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Octreotide in the Management of Postoperative Chylothorax

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Abstract. Chylothorax (KT) may be a complication of thoracic surgery. Its management is not well established and may comprise dietary interventions and surgery. The effectiveness of somatostatin and its analogues has been reported, although their mechanism(s) of action is unclear. We report our experience with octreotide in a series of patients with postoperative chylothorax. Eight patients with KT were treated with a continuous intravenous infusion of octreotide (OCT) at a starting dose of 0.5 μg/kg/hr. They were compared with four additional patients with KT who were treated according to the conventional approach. After a mean of 3.3 ± 1.9 days of treatment, fluid discharge diminished dramatically. In all patients, fluid losses stopped by postoperative day 10.5 ± 2.9 and chest tubes could be removed after 12.8 ± 4.1 days. Compared to a small group of historical controls, OCT reduced significantly the total fluid losses (141.1 ± 89.3 vs 396.7 ± 151.0 ml/kg; $p = 0.003$) and the postoperative length of stay ($p = 0.05$). No patients in the group treated with OCT required parenteral nutrition (compared to all four of the controls; $p = 0.002$) and/or thoracenteses (compared to two of four controls). In postoperative KT, OCT seems to be at least as effective as the conventional approach. Furthermore, OCT may reduce total fluid losses and postoperative length of stay. This may have a beneficial effect on the risk of complications and on hospital costs.

Key words: Chylothorax — Octreotide — somatostatin

Chylothorax (KT) is pleural effusion of fluid rich in triglycerides and chylomicrons. It can be spontaneous (neonatal congenital), posttraumatic, or a complication of a thoracic surgical procedure [1, 12]. In thoracic surgery, chylothorax is often the result of rupturing of the thoracic duct, a thin-walled vessel, driving the chyle from the gastrointestinal tract to the left subclavian vein, which is unable to contract effectively [6, 14]. This condition, when long-standing, may have a profound effect on the clinical status patient due to the loss of significant amounts of proteins and of immunological and nutritional factors. Although not well defined, its usual treatment comprises an early period of dietary management (low-lipid diet and parenteral nutrition), followed by surgical attempts to stop the drainage of chyle. However, surgery is not risk-free and, in some patients, may not be effective. In recent years, the effectiveness of somatostatin and its analogues in the treatment of chylothorax has been the subject of anecdotal reports [2, 3, 5, 10, 11, 13].

We review our experience with chylothorax and its treatment with octreotide, a somatostatin analogue.

Patients and Methods

We prospectively evaluated, in an open study, the effectiveness and safety of octreotide in postoperative chylothorax following pediatric heart surgery. Eight patients were enrolled who presented early postoperative KT. The diagnosis was made clinically after the appearance of a milky drainage from the chest tubes following reintroduction of oral feedings, and it was confirmed by the detection of increased amounts of triglycerides and lymphocytes in the drained fluid (>110 mg/dl and >80% of cells, respectively).

Following the diagnosis of KT, octreotide was administered by continuous infusion through a peripheral vein. The starting dose was 0.5 μg/kg/hr, with a gradual increase until an effect (if any) was seen—that is, clearing and/or consistent reduction of the volume of the drained fluids. Octreotide infusion was gradually tapered and stopped 4–7 days after resolution of the chylous drainage and removal of chest tubes.

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Table 1. Clinical characteristics of the eight patients with postoperative chylothorax treated with octreotide

Patients			
Age (months)	Sex	Cardiac diagnosis	Surgery
7	Female	Double-outlet right ventricle	Complete correction
62	Male	Tetralogy of Fallot	Complete correction
2	Male	Truncus arteriosus	Complete correction
10	Male	D-transposition	Senning
8	Male	VSD + pulmonary stenosis	Complete correction
8	Male	C-TGA + tricuspid atresia + VSD	Cavopulmonary anastomosis
8	Male	c-TGA	Pulmonary artery banding
39	Female	Aortic coarctation	Decoarctation

TGA, transposition of the great arteries; VSD, ventricular septal defect.

Table 2. Comparison of the effects of octreotide with the "conventional" approach

	Octreotide (n = 8)	Historical controls[a] (n = 4)	p value
Median (age, months, range)	8 (2–62)	5.5 (2–276)	NS
Bilateral chylothorax (No.)	5	0	NS
Total fluid losses (ml//kg)	141.1 ± 89.3	396.0 ± 151.0	0.003
Postoperative stay (days)	18.7 ± 7.1	28.2 ± 9.3	<0.05
Days of chylous losses	10.5 ± 2.9	15.75 ± 7.8	NS
Days with chest tubes	12.8 ± 4.2	16.0 ± 6.6	NS
TPN (No.)	0	4	0.002
Thoracentesis (No.)	0	2	

NS, not significant; TPN, total parenteral nutrition.
[a]Cardiac diagnoses: multiple ventricular septal defects, right isomerism with common atrioventricular valve, patent ductus arteriosus, and aortic coarctation.

