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Somatostatin for Postoperative Chylothorax after Surgery for Children with Congenital Heart Disease

Chylothorax is a rare but serious postoperative condition with a high rate of morbidity that may lead to death of children with congenital heart disease. Here we reviewed nine consecutive cases with chylothorax in infants and children following cardiac surgery from March 2002 to February 2003. Somatostatin was added to conservative treatment proctocol to increase effectiveness of therapy in all cases. The duration of somatostatin therapy varied from 7 to 32 days. All cases of chylothorax were successfully treated with intravenous infusion of somatostatin as an adjunctive treatment. Even though two cases showed rebound phenomena, we avoided any surgical procedure in the nine patients who treated with conservative management combined with somatostatin. No significant side effects of somatostatin were observed. It seems that somatostatin is effective, noninvasive and safe therapeutic modality. It can be used as an adjunctive treatment to conservative management to control postoperative chylothorax in children with congenital heart disease.

Key Words : *Somatostatin; Chylothorax; Heart Defect, Congenital; Postoperative Complications; Child*

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INTRODUCTION

Postoperative chylothorax is a rare complication in children who have undergone cardiac surgery for congenital heart disease. When it occurs, it can contribute to patient's morbidity or mortality. The general treatment strategy of postoperative chylothorax is conservative, but surgical reintervention may be indicated in refractory cases. Lymphatic duct ligation or pleurodesis has been considered as the proper surgical intervention (1, 2). With these surgical treatments, however, problems still remain, and the results are not always satisfactory. Furthermore, persistent chylothorax may cause the additional risks to the already compromised patient due to reopening the chest for lymphostasis. Therefore, a noninvasive treatment for postoperative chylothorax would be better for the high-risk patients with congenital heart defect. Over the last years, an additional conservative treatment option with somatostatin has been introduced as a new modality for treatment of postoperative chylothorax (3-5). Thus far, the results have been mostly reported in the literature as individual case reports on children.

In this study, we report our experience in the management of postoperative chylothorax, with emphasis on the efficacy of somatostatin therapy in infant and children with chylothorax after cardiac surgery.

MATERIALS AND METHODS

From March 2002 to February 2003, nine patients developed chylothorax following operations for treatment of congenital cardiovascular disease at Samsung Medical Center. Chylothorax was diagnosed based on the presence of pleural fluid containing at least one of the following three characteristics: 1) milky appearance; 2) pleural fluid triglyceride levels greater than 110 mg/mL; 3) lymphocytic predominance in the fluid cellular component along with sterile cultures (6-8).

The conventional treatment had been undertaken upon recognition of chylothorax in all patients initially. The conventional treatment consisted of drainage of the pleural space by thoracentesis or tube thoracostomy, total parenteral nutrition, enteric rest or diet manipulation such as oral fat intake restricted to medium-chain triglycerides. If the amount of chylous leakage increased in 2 or 3 consecutive days after the conventional treatment, then intravenous somatostatin infusion was instituted. The initial starting dose was 3.5 μg/kg/hr and dosage was increased in a stepwise fashion up to 5, 7, and 10 μg/kg/hr and with a maximum dosage of 15 μg/kg/hr. Calories, electrolytes, proteins and clotting factors were monitored and replaced as necessary. Those patients submitted to cavo-pulmonary procedure (Fontan operation) were

also treated with diuretics, inotropes and vasodilators in order to reduce systemic venous pressure overload. The duration of somatostatin administration was dependent on the patient's response. After cessation of the chylous leakage and resumption of normal dietary habits, we initiated a tapering of somatostatin administration by halving the dosage every day over a 3-day period. Side effects of somatostatin such as hypotension, loose stool, and glucose instability were carefully monitored on a regular basis.

All results are represented as means or median values with ranges.

