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Milk Curd Obstruction in Human Milk-Fed Preterm Infants

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Keywords
Milk curd obstruction · Neonate · Protein · Intestinal obstruction · Fortified breast milk

Abstract
Background: Milk curd obstruction as a cause of intestinal obstruction has been known since 1959, but has nearly disappeared. However, in recent years it has experienced a revival in small premature infants. ***Objective:*** The aim of this study was to evaluate the clinical characteristics of milk curd obstruction (lactobezoar) in preterm infants. ***Methods:*** Data of preterm infants with milk curd obstruction cared for at a large tertiary neonatal intensive care unit between 2012 and 2016 were retrieved from the electronic registry and paper records. ***Results:*** A total of 10 infants (2 girls, 8 boys) were identified: the median birth weight was 595 g (range 270–922), gestational age was 24.4 weeks (23.4–27.0), weight-for-gestational age percentile was 16 (0–62), and age at diagnosis was 28 days (16–64). Five infants (50%) were small for gestational age. All neonates had received fortified human milk (added protein 2.0 g/100 mL, range 0–2.8; added calcium 2,400 µmol/100 mL, range 0–6 844; added phosphate 2,400 µmol/100 mL, range 0–5,178). Seven neonates underwent surgery, and 2 infants died. Hyperechoic masses in extended bowel loops, visualised by abdominal ultrasound, and pale/acholic faeces were hallmarks of milk curd obstruction. ***Conclusions:*** In this study, milk curd obstruction occurred exclusively in infants with a birth weight <1,000 g (2.2%) and <28 weeks' gestational age (2.4%). Male and small for gestational age infants appeared to be at increased risk. Paying attention to the colour of the faeces of infants at risk might help to diagnose milk curd obstruction at an early stage.

Introduction

Intestinal obstruction secondary to clotted milk balls was first described in 1959 using the term "lactobezoar" [1], while the term "milk curd obstruction" was coined in 1969 [2]. Subsequently, several cases have been reported in term and preterm infants receiving formula [3, 4], but the problem apparently vanished with improved formulas mimicking the composition of breast milk. Since 2000, however, milk curd obstruction has experienced a revival in very small premature infants receiving high-caloric density feeds [4, 5]. Here, we report data from a retrospective study on preterm infants with milk curd obstruction, representing the largest series in extremely low birth weight infants described so far.

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Methods

Study Population

We performed a retrospective analysis of all 6,250 newborn infants admitted to the department of neonatology of the Charité – Universitätsmedizin Berlin, Germany, between January 1, 2012, and December 31, 2016. This study population contained 452 infants with a birth weight <1,000 g and 413 infants with a gestational age <28 weeks. During the study period, a total of 25/925 (2.7%) very low birth weight infants (<1,500 g) underwent laparotomy due to different diagnoses.

We retrieved diagnostic codes of all 6,250 babies treated in the department during this time to identify infants with "milk curd obstruction" (ICD10 – code P76.2) and/or "intestinal obstruction" (ICD10 – code P76.8 and P76.9). If one of the codes was detected, we had a look in the medical charts to confirm that the neonate had milk curd obstruction.

Nutrition

All infants with a birth weight <1,500 g were treated according to a standardised feeding regimen based on human milk. Minimal enteral feeding started on the first day of life with expressed own mother's milk or pasteurised donor milk unless objected to by the parents (all parents of the analysed neonates had agreed, none received other enteral fluid than expressed breast milk). Parenteral nutrition was continued until full enteral feeding was well tolerated and restarted if necessary. All neonates received pumped breast milk fortified with breast milk fortifier (Aptamil FMS, Milupa, Friedrichsdorf, Germany, or Nestlé BEBA FM 85 Frauenmilchsupplement Pulver, Nestlé Deutschland, Frankfurt, Germany) with or without additional protein supplement (Aptamil Protein Plus, Milupa). Protein supplementation was aimed at a daily intake of 4.0–4.5 g/kg body weight and tuned to achieve growth along published intrauterine growth charts [6] (approx. 15–18 g/kg body weight/day). Fortification with a multicomponent fortifier (Aptamil FMS, Milupa, or Nestlé BEBA FM 85 Frauenmilchsupplement Pulver, Nestlé Deutschland) was started when a minimum volume of at least 12 × 6 mL (= 72 mL) of breast milk was well tolerated, starting with 1–2 up to 6% of the milk volume. To achieve a protein supplementation of 4.0–4.5 g/kg (daily intake) and/or to achieve the desired growth, an additional protein supplement (Aptamil Protein Plus, Milupa) was necessary in some cases. Due to a glucose imbalance, protein supplementation sometimes has to be started before 6% multicomponent fortifier is added. Even fat is added (Ceres-MCT-Öl) to achieve the desired growth in some cases. The total fluid intake is commenced with 100 mL/kg/day and increased up to 160 mL/kg/day or even more if the weight development requires it.