Patients also had an early, brief period of clear fluids by mouth, followed by feedings with an MCTs formula (Portagen, Mead-Johnson, Rome, Italy).

To verify the potential usefulness of octreotide, we also identified four other patients with KT previously treated at our institution according to the conventional approach with prolonged total parenteral nutrition (TPN) and compared their data with those of patients treated with octreotide. Data were analyzed with the SPSS software, version 11.0 (SPSS, Chicago, IL, USA).

Results

Table 1 illustrates the main clinical characteristics of the eight patients with KT treated with octreotide. All eight patients had an uneventful early postoperative course and they were discharged from the intensive care unit after a mean of 5.2 ± 4.6 days. Following the first few feedings, usually with a formula milk or cow's milk, a whitish drainage from the chest tubes with laboratory confirmation of high levels of triglycerides (> 110 mg/dl) and lymphocytes (> 80%) in the fluid made a diagnosis of KT. Octreotide was started on postoperative day 5 ± 2.6 (range, 2–10) at a starting dose of 0.5 μg/hg/hr, gradually increasing up to 3.4 ± 2.7 μg/kg/hr (range, 0.5–7). After a mean of 3.3 ± 1.9 days of treatment, fluid discharge reduced dramatically and there was a marked change in its appearance (from milky to serous) and biochemical characteristics (decrease of tryglycerides and lymphocytes). In all patients, total disappearance of the fluid loss was achieved by 10.5 ± 2.9 postoperative days (range, 5–14) and chest tubes could be removed after 12.8 + 4.1 days (range, 8–21). Octreotide infusion was gradually tapered and stopped after 12.8 ± 5.1 days (range, 5–22). During treatment, oral feedings were not stopped. After the first 2 ± 0.5 days of clear fluids only, an MCT-enriched formula (Portagen) was gradually introduced in the diet. All patients were discharged in good clinical condition and on diet with Portagen. No side effects of the treatment were observed. Echocardiography ruled out a venous hypertension state as a cause of chylothorax and, for the same reason, no patient had central venous lines at the superior caval vein district.

To verify the usefulness .of octreotide, we compared the clinical course of these eight patients with that of four patient with chylothorax previously treated at our institution (Table 2). Their cardiac diagnoses were multiple ventricular septal defects (VSDs) + coarctation, right isomerism with common

atrioventricular valve, patent ductus arteriosus, and aortic coarctation. All underwent corrective surgery with the exception of the patient with right isomerism, who underwent a cavopulmonary anastomosis (Glenn procedure). Following the development of chylothorax, patients started TPN, compared to none in the group treated with octreotide (Fisher's exact test, $p = 0.002$). Subsequently, after 12.2 ± 3.4 days of TPN, small amounts of clear fluid were introduced by mouth, followed by increased volumes of Portagen. Parenteral nutrition (total and, subsequently, partial) was continued for 20.2 ± 2.5 days (range, 16–35). Despite this approach, these patients underwent repeated thoracenteses (four episodes) and surgeries (thoracic duct ligation in two patients) compared to none in the group treated with octreotide. Also in these patients, echocardiography ruled out a venous hypertension state.

We also compared the total loss of chylous fluids between the two groups. Patients treated with octreotide lost 141.1 ± 89.3 ml/kg compared with patients treated with TPN, who lost 396.7 ± 151.0 mil/kg ($p = 0.003$).

Finally, postoperative length of stay was significantly reduced in patients treated with octreotide compared to controls: 28.2 ± 9.3 vs 18.7 ± 5.7 days ($p = 0.05$).

Discussion

Chylothorax is a relatively rare condition in pediatric patients. Available literature reports an incidence of 0.42–2.5%. It may be spontaneous (usually in neonates) or acquired as a result of thoracic surgical procedures [2]. In these patients, chylothorax may follow a direct lesion of the thoracic duct or depend on a condition of venous hypertension at the superior caval vein level. The diagnosis of chylothorax is made clinically based on the milky appearance of the drained fluid from the pleural spaces following the reintroduction of oral feedings and also on the presence of high levels of triglycerides (> 110 mg/dl) and lymphocytes (> 80% of cells) in the drained fluid [1]. Because chylothorax is rare, it has been difficult to determine the optimal therapy. Most published series are retrospective, comprise adult patients, or are limited to anecdotal reports [2–5, 8–11, 13].

