0.377
Comorbidity			
BPD	52 (40.3)	7 (53.8)	0.345
ROP	32 (24.8)	3 (23.1)	0.89
PDA	58 (45)	7 (53.8)	0.54
Sepsis	16 (12.4)	1 (7.7)	0.618
IVH	29 (22.5)	5 (38.5)	0.198
MOP	2 (1.6)	2 (15.4)	0.004

• Values are presented as number (%) or mean ± standard deviation

• BPD, Bronchopulmonary dysplasia; ROP, Retinopathy of prematurity; PDA, Patent ductus arteriosus; IVH, Intraventricular hemorrhage; MOP, Meconium obstruction of prematurity

Table 2. Feeding-related characteristics comparison between patients with and without FIF

	Feeding intolerance (-) N=129 (90.8%)	Feeding intolerance (+) N=13 (9.2%)	p-value
Timing of first fortifier administration (days)	18.8±12.19	14.5±4.81	0.016
Timing of first fortifier administration (PMA)	32.0±2.64	31.3±2.790	0.400
Timing of reaching enteral feeding ≥ 100mL/kg/D (days)	12.6±11.05	13.3±5.91	0.82
Duration of parenteral nutrition (days)	12.7±11.60	15.6±9.05	0.376

• Values are presented as number (%) or mean ± standard deviation

• PMA; Post-menstrual age, 100mL/kg/D; 100 ml per kg per day

Table 3. Clinical manifestations of FIF

Symptom	N
Vomiting	1
Regurgitation	1
Increase of residue	4
Increase of abdominal circumference	11
Increase of apnea alarm	4

• Allowing documentation of multiple symptoms from each patients

• Values are presented as numbers

Table 4. Multivariable risk factor analysis for FIF

	p-value	95% Confidence Interval
Gestational age (weeks)	0.497	0.718-1.981
Body weight at birth (gram)	0.087	0.991-1.001
Small for gestational age	0.660	0.038-7.935
Male sex	0.851	0.236-5.763
1 minute Apgar score	0.905	0.521-1.781
5 minute Apgar score	0.444	0.581-3.453
Cesarean delivery	0.816	0.173-3.986
Multiple gestation	0.040	0.048-0.935
Timing of reaching enteral feeding ≥ 100mL/kg/D	0.031	0.614-0.977
Duration of parenteral nutrition (days)	0.007	1.090-1.742
Timing of first fortifier administration (days)	0.0023	0.712-0.975

Conclusion

- FI occurred in 9.2% of very low birth weight infants after HMF administration in our study.
- Multiple gestation, history of meconium obstruction of prematurity, and early HMF administration were statistically significant risk factors for FIF.
- Earlier administration of HMF after birth was associated with FI. These findings need to be replicated by other studies before generalization.

References

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