Data Collection

All data were collected from medical charts (paper or electronic records). The basic data comprised sex, gestational age, birth weight, treatment of patent ductus arteriosus, respiratory support, and age at clinical onset of milk curd obstruction. We further collected data about symptoms and nutrition at the time of onset, including the kind of milk (own mother's milk, human donor milk, or preterm formula), supplementation of the milk, parenteral nutrition, daily fluid intake, oral and parenteral medication, and the subsequent clinical course.

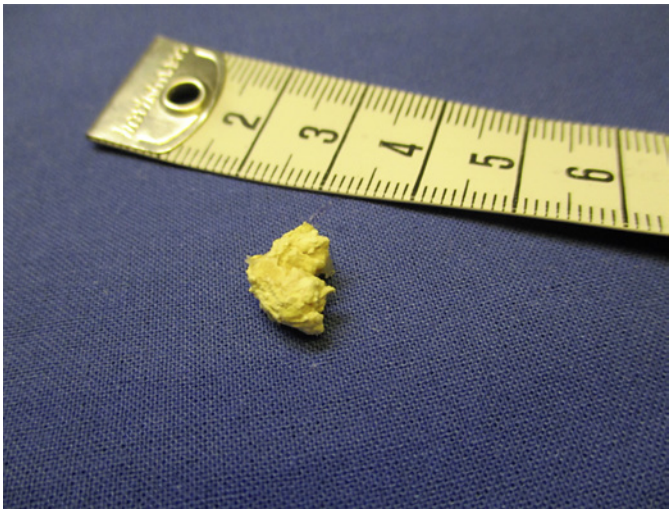

Fig. 1. Pale/acholic faeces.

Statistical Analysis

The patient's baseline characteristics are described as the median and range or total numbers with percentages. Calculations were made using IBM® SPSS® Statistics version 22.

Results

A total of 10 infants (8 boys) with milk curd obstruction were identified (Table 1), all of whom had a birth weight <1,000 g and a gestational age <28 weeks. Eight had undergone treatment for patent ductus arteriosus 7–61 days (median 17) prior to the onset of milk curd obstruction (ibuprofen only, $n = 5$; paracetamol after failed ibuprofen, $n = 2$; surgical ligation after failed ibuprofen, $n = 3$). None of the infants had had abdominal surgery prior to milk curd obstruction. While symptoms at the onset of milk curd obstruction were non-specific (Table 2), pale or acholic stools (Fig. 1) were present in all cases. Review of abdominal ultrasound images revealed extended bowel loops containing hyperechoic masses (7/10 neonates; Fig. 2) and impaired peristalsis movements (8/10 neonates).

Half (50%) of the neonates had to go on partial parenteral nutrition again with the beginning of intestinal symptoms. The diagnosis was made clinically, via abdominal radiography, ultrasound, and during surgery (Table 2). Seven neonates had to undergo surgery (Table 2), and 2 infants eventually died 3 and 30 days after the onset of milk curd obstruction, respectively.