RESULTS

Table 1 shows details of patient, age at time of surgery, the cardiac diagnosis, the type of operation performed, interval to diagnosis of chylothorax after cardiac operation and the maximal drainage volume per day. The patients ranged in age from 1 week to 4 yr old. They were diagnosed of chylothorax between postoperative day 2 and day 16. The maximal daily volume of drainage ranged from 10 to 127 mL/kg per day. Only one patient (patient 1) experienced chylopericardium combined with chylothorax.

Table 2 indicates result of the treatment and the final outcome for each case. The duration of somatostatin therapy varied from 7 to 32 days with a median duration of 18 days.

Table 1. Characteristics of patients with chylothorax

Case No.	Age (Sex)	Cardiac defect	Type of operation	Diagnosis (POD)	Drainage amount*
1	2 yr 10 mo (F)	PA/VSD, DORV	Fontan	2	75
2	4 yr 5 mo (F)	Corrected TGA, VSD, PS	Double switch operation	4	11
3	3 yr 10 mo (M)	DILV, VSD, L-TGA,	Fontan	5	10
4	3 yr (F)	AVSD, DORV,	Fontan	3	71
5	6 mo (F)	AVSD	Repair	5	19
6	1 wk (M)	DORV, VSD, IAA	Repair	12	76
7	1 wk (M)	PA/VSD, PDA	RMBT	16	30
8	3 mo (M)	AVSD, SV, PA, TAPVR, MAPCA	RMBT, TAPVR repair, MAPCA unifocalization	11	29
9	2 wk (F)	TGA, VSD	ASO	16	127

ASD, atrial septal defect; ASO, arterial switch operation; AVSD, atrioventricular septal defect; DILV, double inlet left ventricle; DORV, double outlet right ventricle; IAA, interruption of aortic arch; MAPCA, major aortopulmonary collateral arteries; PA, pulmonary atresia; PDA, patent ductus arteriosus; POD, post operative day; PS, pulmonary stenosis; RMBT, right modified Blalock-Taussig shunt; SV, single ventricle; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries; VSD, ventricular septal defect.
*, maximal daily drainage (mL/kg/day).

A decrease in drainage was observed at an average of 3.1 days after the initiation of somatostatin, as the dose of somatostatin had increased enough to produce an effect (Fig. 1). All cases of chylothorax were successfully treated with conservative management combined with intravenous infusion of somatostatin. The median duration to reduce to 5 mL/kg per day of lymph drainage was 5 days (range 1 to 25 days). In patient 6 and patient 9, a rebound phenomenon of chylothorax was noted upon the reduction of somatostatin therapy, but the rebound effusion responded promptly when the dose of somatostatin was boosted (Fig. 2). No increase in drainage was observed when their normal diet was resumed. All nine patients had recovered completely from postoperative chylothorax by the use of somatostatin, and could avoid any invasive surgical interventions.

Patient 4

A 3-yr-old girl with a double outlet right ventricle and atrioventricular septal defect required a Fontan operation. The postoperative course was complicated by chylothorax after 3 days of operation. Her chylothorax was managed with total parenteral nutrition and diet modification firstly. However pleural effusion persisted. The patient was started on somatostatin continuous infusion of 3.5 μg/kg/hr when her pleural fluid losses were still 510 mL/day. But the chylous leak was increased for the next 8 days. At that time, her cardiac catheterization showed near complete occlusion of superior vena cava with large thrombus. Because the volume of daily leakage was up to 1,000 mL and the patient was in an unstable condition, we decided to attempt an exceptional increase in the somatostatin dose at 15 μg/kg/hr before considering the surgical management. She had a distinguished course of treatment. The volume of daily chylous leakage was decreased dramatically. Chylothorax ceased completely on day 35 without any surgical intervention. In this patient, superior vena cava syndrome was considered a contributing fac-

Table 2. Outcomes of patients with somatostatin therapy

Case No.	Duration[1]	Duration[2]	Rebound phenomena	Side-effect of somaostatin	Outcome
1	26	11	-	None	Successful CM
2	15	1	-	None	Successful CM
3	15	5	-	None	Successful CM
4	32	25	-	None	Successful CM
5	17	4	-	None	Successful CM
6	26	14	-	None	Successful CM
7	18	5	-	None	Successful CM
8	7	1	-	None	Successful CM
9	30	19	+	Loose stool	Successful CM

Duration 1, duration of somatostatin therapy (day); Duration 2, duration to reduction of chylous leakage to 5 mL/kg/day (day); CM, conservative management.

