First Use in Japan of Exclusive Human Milk Diet: Case Report Series

Masafumi Aoki1, Sakurai Motoichirou1, Katsumi Mizuno1*, Yuya Nakano1, Hideyuki Asai1 and Keil M Hawthorne2

1Department of Pediatrics, Showa University School of Medicine, Tokyo, Japan
2Department of Pediatrics, University of Texas at Austin, USA

Abstract

Background: Several studies have confirmed the benefits of an exclusive human milk diet for premature infants; however, a donor human milk-based fortifier has not been available in Japan.

Case Presentation: A donor human milk-based fortifier was recently used for the first time ever in Japan, given in conjunction with mother’s own milk to three premature infants. Details of these three infant case studies are reported here. These infants received the donor human milk-based fortifier as part of a rescue nutritional intervention due to poor weight gain in the presence of meconium ileus and perforation. Infants demonstrated good tolerance and weight gain while receiving the exclusive human milk diet.

Conclusion: This is the first report of infants receiving an exclusive human milk diet in Japan, consisting of mother’s own milk with a donor human milk-based fortifier for additional calories and nutrients. Infants demonstrated good tolerance and experienced improved weight gain while receiving the product.

Keywords: Human milk; Donor human milk; Premature infant; Preterm infant

Introduction

The World Health Organization and American Association of Pediatrics recommend that infants receive Donor Human Milk (DHM) when a mother is not able to provide enough of her own milk [1,2]. Donor human milk is breast milk that has been expressed and then processed and pasteurized by a human milk bank for infants. Often DHM is pooled from multiple mothers so as to provide a consistent level of nutrients. Premature infants have unique nutritional needs and require additional energy and nutrients; therefore, fortification of human milk, whether Mother’s Own Milk (MOM) or DHM has become common practice. Originally, fortification was done with a bovine-based human milk fortifier. Since 2005, a DHM-based human milk fortifier has been available in the US; however, this product is not available for use in Japan. Currently the only human milk fortifier available in Japan is a bovine-based fortifier called HMS2 (Morinaga Co. Ltd, Tokyo, Japan). An exclusive human milk diet is defined as the use of only human milk products by fortifying MOM or DHM with a DHM-based human milk fortifier.

Much research has been published over the past decade about the benefits of an EHM diet for premature infants including decreased rates of necrotizing enterocolitis, late-onset sepsis, retinopathy of prematurity, and bronchopulmonary dysplasia [3-6]. However, little has been documented about its use and benefits on a global scale.

Worldwide, more than 40 countries have established human milk banks to provide DHM to premature infants [7]. A survey of physicians in the Japanese Neonatologist Association found that approximately three-fourths of respondents were interested in having a human milk bank in order to provide a safe method of providing pasteurized DHM to infants in need [8]. In 2014, the first human milk bank was established at Showa University’s Koto Toyosu Hospital with the support of the Ministry of Health, Labor, and Welfare. This facility stores pasteurized DHM to be offered to fragile, premature infants in the Neonatal Intensive Care Unit. In May of 2017, the Japanese Human Milk Bank Association was established with the primary purpose of promoting MOM and DHM in neonatal medicine throughout Japan [9].

*Correspondence: Katsumi Mizuno, Department of Pediatrics, Showa University School of Medicine, Tokyo, Japan, E-mail: katsuorobi@med.showa-u.ac.jp
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Case Series

This report details the first three infants in Japan to receive an exclusive human milk diet. These infants received the DHM-based human milk fortifier as part of a rescue nutritional intervention due to poor weight gain in the presence of meconium ileus and perforation. Parents of all infants were consented with a consent form approved by the Ethics Committee of Showa University School of Medicine.

Case 1

Born at 28 weeks and 4 days, Baby 1 had a birth weight of 740 g and APGARS 3 and 5. She was treated with surfactant for respiratory distress syndrome. On Day of Life (DOL) 0 she was given a glycerin enema for meconium related ileus, followed by a lower gastrointestinal study showing improved ileus on DOL 4.

Parenteral nutrition began at the time of hospitalization, and enteral feeds were initiated on DOL 7. Although there was abdominal distension, feeds were increased steadily and reached full feeds in less than 2 weeks.

With the decrease of parenteral nutrition, the glucose values before feeding were 40 mg/dL to 50 mg/dL, and diazoxide was administered because hyperinsulinemia was recognized, but this led to diuretic reduction and it was abandoned.

Enteral nutrition included HMS2 bovine-based human milk fortifier added to MOM at 150 mL/kg/day to 160 mL/kg/day with a glucose infusion of 20 mL/kg/day. Weight gain was slow at 7 to 10 g/day and cholestasis gradually progressed. Direct bilirubin increased to 1.5 mg/dL and 1.6 mg/dL on DOL 20 and 33 of age, respectively. Bile acids were 41.5 umol/L on DOL 33.

A DHM-based human milk fortifier became available for this patient. Fortification with +6 kcal/oz DHM-based human milk fortifier to MOM was started on DOL 40 and glucose levels became stable, with the glucose infusion required for only 4 days. In addition, we saw improvement in cholestasis with direct bilirubin reducing to 0.4 mg/dL and bile acids at 25 umol/L on DOL 61, along with improvement of abdominal distension and weight gain (37 g/d average during weeks 35 to 37 Post-Menstrual Ages: PMA).