Table 1. Clinical characteristics of the 10 preterm infants with milk curd obstruction

Basis characteristics	
Male sex	8 (8)
Gestational age, weeks/days	24/5 (23/4–27/0)
Birth weight, g	595 (270–922)
Birth weight percentile	16 (0–62)
Small for gestational age (<10th percentile)	5 (50)
Treatment for patent ductus arteriosus	8 (80)
Nutrition with human milk[a]	10 (100)
Full enteral feeding achieved prior to onset of milk curd	9 (90)
Day of life on which full enteral feeding was achieved	16 (12–49)[b]
At time of diagnosis of milk curd obstruction	
Age, days	28 (16–64)
Postmenstrual age, weeks/days	28/6 (27/1–33/6)
Actual body weight, g	930 (480–1,600)
Enteral protein supply, g/kg/day	4.27 (1.69–6.57)
Sum of parenteral amino acid and enteral protein supply, g/kg/day	5.02 (2.75–6.57)
Total fluid intake, mL/kg/day	161 (153–200)
Protein added per 100 mL milk, g/100 mL	2 (0–2.8)
Calcium added per 100 mL milk, μmol/100 mL	2,400 (0–6,844)
Phosphate added per 100 mL milk, μmol/100 mL	2,400 (0–5,178)
Outcome	
Abdominal surgery for intestinal obstruction	7 (70)
Enterostomy	6 (60)
Bronchopulmonary dysplasia (O_2 requirement at 36 weeks' gestational age)	9 (90)
Death prior to discharge	2 (20)

Data are presented as *n* (%) or the median (range).
[a] No neonate received other enteral fluid than expressed breast milk.
[b] One infant did not achieve full enteral feeding prior to the onset of milk curd obstruction.

Table 2. Symptoms and procedures in neonates with milk curd obstruction

Symptoms of milk curd obstruction										
Patient No.	1	2	3	4	5	6	7	8	9	10
Age at onset of symptoms, days	40	23	28	24	64	26	16	62	32	28
Feeding intolerance	x		x	x	x	x			x	x
Increased (bilious) nasogastric aspiration	x		x	x	x	x		x	x	x
Volvulus suspected			x	x						
Ileus	x	x	x	x		x	x		x	x
Abdominal distension	x	x	x		x	x	x	x	x	x
Pale/acholic faeces (prior to surgery)				x		x	x	x	x	x
Pale/acholic faeces (seen during surgery)	x	x	x	x	x					
Decreased stooling frequency	x			x	x	x	x	x	x	x
Diagnostic and surgical procedures										
Abdominal ultrasound	x	x	x	x	x	x	x	x	x	x
Abdominal X-ray (* with contrast agent)	x*	x	x	x	x			x	x*	x
Laparotomy	x	x	x	x	x				x	x
Bishop-Koop anastomosis	x									
Enterostomy		x		x	x				x	x

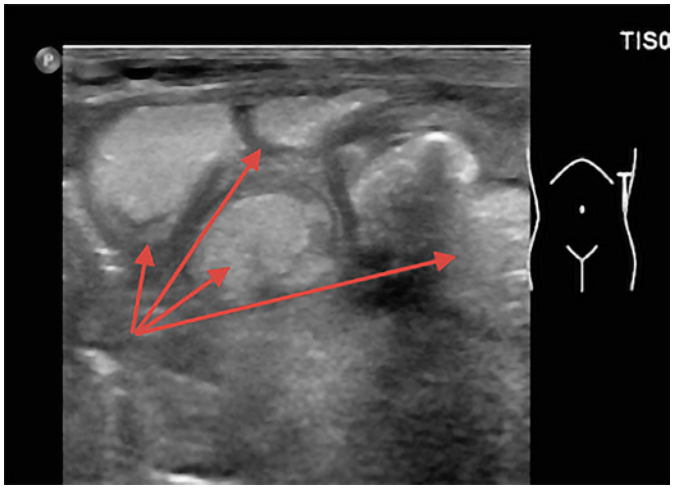

Fig. 2. Extended bowel loops containing hyperechoic masses.

Discussion

In this retrospective study, milk curd obstruction occurred exclusively in infants with a birth weight <1,000 g and <28 weeks' gestational age. Male and small for gestational age infants were at increased risk. The calculated rate among infants <28 weeks' gestational age was 2.4%, while it was 2.2% in infants with a birth weight <1,000 g. This contrasts to a reported incidence in infants born <1,000 g of 6% in a single-institutional study [3]. In a series of 381 consecutive preterm infants <26 weeks' gestation, milk curd was the pathology prompting laparotomy in 4/57 infants (7%) [7].