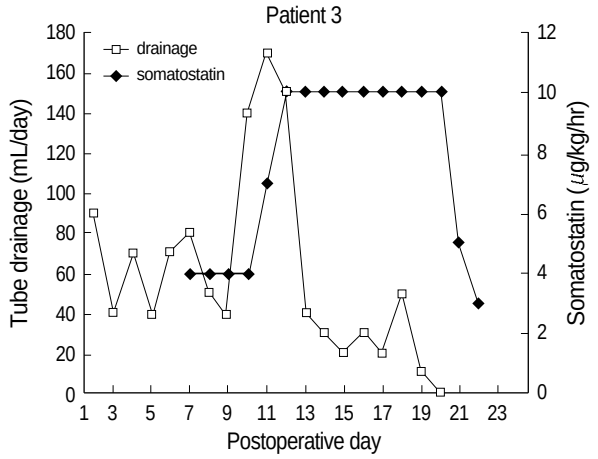

Fig. 1. Clinical course of patient number 3.

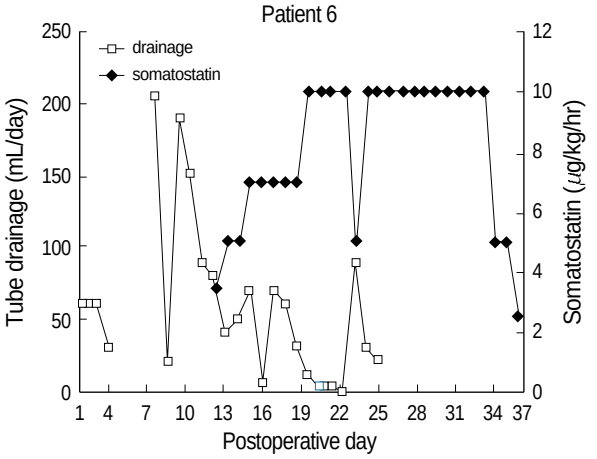

Fig. 2. Clinical course of patient number 6.

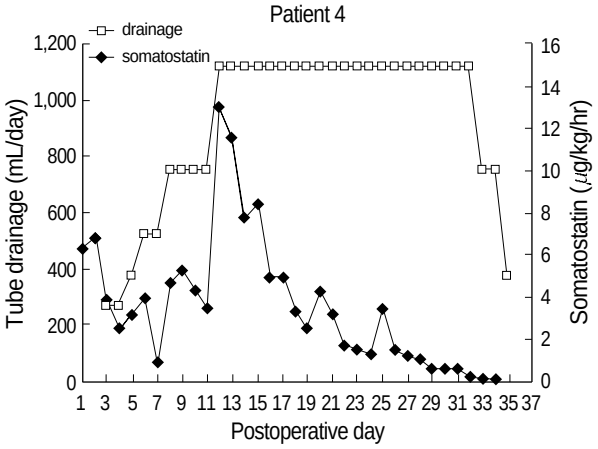

Fig. 3. Clinical course of patient number 4.

tor for the prolonged chylous drainage, but the high dose somatostatin infusion was tolerated for 21 days without any apparent side effects (Fig. 3).

Patient 9

10-day-old girl born with transposition of great arteries and ventricular septal defect underwent arterial switch operation and closure of ventricular septal defect. On postoperative day 9, she had second operation for wound debriment and repair of surgical wound. After that day, drainage from chest tube became large up to 300 mL/day, when her chylothorax was confirmed. Her chylous drainage was persistent after conservative managements, so we added infusion of somatostatin. Her chylous leakage decreased to 40 mL/day by postoperative day 32. She developed loose stool for 2 days during the infusion of somatostatin, but the diarrhea spontaneously resolved. Aside from this, there were no apparent adverse effects of the somatostatin.

