Can Octreotide be the First Line Treatment for Chylothorax?

SONTHAKIT LEELAHANON, MD*,
WIRACHAI SONTIMUANG, MD**,
VARAPORN TEPAKORN, MD**,
WATTANASAK PETLEK, MD**,
PAKPOOM POCHANART, MD**,
SATIT RUANGPEG, MD**

Abstract

Background : Chylothorax is a rare but serious condition with a high rate of morbidity that may lead to death. It may be spontaneous or a complication of cardiac surgery. Treatment of this potentially harmful condition is not well established and may comprise dietary interventions. In order to avoid surgery, somatostatin and octreotide have been recently suggested as new modalities for the treatment of chylothorax.

Objective : To study the efficacy of octreotide for the treatment of chylothorax.

Method : Cases reports.

Result : The authors report two cases of chylothorax successfully treated with intravenous infusion of octreotide as an adjunct to conventional treatment. Furthermore, the authors report their last case who were treated successfully with octreotide as the first line drug without diet modification.

Conclusion : It seems that octreotide is effective, noninvasive and safe. It can be used as an optional or first line treatment for chylothorax.

Key word : Octreotide, Chylothorax

LEELAHANON S, PETLEK W, SONTIMUANG W, POCHANART P, TEPAKORN V, RUANGPEG S
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* Division of Cardiovascularthoracic Surgery,
** Division of Pediatric Surgery, Department of Surgery, Queen Sirikit National Institute of Child Health, Bangkok 10400, Thailand

Chylothorax is a rare but potentially serious complication of pediatric cardiac operations with an incidence of 0.56 per cent to 1.9 per cent[1]. Most cases of chylothorax are operative injury but can occur as a congenital cause. Disruption of the thoracic duct or accessory lymphatic channels is the pathology of this disease. The majority of chylothorax cases respond to conservative management with bowel rest, medium chain triglyceride or total parenteral nutrition. For unabated drainage that lasts longer, surgical interventions including pleurodesis, ligation of lymphatic ducts, ligation of the main duct at the aortic hiatus and pleuroperitoneal shunting are advocated, though not always effective. Furthermore, the need for chest tube insertion, total parenteral nutrition and prolonged hospital stay increase the morbidity and expenses of patients with chylothorax. Neonates and post-operative children have limited reserves and they are at increased risk of developing life-threatening complications such as lymphocytopenia, hypoproteinemia and serious electrolyte and acid-base disturbances[2]. The need for long-term central venous access in the presence of a depressed immune system puts them at risk of sepsis[2]. In order to eliminate these adverse effects, somatostatin and its synthetic analogue (octreotide) have been recently suggested as new modalities for the treatment of chylothorax. The authors report two cases of post-operative chylothorax and one case of congenital chylothorax who were successfully treated with intravenous infusion of octreotide.

CASES REPORT

Patient 1

A 3-year-old girl underwent left thoracotomy for clipping of patent ductus arteriosus. As the patient resumed feeding on the day after operation, milky fluid was noted in the chest drain. Chylothorax was confirmed by a high level of triglyceride. Initially, a fat free diet and partial parenteral nutrition were used. However, chyle leakage did not stop after treatment for 9 days. Thus, feeding was withheld and total parenteral nutrition was introduced for another five days but was still unsuccessful. Leakage continued about 20-40 ml/day. Finally, octreotide was added at the rate of 0.5 μg/kg/hour intravenously. Dramatically, chyle was completely stopped the next day. Normal diet was started and no further chyle leakage was found. Octreotide was infused for 4 days and chest drain was subsequently removed. Neither side effect nor complication was found.

Patient 2

A 4.1 kg term male neonate had respiratory distress since birth. His mother had a history of polyhydramnios and cesarean section was done due to cephalopelvic disproportion. His APGAR scores were 6,8. He was intubated and respiratory dependent. Physical examination showed decreased breath sound of the left lung and chest X-ray revealed massive left pleural effusion with mediastinal shifting to the right. Echocardiogram was normal. Left thoracocentesis was done at which the clear pleural fluid was removed. Effusion examination showed WBC 11,800 cells per mm^3 with lymphocyte 97 per cent and PMN 3 per cent. Because left thoracostomy tube was inserted and a large amount of pleural fluid about 250 ml was drained, the patient was markedly improved. For diagnosing chylothorax, enteral feeding was given and subsequently the pleural fluid was changed from a clear to milky color with a high level of triglyceride. With total parenteral nutrition and complete bowel rest, chyle leakage was decreased from 74 ml/kg/day to 15 ml/kg/day but this output level was still unacceptably high. To reduce hospitalization time, octreotide 0.5 μg/kg/hour was started on the fifth day. The next day, the drainage had markedly decreased to 3 ml/kg/day and the patient was able to take a normal diet. It was further decreased and finally stopped after 3 days of drug infusion. Octreotide was continuously infused for 5 days without any side effects. This patient was discharged without any complications or recurrences.

Patient 3

Similar to the first patient, a 5-year-old boy had a left pleural effusion as chyle on the second day post-operatively after clipping of the patent ductus arteriosus. Intravenous octreotide infusion of 0.5 μg/kg/hour was started immediately. Although this patient was kept on a normal fat content diet, chyle leakage was completely stopped within 24 hours. Octreotide was infused for 2 days and stopped with neither recurrences nor complications.