The DHM-based human milk fortifier was given daily for three weeks. There were no feeding issues while receiving the DHM-based human milk fortifier and it was determined to be well tolerated. HMS2 bovine-based human milk fortifier was restarted when weight reached 1700 g. However, weight gain slowed down to 17 g/d.

Case 2

Baby 2 was born at 25 weeks and 2 days, with a birth weight of 715 g, length of 31.0 cm, head circumference of 21.0 cm, and APGARS 3 and 8. He was treated with indomethacin for patent ductus arteriosus four times in the first five DOL. Enteral feeds were initiated on DOL 2 with unfortified MOM (0.5 mL given 8 times a day and increased by 0.5 mL each day). On DOL 4 he was diagnosed with meconium ileus and underwent an intestinal dilation. Enteral feeds were stopped. Gastrografin enemas were conducted on DOL 8, 9, and 10. On DOL 10, Baby 2 had an ileostomy placed due to intestinal perforation and peritonitis from the meconium related ileus. No bowel was removed. While he had the ileostomy, Baby 2 received about 130 mL/kg/day to 140 mL/kg/day of unfortified MOM enteral feeds, providing 1.1 g to 1.4 g protein/kg/day and 75 kcal/kg/day to 90 kcal/kg/day along with 30 mL/kg/day to 40 mL/kg/day parenteral nutrition providing an additional 1 g to 1.4 g protein/kg/day and 15 kcal/kg/day to 20 kcal/kg/day.

Weight gain before the closure of the ileostomy was fair, averaging 14 g/kg/day from DOL 10 to 76. On DOL 76, closure of the ileostomy was performed, amino acid infusion was discontinued, and weight was 1595 g. Full feeds of unfortified MOM at 140 mL/kg/day were reached on DOL 94. MOM was analyzed and composition was determined to be 1.0 g protein/dL and 72 kcal/dL (21.2 kcal/oz).

Weight was 1521 g, down 74 g from the date of ileostomy closure. Due to this poor growth, the DHM-based human milk fortifier was obtained and started on DOL 101 with +6 kcal/kg/day added to MOM at 150 mL/kg/d when the infant was 39 weeks, 5 days PMA. After starting the DHM-based human milk fortifier, weight gain improved and averaged 12 g/kg/day from DOL 101 to 129. There were no feeding issues while receiving the DHM-based human milk fortifier and it was determined to be well tolerated.

Case 3

Born at 25 weeks and 2 days, Baby 3 had a birth weight of 666 g and APGARS 6 and 8. She received indomethacin for treatment of patent ductus arteriosus in the first few days of life. On DOL 5, she received intestinal dilation due to meconium related ileus, and later had a gastrografin enema. On DOL 9, Baby 3 had an ileostomy placed due to significant dilation of the intestine although no perforation was seen. Closure of the ileostomy occurred on DOL 69.

While she had the ileostomy, Baby 3 received about 110 mL/kg/day to 120 mL/kg/day of enteral feeds providing 0.8 g to 1.0 g protein/kg/day and 65 kcal/kg/day to 80 kcal/kg/day along with 40 mL/kg/day to 50 mL/kg/day parenteral nutrition providing an additional 1.8 g to 2.0 g protein/kg/day and 25 kcal/kg/day to 30 kcal/kg/day.

Weight gain before the closure of the ileostomy was fair, averaging 14 g/kg/day from DOL 41 to 69. On DOL 69, closure of the ileostomy was performed, and weight was 1576 g. On DOL 106 amino acid infusion was discontinued and full feeds at 140 mL/kg/day were reached on DOL 108.

The DHM-based human milk fortifier was started on DOL 101 with +6 kcal/kg/day added to mother’s own milk when the infant was 41 weeks, 5 days post-menstrual age and was continued until DOL 136. Growth improved while the infant received the DHM-based human milk fortifier with the infant’s weight gain velocity at 25 g/d during this time. Weight increased from 1525 g to 2395 g during this period, and length increased from 39.6 cm to 47 cm (1.5 cm/wk average), and head circumference increased from 30 cm to 34 cm (0.8 cm/wk average). There were no feeding issues while receiving the DHM-based human milk fortifier and it was determined to be well tolerated.

Discussion and Conclusions

This is the first report of infants receiving an exclusive human milk diet in Japan, consisting of MOM with a DHM-based fortifier for additional calories and nutrients. Infants demonstrated good tolerance without any adverse events and experienced improved weight gain while receiving the product. This tolerance and improved weight gain was also seen previously in US reports [5,6].

Use of this DHM-based fortifier with MOM or pasteurized DHM further strengthens the recent focus by Japan physicians on human milk, including both the exclusive human milk diet and the new
human milk bank for premature infants. A DHM-based fortifier may be a useful nutritional intervention for premature infants who struggle with growth and gastrointestinal issues. More consideration of the use of this fortifier product will be helpful for improving nutritional care of premature infants.

**Declarations**

- Ethics approval and consent to participate: This study was approved by the Ethics Committee of Showa University School of Medicine; Study ID #2714. Parents were consented with an approved consent form.
- Consent for publication: Written informed consent was obtained from the patient’s legal guardians for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.
- Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
- Competing interests: KH receives honorarium as a speaker for the manufacturer of the donor human-milk based fortifier but does not receive any funding for research.

**Authors' Contribution**

MA, SM, KM, YN, and HA collected and analyzed the patient data, and contributed to information in the manuscript. KH wrote the manuscript in English. All authors approved the final manuscript.

**References**