DISCUSSION

Chylothorax is a rare, but potentially serious complication of pediatric cardiac operations. It was estimated to occur at an incidence of 0.25% to 0.8% following cardiovascular procedures (9, 10). The standard treatment for postoperative chylothorax includes conservative therapy with pleural space evacuation, enteric rest or fat-free nutrition, and total parenteral nutrition (11). If this is not successful, operative treatment such as pleurodesis, ligation of the thoracic duct and pleuroperitoneal shunt is indicated (12, 13). However, these surgical treatments have some limitations. Pleurodesis is a painful procedure and the long-term results can vary. Ligation of the thoracic duct may fail as a result of anatomic variations of the thoracic duct or due to a failure for identifying the chylous leakage sites (6).

There have been several anecdotal reports in the literature related to using somatostatin for treating chylothorax as a complication of thoracic procedures in adults (3-5). Somatostatin is a peptide hormone that acts as a neurohormone as well as a paracrine agent, and it is present in the central nervous system, gastrointestinal tract and pancreas (14). The exact mechanisms involved for the drying effect of somatostatin on lymphatic leakage are not wholly understood. The effectiveness of somatostatin may be due to its ability to decrease the hepatic venous pressure gradient, to decrease the intestinal absorption of fats, to decrease the triglyceride concentration in the thoracic duct and to attenuate splanchnic blood flow (15-17). In addition, it could be that the lymphatic vessels contain somatostatin receptors, like the blood vessels in the splanchnic area, and that their constriction reduces the lymph production (18, 19).

In 1998, Rimensberger et al. (20) reported the successful use of somatostatin in children to control increasing chylous drainage under conservative treatment. In addition, the authors described several pediatric cases of postoperative chylothorax that were treated with somatostatin (21-23). In our study,

3 patients underwent surgical procedure for their congenital heart disease during the neonatal period. In our cases, no serious complications associated with unabated chylous drainage were encountered, which is in contrast to the previous reports (21, 22). This is probably due to the prompt use of intravenous somatostatin after the diagnosis of chylothorax during the postoperative period.

Opinions vary in the literature regarding the appropriate dose and type of administration for somatostatin for children with postoperative chylothorax. The starting dose was 3.5 μg/kg/hr according to the case report of Rimensberger et al. (20). Buettiker et al. suggest that chyle production began cessation at a dose of 10 μg/kg/hr, but they also tried increasing the dose up to 12 μg/kg/hr for chylothorax refractory to the conventional dose (21). In our study, we increased the dosage of somatostatin up to 15 μg/kg/hr in one case without observing any serious side effects. Somatostatin is currently used for the therapy of diverse pediatric diseases such as acromegaly, intractable diarrhea and gastrointestinal bleeding (24-29). Because this therapy is still experimental, further studies that take into consideration the duration and tolerable dosages are necessary to assess the safety of its administration in children.

Superior vena cava thrombosis is also well known to be a risk factor for the failure of non-operative management of chylothorax (1). It is usually recommended that such patients be considered for earlier operative intervention when this complication is associated with chylothorax. In our case, however, the patient's poor general condition led us to attempt somatostatin trial before any invasive steps. The satisfactory outcome in this patient may be speculated as the results of somatostatin and/or the development of collateral lymphatic channels.

The side effect of somatostatin is primarily related to the suppressed actions of gastrointestinal motility and secretion, and this includes hypotension, loose stool, malabsorption, nausea, flatulence, liver dysfunction and hyperglycemia (15). In all 9 patients, no significant side effects were observed that necessitated medical intervention or discontinuation of somatostatin.

The results of our case series are suggesting the value and safety of somatostatin in pediatric patients with postoperative chylothorax. The continuous infusion of somatostatin may be of particular benefit if the patient is in a poor general condition, and additional risks may be introduced with repeated surgery. A larger prospective study needs to be undertaken to verify our investigations.

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