DISCUSSION

Cardiothoracic operations are the most common causes of chylothorax in children[1,3,4]. Direct trauma to the thoracic duct or adjacent lymphatic pathways is believed to be the usual cause. Systemic venous hypertension after some cardiac operations may promote chylothorax formation. Another very rare cause of chylothorax is congenital. A conserva-

tive treatment strategy is currently recommended to avoid unnecessary early operation. Initial treatment is pleural drainage and use of a diet [such as formula with medium chain triglycerides (MCT)] that lacks long chain fatty acids or total gut rest with total parenteral nutrition[4]. However, patients may present with massive lymph drainage, which will result in critical losses of fluid, lymphocytes, proteins, coagulation factors, and antibodies, thus increasing morbidity and mortality. This is particularly true in small babies, for whom early operation is advocated. A significant increase in triglyceride and chylomicron concentrations can occur after MCT oil intake, and water alone can increase the chyle flow by 20 per cent[5]. These findings perhaps explain the poor resolution of chylothorax in a study of 49 patients on an MCT diet (38% after 14 days, 77% after 45 days)[3]. With total parenteral nutrition, chylothorax resolved in 77 per cent of patients in another study but at the cost of a mean pleural drainage time of 11.9 days[4]. Total parenteral nutrition itself might engender problems related to infection, thrombosis, or cholestasis.

Surgical treatment of chylothorax is neither straightforward nor well established and is recommended after the failure of dietary management, usually after 3 to 4 weeks[1]. Ligation of the thoracic duct with adjacent leaking lymphatics is the preferred surgical option but can involve an extensive thoracotomy[1]. Ligation of the duct at the diaphragmatic hiatus through an abdominal approach avoids a thoracotomy, as does chemical pleurodesis using talc. The insertion of an externalized pleuroperitoneal shunt for up to 3 months was followed by resolution of chylothoraces in 84 per cent of children[5].

As medical treatment is prolonged and surgical options are difficult, other treatments have been explored. The first report of using somatostatin to treat ruptured thoracic duct after supraglottic laryngectomy for carcinoma of the larynx was from Ulibarn et al in 1990[6]. Subsequently, Rimensberger et al[7] successfully used 14 days' somatostatin infusion (3.5 to 7 μg/kg/hour) in an infant with persistent bilateral chylothoraces after cardiac operation. Kelly and Shumway [8] also concluded that somatostatin was an effective therapeutic option for treatment of post-operative chylothorax. Somatostatin reduced gastric, pancreatic and intestinal secretions[9]. Somatostatin also causes a decrease of hepatic venous pressure gradient and a mild but sustained decrease of splanchnic blood flow without influencing systemic hemodynamics[7]. Furthermore, it inhibits intestinal motility[10]. These could be useful in an attempt to decrease chyle production. Pettitt et al[2] used somatostatin 5 μg intravenous injection every 12 hours for 3 days for treatment of persistent chylothorax in a neonate with hypoplastic left heart syndrome after Norwood procedure. They reported that within hours of the first injection, chest tube drainage decreased dramatically and stopped after 3 days. Aside from some transient cutaneous flushing, there were no apparent adverse effects.

Octreotide is a parenteral synthetic analogue of the naturally occurring hormone somatostatin; it has similar activity, greater selectivity and a longer half-life. Octreotide inhibits several pituitary and gastrointestinal hormones. The inhibition of serotonin and other gastrointestinal peptides results in increased intestinal absorption of water, decreased pancreatic and gastric acid, and increased intestinal transit time [5]. Importantly it also increases splanchnic arteriolar resistance and decreases gastrointestinal blood flow and, thus, secondarily reduces lymph flow[5]. Indications of octreotide therapy are endocrine tumors, variceal bleeding in portal hypertension, and reduction of lymph flow in chylous ascites[11]. It decreases the volume of high output intestinal fistula[12]. Pratap et al[5] used octreotide 1-4 μg/kg/hour in children with post-operative chylothorax in addition to an MCT diet in the hope that decreasing lymph production by non-dietary means would hasten its resolution. All-4 patients responded to the infusion and drain could be removed within 5 days of treatment. They discontinued octreotide within 10 days with no recurrence of the chylothoraces and without side effects or complications.

Octreotide can also be administered by subcutaneous injection. Demos et al[12] used octreotide 100 μg tid subcutaneously for 17 days to treat persistent chylothorax in adults. Cheung et al[10] used subcutaneous octreotide starting at a dose of 10 μg/kg/day in 3 divided doses and stepwise increased the dosage by 5 to 10 μg/kg/day every 72-96 hours. They also found that octreotide reduced the ratio of triglyceride concentrations in the lymph to that in the serum from 4.2 to 0.72.

It has been shown that somatostatin at a near physiologic dose reduces canine thoracic duct lymph flow rate. Reduction of chylomicron synthesis and transport into the lymphatic duct occurred through perturbation in the splanchnic circulation which was

demonstrated in a study on[13]. Markham et al[14] also randomly experimented in dogs and concluded that octreotide was effective in treating thoracic duct injury, leading to an early decrease in drainage and early fistula closure.

Reported side effects of octreotide include diarrhea, dizziness, thrombocytopenia and hepatotoxicity. These were not found in the presented patients. They were all rapidly cured after octreotide infusion. Furthermore, the last patient improved without diet modification. This suggests that the first line treatment of chylothorax may change from diet treatment to octreotide infusion.

Although it is impossible to determine the timescale of chylothorax resolution, had octreotide not been used. The authors' preliminary experience strongly suggests that octreotide is effective, noninvasive, and safe. Octreotide appears to reduce the morbidity, hospitalization, and costs related to this troublesome complication. Controlled studies are required to confirm these observations and the effects of octreotide treatment on morbidity and mortality.

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