Congenital Chylothorax in Preterm Infants – A New Approach in Dietary Treatment with Skimmed Breast Milk

Michaela Höck
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde
https://orcid.org/0000-0001-7855-0617

Alexander Höller
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde

Marlene Hammerl
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde

Karina Wechselberger
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde

Jakob Krösslhuber
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde

Ursula Kiechl-Kohlendorfer
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde

Sabine Scholl-Bürgi
Medizinische Universität Innsbruck Department für Kinder- und Jugendheilkunde

Daniela Karall (✉ daniela.karall@i-med.ac.at)
Medical University of Innsbruck

Research

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Abstract

Background

Congenital chylothorax (CC) is a rare but potentially life-threatening condition in newborns. It is defined as an accumulation of chyle in the pleural cavity. The few publications regarding medical management and therapeutic dietary intervention motivated us to share our experience.

Methods

Neonates diagnosed with congenital chylothorax and treated at Innsbruck Medical University Hospital between 2013 and 2019 (n = 5, gestational age: 36 3/7, 32 5/7, 36 4/7, 35 0/7, 35 4/7) were eligible for this report.

The cornerstones of treatment for chylothorax conventionally consist of chest tube drainage (CTD), respiratory support, dietary restriction of long-chain triglycerides (LCT) or total parenteral nutrition (TPN). In further course the introduction of a medium-chain triglyceride (MCT)-based formula followed by an overlapping switch to a formula with low LCT and high MCT, containing the essential long-chain fatty acids (LCFA), is attempted. As soon as possible, the change is made to breast milk feeding or breastfeeding. In two patients we used fat-modified (skimmed) breast milk to avoid discontinuation of breast milk feeding.

Results

The early introduction of LCFA in the form of breast milk after resolution of chylothorax was associated with favourable outcome (no recurrence of pleural effusion and adequate weight gain).

Conclusion

The first-line therapy of chylothorax is a combination of respiratory stabilization and dietary modification. The purpose of this report is to point out the feasibility of a fast change from LCT fat-free nutrition to full-fat nutrition once the chylothorax has dissolved, especially the early introduction of breast milk feeding / breastfeeding in infants with chylothorax.

Background

Congenital chylothorax, the accumulation of chyle (lymphatic fluid of intestinal origin) in the pleural space, is a rare – 1:5,000–10,000 live births – but potentially life-threatening condition and requires multimodal management strategies [1].

Treatment is typically stepwise, starting with stabilization of the respiratory situation via chest tube drainage (CTD) and respiratory support. Nutrition management for chylothorax includes adhering to a regime where the fat source is primarily medium-chain triglyceride (MCT). As breast milk (BM) contains
high concentrations of long-chain triglycerides (LCT), patients are usually transitioned to an MCT-containing formula like Monogen®, which is a milk protein-based powdered formula that is low in fat (25% of calories), of which 90% is in the form of MCTs [2]. MCTs are transported directly into the portal circulation, contributing little to chylomicron formation and minimizing the volume of lymph flowing along the thoracic duct [3]. However, breast milk (BM) contains the appropriate nutritional components and digestive enzymes, but also immunologically effective and protective components like antibodies, lysozyme, neuregulin-4 and lactoferrin. Completely weaning children with chylothorax off breast milk means the loss of these components, which are essential for an enhanced neurological development. Moreover, special milk formulas are not freely available in developing countries and are far too expensive, so that the use of fat-free human milk was already reported by Chan in 2007 [4]. The use of skimmed milk was found to be equivalent or even better to specialized formulae and can be a therapeutic option [5]. Octreotide, a long-acting analogue of somatostatin, is an additional strategy in the treatment of chylothorax, because it inhibits lymphatic fluid production by acting on somatostatin receptors in the splanchnic vessels [6].

Considering the importance of breast milk feeding, especially in preterm infants [7], we used skimmed breast milk (SBM) to avoid its discontinuation. Further, we report the early introduction of long-chain fatty acids (LCFA) in the form of breast milk after resolution of chylothorax with favorable outcome in neonates with congenital chylothorax.

**Methods**

Neonates diagnosed with congenital chylothorax and treated between 2013 and 2019 at Innsbruck Medical University Hospital (n = 5) were eligible for this report.

In two patients we administered skimmed breast milk, which is defined as the nearly fat-free fraction of breast milk and can be produced via centrifugation or spontaneous separation. We decided to use a centrifugation-based method because it was shown to be more effective at separating fat in human milk. BM was expressed and stored at 0°-4 °C in a refrigerator for maximal 24 hours until it was processed at the local human milk bank. Expressed breast milk (EBM) was then transferred to sterile conical centrifuge tubes (Falcon™ 50 ml polypropylene conical tubes) and centrifuged for 10 minutes at 2000 rpm and 5 °C (Centrifuge 5810R®, Eppendorf). Separation of the fat fraction and the skimmed portion was clearly visible (shown in Fig. 1). Aspiration of the fat-free fraction was performed with a syringe and an attached sampling straw. Skimmed breast milk was either stored at 0°-4 °C and fed within 24 hours from the time BM was expressed or stored at ≤ -18 °C for at least 24 hours and used thereafter. After thawing, SBM was used within 24 hours and not frozen again [8].