We compared our results to data of a total of 48 infants born <1,000 g reported in 16 publications [3–5, 7–19] retrieved from a Medline search (1959–2017) employing the terms "lactobezoar neonate" or "milk curd neonate." Of 58 publications identified, 16 reported milk curd obstruction in infants born <1,000 g. We also included data on infants <30 weeks of gestation if individual birth weight data were not available. Nine reports used the term "lactobezoar" (26 infants) [9–17], and 7 the term "milk curd" (22 infants) [3–5, 8, 18, 19]. The largest cohort reported on 9 patients [4]. The virtual cohort compiled from the literature had a higher gestational age (23–31 weeks), a higher birth weight (505–990 g), and lower age at diagnosis (3–70 days, median 16 days) than the cohort described here. Nutrition consisted of fortified human milk (n = 21), preterm formula (n = 22), both (n = 1), or was not reported (n = 4).

The cause of milk curd obstruction remains enigmatic. Improper formula composition has been an alleged cause when formula feeding was commonly practiced in preterm infants. Milk curd obstruction has been reported in 2 infants fed medium-chain triglyceride-rich formula as part of the management of chylothoraces [12]. However, more recent reports [3, 4, 15, 20], including this one, demonstrate that milk curd obstruction may also occur in very preterm infants fed fortified human milk.

Biochemical analysis of obstructing lactobezoars has yielded either clots consisting entirely of inspissated milk [3] or fatty acid calcium stones [21]. It has been shown previously that poor absorption of fat and calcium can result in calcium soap formation [22]. Thus, digestive immaturity may be critical for milk curd formation. At 4 weeks of age, more than 25% of infants <28 weeks of gestation have biochemical signs of severe exocrine pancreatic insufficiency, as determined by a low (<100 μg/g) pancreatic-specific elastase-1 stool content [23]. Low intraluminal levels of endogenous enzymatic activity appear to be relevant for the digestion of milk, as supplementation with exogenous pancreatic enzymes improves weight gain in preterm infants displaying growth restriction despite intensified enteral nutrition [24]. We assume that milk curd formation evolves secondary to an imbalance between enteral food supply and digestive capacity [11].

Despite lack of evidence from randomised controlled trials [25, 26], supplementing human milk with calcium and phosphorus, usually via multicomponent fortifiers, has become common practice in most neonatal units caring for extremely low birth weight infants. To achieve extrauterine growth similar to intrauterine trajectories, very preterm infants require more protein than the amounts provided by breast milk [27]. Results of several randomised controlled trials suggest that the gap cannot be overcome by increasing the amounts of amino acids provided by parenteral nutrition [28–30], whereas adding protein to human milk promotes the growth of extremely preterm infants [31–34]. However, there is an apparent ceiling at around 4 g/kg/day [35].

Prevention and early treatment of milk curd obstruction, to avoid severe complications and the need for surgery, requires awareness of the disease, as well as tools for diagnosis and screening. In abdominal ultrasound imaging with linear or curved array transducers, milk curd obstruction was characterised by extended bowel loops containing hyperechoic masses. This feature allows for a tentative diagnosis of milk obstruction by non-invasive means. As we found pale or frankly acholic stools in all cases, we introduced stool colour cards developed as a

screening tool for early detection of biliary atresia [36] to judge the stool colour in infants at risk, i.e., those <28 weeks of gestation and birth weight <1,000 g. When the faeces turn pale, we reduce the enteral protein supply until the colour normalises and the status of the baby improves. Abdominal ultrasound is used to look for echogenic intraluminal masses in the intestine. In suspicious cases, breast milk fortification is stopped and resumed after remission at lower concentrations while increasing the total amount of fluid. With this strategy in place, we did not encounter new cases of milk curd obstruction.

One limitation of our study is that we did not have a matched control group for our analysed cases. This was due to the very special neonatal population.

Conclusions

Milk curd obstruction is a rare but grave disease seen in a small fraction of extremely preterm infants fed fortified human milk. Being male and small for gestational age are apparent risk factors for milk curd obstruction. Pale/acholic stools and dilated bowel loops containing hyperechoic masses on abdominal ultrasound examination may be taken as early signs, which should prompt the temporary omission or reduction of fortifier.

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Statement of Ethics

The study was approved by the local institutional review board (Ethikkommission der Charité – Universitätsmedizin Berlin, No. EA2/147/16).

Disclosure Statement

The authors have no conflicts of interest relevant to this article to disclose.

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