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Octreotide for chylous effusions in congenital diaphragmatic hernia

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Abstract

Background/Purpose: Chylothorax is a frequent complication in congenital diaphragmatic hernia (CDH) infants and is associated with significant morbidity. The optimal treatment strategy remains unclear. We hypothesize that octreotide decreases chylous effusions in infants with CDH.

Methods: This is a retrospective study of all infants with CDH admitted to our institution from October 2006 to October 2011.

Results: Eleven (12%) infants developed a chylothorax. Five infants were managed conservatively with thoracostomy and total parenteral nutrition. Six infants were started on octreotide therapy. None of the infants required surgical intervention to stop the effusion. There was no significant difference in survival to discharge, length of stay, or average daily chest tube output between groups. There appeared to be a temporally associated drop in chest tube output upon initiation of octreotide in two infants; however, the overall rate of decline in chest tube drainage was unchanged. In addition, there were infants in the conservative group who demonstrated a similar drop in daily chest tube output despite the absence of octreotide.

Conclusions: Our data suggest that the majority of chylous effusions in CDH infants resolve with conservative therapy alone.

Chylothorax is reported in 6%–27% of infants with CDH [1–6]. This complication contributes significantly to the morbidity already associated with CDH, adding problems such as nutritional deficiency, hypoproteinemia, electrolyte abnormalities and a compromised immune system [2,5]. Effective management remains a challenge and many treatment strategies are controversial. Initial approaches to

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management include tube thoracostomy, withholding of enteral feeds and administration of total parenteral nutrition [1,2,4,6,7]. In cases that are refractory to this conservative management, surgical interventions such as pleurodesis, thoracic duct ligation or pleurectomy, are considered [2,5].

Octreotide, a somatostatin analogue, has been used in patients with refractory chylothorax that do not respond to conservative management; however, no randomized studies in the neonatal population are available [7]. The exact mechanism of this therapy is uncertain, but is thought to cause vasoconstriction of splanchnic vessels, thereby reducing gastrointestinal secretions and intestinal absorption, which ultimately reduces the flow of chyle. Reported adverse effects of this medication include transient impairment of liver function, transient hypothyroidism, abnormal glucose homeostasis, and necrotizing enterocolitis [8].

Octreotide is used frequently as second-line treatment in patients who develop chylothorax following congenital heart surgery [9–11]. While there are no published controlled clinical trials regarding its use in this population, multiple large case series report success [7–13]. In one of the larger studies, 19 patients with congenital heart disease who developed postoperative chylothorax were treated with octreotide after failed conservative management [9]. Sixty-three percent of those patients demonstrated complete resolution of the chylothorax at an average of about 11 days after starting octreotide.

Use of octreotide for chylothorax in infants with CDH has been reported in only 11 cases with variable success [2,6,14,15]. Four of these cases were reported to have a dramatic reduction in chest tube drainage after initiation of octreotide with resolution of the effusion after 5–13 days of treatment [6,14,15]. In the remaining seven cases, octreotide failed to decrease chest tube output [2,6]. Most of those cases came from a single retrospective series of six patients in which octreotide did not consistently reduce chest tube drainage in any of the infants [2]. Our institution has used octreotide frequently in this population. The aim of this retrospective study was to determine if octreotide decreases chylous effusions in infants with CDH.

1. Methods

A retrospective analysis of infants with a diagnosis of CDH admitted to Cincinnati Children's Hospital Neonatal Intensive Care Unit from October 2006 through October 2011 was performed. Eighty-nine infants were identified for review. Infants with a diagnosis of pleural effusion with chest tube output >15 mL per kg per day were then identified. Chylothorax was diagnosed based on pleural fluid that was documented to be sterile and that had a lymphocyte count of more than 70%. Data on sidedness of the diaphragmatic defect, severity of the defect (based on prenatal total lung volume (TLV) or observed to expected lung area to head circumference ratio (O:E) where mild equals TLV > 40 mL or O:E > 45, moderate equals TLV = 20–40 mL or O:E = 25–45, severe equals TLV < 20 mL or O:E < 25) and need for extracorporeal membrane oxygenation were collected. Those infants with chylous effusions who received octreotide were compared to those who did not receive this therapy. The primary outcome measured was duration of effusion. Secondary outcomes measured were survival to discharge, length of stay, total chest tube output, average daily chest tube output, and culture positive sepsis. Since the duration of chest tube output was variable in the six patients treated with octreotide, some days included data from only one to two patients. To insure that our analysis was not overly weighted toward a single patient, we only included days that represented three or more patients in our results in Fig. 2. Statistical analysis was conducted using Microsoft Excel. Comparison between the two groups was made using a Student's *t*-test and chi-squared analysis. $P < 0.05$ was considered statistically significant.

2. Results

During the 5-year study period, 89 infants with CDH were identified (78 left sided, 11 right sided). Thirty (34%) infants developed a pleural effusion requiring chest tube drainage, of which, 11 were confirmed chylous by pleural fluid analysis. The remaining 19 infants with a pleural effusion were excluded from this study because 10 of the effusions were not chylous and 9 were indeterminate as no pleural fluid was sent for analysis. All of the infants with a chylothorax had a left-sided diaphragmatic defect. Seven of these infants developed a chylothorax after CDH repair, four developed a chylothorax prior to repair. The average survival rate for infants with chylothorax, nonchylous effusions, and no pleural effusions was 64%, 50%, and 70%, respectively, while the average length of stay for these three groups was 82, 105, and 64 days, respectively.

Initial management consisted of cessation of enteral feeds, total parenteral nutrition and chest tube drainage. Five of the 11 infants with chylothorax were managed successfully with this conservative approach alone and required chest tube drainage for an average of 9 days (range 2–18 days). These infants were all male with an average gestational age of 38 weeks. Three of these infants had a moderate-sized diaphragmatic defect and two had a severe defect. Those two infants with a severe diaphragmatic defect required ECMO. The remaining six infants who did not demonstrate a decrease in chest tube output with conservative management were started on octreotide therapy. This therapy was initiated on average 8 days into the pleural effusion. The octreotide dosing range used in these patients (1–13 μg/kg/h) was consistent with previously published octreotide dosing regimens [8]. These infants required chest tube drainage for an average of 29 days (range 10–51 days). Five of the infants in this group were female and one was male, with an average gestational age of 37 weeks. Two of these infants