**Results**

Patient 1 (36 + 4 weeks):
A diet with an MCT-based formula (Monogen®) was started on the first day of life (DOL). However, even with total parenteral nutrition (TPN), the chyle amount did not decrease. On day 16, therapy with somatostatin (octreotide) was initiated and slowly increased to a peak dose of 5 µg/kg/h. After clinical improvement somatostatin was reduced and discontinued on day 26 (cumulative dose 2.83 mg). Chyle amount decreased gradually and enteral nutrition with Monogen® was restarted on day 18, reaching an amount of 150 ml/kg/day on day 23, when parenteral nutrition was discontinued. The infant was discharged at 40 + 4 weeks and 3750 g (50th percentile) on the 27th DOL on Monogen® and was transitioned to full-fat formula nutrition on day 77. Breast milk was never given.

Patient 2 (35 + 0 weeks):

After one week of TPN, an almost fat-free formula (Basic F®) was introduced. On full enteral nutrition, recurrence of pleural effusion and respiratory deterioration led to the introduction of therapy with somatostatin with a maximal dose of 10 µg/kg/h on the 14th DOL. Nutrition with Basic F® was continued again and diet was gradually changed to Monogen® to introduce some LCFA on day 29. Somatostatin was discontinued on day 41 (cumulative dose 15.65 mg). The patient was discharged on Monogen® and LCFA and vitamin substitution once a week (until the 84th DOL) on day 43 at 41 + 0 weeks, 4415 g (90th percentile). Breast milk was gradually introduced at the 56th DOL.

Patient 3 (32 + 5 weeks):

TPN was performed until the 13th DOL. Additionally, therapy with somatostatin was commenced on day 3, reaching a maximal dose of 10 µg/kg/h on day 5 and discontinued on day 32 (cumulative dose 12.6 mg). After two weeks Basic F® was introduced and replaced by Monogen® one week later. LCFA and vitamins were substituted once a week (until the 54th DOL). The patient was dismissed on day 43 at 38 + 5 weeks and 2885 g (10th percentile). Breast milk was gradually introduced at the 47th DOL.

Patient 4 (36 + 3 weeks):

After one week of TPN, effusion amount decreased and enteral nutrition with Basic F® was introduced. Subsequently, effusion amount and tachydyspnoe worsened again. For this reason, somatostatin was started on day 16 at a maximum dosage of 15 µg/kg/h and discontinued on the 56th DOL (cumulative dose 32.9 mg). Moreover, parenteral nutrition was introduced for another two weeks. After stabilization, Basic F® was restarted on day 35 and converted to skimmed milk within two weeks. LCFA and vitamins were substituted once a week till the 57th DOL. Under this regime weight gain was adequate and chylothorax did not recur. From the 60th day on, the patient was fully breastfed and was dismissed on the following day at 45 + 0 weeks and 4105 g (35th percentile).

Patient 5 (35 + 4 weeks):

This was a female neonate with confirmed *RAF1* mutation (Noonan syndrome). Ligation of a persistent ductus arteriosus Botalli at the age of 28 days revealed congenital lymphatic system malformations and subsequently a chylothorax. The patient was on parenteral nutrition for five days, and somatostatin was
additionally given at a maximal dose of 10 µg/kg/h for 24 days (cumulative dose 8.31 mg). Since day 42, when pleural effusions resolved, the patient was fed with skimmed breast milk and reached full enteral feeding ten days later.

A summary of patient characteristics and CC management at the NICU Innsbruck is given below (shown in Fig. 2).

**Discussion**

Congenital chylothorax is an uncommon but serious entity in neonates. Due to the rarity of this disorder a universal consensus on management of CC is unavailable and current dietary treatment recommendations are based on individual case reports or case series [9]. Over a period of seven years we identified a total of five preterm infants with congenital chylothorax.

The accumulation of lymphatic fluid with high levels of triglycerides (>110 mg/dl), proteins (>20 g/L), and lymphocytes (>80% of cells) implicates large losses of nutrients and immune cells and put patients at risk of malnutrition and impair their immune system [10]. So, when dealing with the effusion, nutritional management is a key issue and a balance is needed between achieving sufficient caloric intake and minimizing chyle production. Moreover, a rapid conversion to regular alimentation (preferably breast feeding) is especially important for preterm infants as the growing brain is strongly dependent on the supply of balanced fatty acid nutrition [11]. Enteral feeding with MCT bypasses the intestinal lymphatic system, as they are absorbed directly into the portal venous system. Thus, therapy of chylothorax calls for MCT-based nutrition with adequate LCFA supplementation, as they are needed as essential part and precursors for membranes and other metabolic processes. This reduces the chyle flow. However, even the intake of sterile water can stimulate chyle flow by 20% [12]. Therefore, total parenteral nutrition should be applied until the pleural effusions have resolved [13]. Thereafter, diet needs to be cleared of long-chain fatty acids over several weeks or even months. Thus, chylothorax is considered an absolute contraindication for breastfeeding as human milk has a high long-chain fatty acid content [14].