Its treatment is not well established, although Beghetti et al. [1] proposed a therapeutic algorithm. The chyle is rich in trigycerides absorbed by the gut, therefore, a nutritional approach may be attempted, reducing the dietary uptake of lipids. This can be accomplished using commercially available formulas enriched with MCTs, which are not carried by the chyle. This allows a satisfactory nutritional supply, despite the reduction of the lymphatic flow from the gastrointestinal tract. Usually, if the nutritional approach fails, TPN is introduced, which is followed by direct ligation of the thoracic duct after 3 or 4 weeks. Alternatively, pleurodesis or placement of a pleuroperitoneal shunt can be performed [15]. However, this approach is not risk-free: during the period of nutritional management, patients may suffer nutritional impairment and are prone to develop systemic infections due to the loss of immunoglobulins and lymphocytes with the drained fluid. Moreover, surgery may not be effective and the suggested procedures are not free of complications [1, 7].

In 1990, Ulibarri et al. [13] reported the effectiveness of somatostatin in an adult with chylothorax. Subsequently, anecdotal reports have been published and only few pediatric patients have been treated with somatostatin or its analogues for postoperative chylothorax. Markham et al. [6] published the only controlled trial of octreotide in the experimental animal with surgically induced chylothorax, and they noted a significant reduction of fluid drainage in the octreotide-treated animals. Rimensberger et al. [10] reported a 4-month-old infant treated with octreotide, and Cheung et al. [3] described the effectiveness of octreotide in two children with postoperative chylothorax. In a previous report from our institution, we also described the apparent effectiveness of octreotide in two pediatric patients [11]. Several other case reports have been published on octreotide in patients with postoperative or congenital chylothorax [4, 9], as a small series discussing the surgical approach [8]. Somatostatin and related peptides inhibit growth hormone secretion. Moreover, they are particularly active on the gastrointestinal tract. Although the mechanism(s) of action is not clearly understood, they probably act through a reduction of the gastrointestinal blood flow and, consequently, of the lymphatic drainage from the gut. This decrease of the lymphatic flow through the thoracic duct would favor coalescence of the "wound edges" within its thin walls and, eventually, its healing. If this were true, somatostatin and its analogue should not work in patients with chylothorax due to a superior caval vein hypertension, a condition that was ruled out in all our patients. Somatostatin has a short half-life and should be administered intravenously; therefore, analogues with longer half-lives have been developed and administered either parenterally or subcutaneously. In our patients, we used octreotide, a recently developed analogue. Side effects of somatostatin are hypotension, hyperglycemia, and abdominal distension, but no severe complications of this treatment have been reported.

In our patients, there were no significant side effects, but there was a mild increase in stool fre-

quency (four per day) in one patient. Treatment with octreotide avoided parenteral nutrition and reduced the risks related to a prolonged hospital stay and long-lasting chylous drainage—that is, infection, nutritional deficits, and psychological discomfort. It should be noted that no patient treated with octreotide required parenteral nutrition. This issue should not be disregarded because of the risks of metabolic and infectious complications of parenteral nutrition. Also, patients treated with octreotide did not require albumin infusions and/or thoracenteses. Our results show a significant reduction in hospital stay and, more important, the total amount of fluid loss. We believe that this effect may be attributed to octreotide because its infusion led to a marked reduction of fluid loss by a mean of 3.3 days, whereas after the same time controls did not have a significant reduction. Octreotide may be effective at least as the initial approach, independent of its etiology, provided a condition of increased central venous pressure has been ruled out. In fact, if the etiology of KT is a caval vein hypertension state, it is unlikely that drainage of the chyle can be improved through pharmacological methods only.

Our study has several limitations. First, it is not a randomized, placebo-controlled trial. Second, the sample is small, however, this is the largest series studied to date since chylothorax is very rare and it would be extremely difficult to obtain enough patients for a controlled trial. Despite this, statistical analysis revealed that octreotide may at least be effective as the conventional approach. Also, to our knowledge, this is the first attempt to compare this new treatment option with the conventional approach.

In conclusion, octreotide seems to be helpful in the management of postoperative chylothorax. Compared to the conventional approach, its effectiveness seems similar, with the advantages of reduced hospital stay and duration of chest tube use, reducing the losses of nutritional and immunological factors. This issue is important, particularly in pediatric patients.

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