The dietary management of our five patients consisted of TPN, which was performed until pleural effusions resolved (mean 12.4 days). To avoid a prolonged parenteral nutrition and its possible adverse effects including a high risk of sepsis, nutritional support was provided in the form of adequate caloric intake and enteral feedings were gradually introduced using a low-fat formula. Basic F® was given to Patient 2 (for 22 days), to Patient 3 (for seven days) and to Patient 4 (for ten days), respectively. LCFA like clinoleic acid and vitamins (Vitalipid®, Soluvit®) were substituted once a week. In further course the introduction of a medium-chain triglyceride (MCT)-based formula containing some LCFA (16% of energy) was attempted. Patient 1 immediately received Monogen®, Patient 2 at the 29th DOL and Patient 3 at the 21st DOL. About 80% of infants with chylothorax respond to conservative dietary management [15]. Nevertheless, chylothorax did not resolve in any of our patients under this regime, and therefore treatment with somatostatin was started additionally. The initial dose varied from 0.5 to 1 µg/kg/h and the maximum dose applied was 15 µg/kg/h. In human milk somatostatin is found in high concentrations, thus contributing a direct beneficial effect toward reducing lymph production when human milk is
continued in infants with chylothorax [16]. If breast milk feeding is continued, medication with octreotide could be avoided and uncommon but potentially life-threatening side-effects like necrotizing enterocolitis (NEC) [17], pulmonary hypertension or aggravation of bronchopulmonary dysplasia (BPD) might possibly be prevented [18].

Breast milk has proven to have beneficial effects and is strongly recommended for all infants, particularly for preterm infants because of its nutritional, immunologic and psychosocial advantages [19]. Abstaining from breast milk causes infants to not be optimally protected against serious diseases of preterm infants like gastrointestinal infections or NEC. Furthermore, a chylothorax diagnosis can be disappointing for parents, especially for those who had intended to provide breast milk as the primary form of nutrition for their infant. Consequently, the mother-child interaction may suffer because of the missing physical contact. Against this background, we aimed to successfully introduce a dietary regimen of fat-modified breast milk fortified with additional fat, calories, and essential fatty acids that can provide the immune, nutritional and bonding benefits of breast milk without exacerbating chylous effusions. Accordingly, in Patients 4 and 5 we administered skimmed breast milk instead of an MCT-based formula after resolution of chylothorax on day 40 and 42, respectively. The literature shows reports on several cases of successful use of fat-free (skimmed) breast milk [4, 20–23]. More and more clinics worldwide are introducing skimmed breast milk instead of special fat-free nutrition. This can be provided via centrifugation (at minimum 2500 rcf for 15 min; which is approx. 3000–3500 rpm depending on the centrifuge) or by placing the milk in the refrigerator and leaving it undisturbed until the fat fraction and the transparent, fluid skimmed portion spontaneously separate, so that it is also practicable after discharge. Skimmed milk has had the long-chain fatty acids removed (fat content is less than 0.1%), is lower in calories, essential fatty acids and fat-soluble vitamins, which have to be parenterally replaced. However, it retains levels of electrolytes, protein and lactose that are similar to those of normal breast milk, and it can thus be assumed that the immunologically protective components of breast milk that are contained in proteins are largely preserved during the procedure.[4]

**Conclusion**

The therapy regimen practiced at our institution for congenital chylothorax, including the use of fat-free human milk, was successful in all five patients, meaning no further re-accumulation of pleural fluid and an adequate weight gain. From patient to patient we improved our treatment strategy, and with the last two patients we feel we achieved a good plan to suit the wishes of mother and child.

The use of skimmed breast milk offers benefits to mothers who wish to resume breast feeding after resolution of chylothorax and has proven positive effects, above all in preterm infants as optimal nutrition with protective components superior to formula feeding.

**Abbreviations**

BPD Bronchopulmonary dysplasia
Monogen® Formula with low LCT (16%) and high MCT (84%) contains the essential fatty acids docosahexaenoic acid (DHA) and arachidonic acid (AA)

octreotide Synthetic long-acting analogue of somatostatin

Declarations

Ethics approval and consent to participate
The research was conducted ethically in accordance with the World Medical Association Declaration of
Helsinki.

Consent for publication

The manuscript does not contain any individual person's data in any form (no individual details, images or videos).

Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests" in this section.

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Author Contributions

MH, KW, MH, JK and UKK treated the patients at the neonatal intensive care unit. DK, AH and SSB provided expertise for nutritional advice. MH, KW, MH, JK, UKK and DK drafted the manuscripts, collected data on the patients, and reviewed the literature for data on other known patients suffering from congenital chylothorax. All authors critically reviewed the manuscript and approved the final version.

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Figures

Figure 1

Clearly visible separation of fat and fat-free fraction after centrifugation.
Figure 2

Algorithm of CC management at the NICU Innsbruck.