INTRODUCTION

Many advances in surgery for patients with congenital heart disease, including earlier intervention, have improved patient survival. However, important morbidity continues to complicate the postoperative care of these patients. Chyloous pleural effusion, or chylothorax, is an early postoperative complication. The postoperative leakage of lymphatic fluid into the pleural space may result from the surgical disruption of the thoracic duct or one of its main tributaries, or increased pressure within the intrathoracic lymph system (increased pressure in the systemic vein exceeding that in the thoracic duct). Patients usually remain asymptomatic until a large volume of chyle accumulates. Therefore, fluid accumulations may remain unrecognized for an important period of time. Loss of this fluid by therapeutic drainage can lead to nutritional depletion, fluid and electrolyte loss, hypolipemia, and lymphocytopenia of T cells, which can contribute to immunodeficiency.

Recent studies suggest an increase in the prevalence of postoperative chylothorax from the previously reported 1% or less to 2.5% to 4.7%, which has been attributed to the increased...

POSTOPERATIVE CHYLOTHORAX AFTER CARDIOTHORACIC SURGERY IN CHILDREN: EXPERIENCE AT NICVD

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Background: A definitive management strategy for postoperative chylothorax remains elusive. We reviewed our experience in the management of chylothorax in children after congenital heart surgery.

Methods: The case records of 51 patients, with a median age of 11 months (range, 4 days to 19.6 years), diagnosed to have postoperative chylothorax between 1981 and 2013 were reviewed. The responses of patients to nutritional modifications, octreotide therapy, and surgical interventions were noted.

Results: The prevalence of postoperative chylothorax, which developed at a median of 9 days after operation (range, 0 to 24 days), was 0.85% (51 of 5,995). Four patients died, and among the 47 survivors the median duration and total volume of chylous drainage was 15 days (range, 1 to 89 days) and 156 mL/kg (range, 3 to 6,476), respectively. The duration of chyle output was significantly longer after the Fontan-type procedures. Twenty-one patients were diagnosed between 1981 and 1999 and managed by nutritional modifications, 2 of whom required further surgical interventions. Of the 30 patients diagnosed between 2000 and 2013, 12 responded to nutritional modifications alone while 18 were started on octreotide therapy at a median of 19.5 days (range, 7 to 35 days) after the onset of chylothorax. Fifteen of the 18 (83%) patients responded to octreotide therapy at 15.3 ±5.5 days after starting octreotide, while 3 required further surgical interventions. None developed side effects from octreotide therapy.

Conclusions: Chylothorax increases duration of hospitalization after cardiovascular surgery in children. Early diagnosis may reduce the duration of chylothorax. Nutritional strategies remain the cornerstone for management of postoperative chylothorax. The impact of octreotide and surgical intervention is limited when reserved for patients with severe or prolonged drainage.

Key Words: chylothorax, Cardiac Surgery, Congenital heart disease.
complexity of the surgery being performed and possibly earlier reintroduction of feeding after surgery.\textsuperscript{7,8} Whereas the morbidity and mortality relating to excessive loss of chyle are well-documented,\textsuperscript{5,6,9} a definitive management strategy for postoperative chylothorax remains elusive.\textsuperscript{10} A commonly adopted management strategy is a period of conservative management with the use of medium-chain triglycerides or total parenteral nutrition, followed by surgical interventions as pleurodesis, ligation of the lymphatic ducts, and pleuropertitoneal shunting for nonresponders.\textsuperscript{1,4,7,11} Over the past few years, octreotide has increasingly been incorporated into the management algorithm of postoperative chylothorax.\textsuperscript{7,12} Published treatment strategies which aim to decrease or stop the lymphatic lymph flow are: long chain fatty acid free, median chain triglyceride (MCT) enriched diet, total parenteral nutrition (TPN), octreotide therapy, optimization of hemodynamics (recanalisation of closed central veins), or closing the leakages by supraphrenic ligation or pleurodesis.

In the present study, we reviewed our experience in the management of chylothorax that occurred after congenital heart surgery in a relatively large cohort of 51 patients.

METHODS

Fifty-one patients who developed chylothorax after surgery for their underlying congenital heart disease between 1981 and 2013 were identified from the hospital database. The diagnosis of chylothorax was made based on one or more of the following abnormalities of the milky fluid draining from the chest tube: (1) positive Sudan staining of fat globules; (2) elevated triglyceride (>1.1 mmol/L); and (3) lymphocyte predominance (>80\%).\textsuperscript{6,12,33} Their case records were reviewed with the following data collected: demographic information, cardiac diagnoses, types of surgical procedures, the onset, duration and management of chylothorax, the daily chyle output volume, laboratory investigation findings including total white cell counts and serum albumin levels, and postoperative complications and outcomes. To define the overall prevalence of chylothorax, the total number of operations performed during the same period was retrieved from the hospital database. The Institutional Review Board approved the study and waived the need for patient consent.

Institutional Management Strategy

Conservative management with nutritional modifications was the mainstay of management before 2000. The indications for octreotide therapy were persistent chyle leak for more than 2 weeks and significant drainage that exceeded 10 mL/kg/day, in which case octreotide would be started even after 1 week of conservative treatment. Weaning of octreotide would be commenced after 3 days of insignificant chyle output (<10 mL/day)\textsuperscript{12}. The patients were monitored for potential complications of octreotide therapy, including hyperglycemia or hypoglycemia, cardiopulmonary side effects, and gastrointestinal disturbance.

RESULTS

The 51 patients (26 males), with a median age of 11 months (range, 4 days to 19.6 years), were identified from a total of 5,995 congenital heart patients who had undergone operations over the 33-year period, giving an overall prevalence of 0.85%. Between 2000 and 2013, the prevalence of chylothorax was 2.27% (31 of 1,364), which was significantly greater that the 0.45% (21 of 4,631) between 1981 and 1999. The mortality was 7.8% (4 of 51). Four patients died at a median of 53 days (range, 24 to 103) after the operations, the causes of death being uncontrolled sepsis in 2, heart failure in 1, and pulmonary hypertensive crisis in 1. For the 47 survivors, the median duration of hospital stay was 32 days (range, 13 to 135).

Table I summarizes the cardiac diagnoses and
operations. The most frequent cardiac lesions were those with right ventricular outflow obstruction, including tetralogy of Fallot and pulmonary atresia with or without ventricular septal defect. The most frequently performed operations are those involving repair or reconstruction of the right ventricular outflow tract.

Chylothorax

Chylothorax developed at a median of 9 days after operation (range, 0 to 24). It was left-sided in 16, right-sided in 17, and bilateral in 18 patients (Fig I). 5 patients had an additional pericardial effusion. For the 47 survivors, the median duration for chylous drainage was 15 days (range, 1 to 89), and the median total volume of chyle output was 156 mL/kg (range, 3 to 6,476). The duration of chyle output was significantly longer after the Fontan-type procedures when compared with that after systemic-to-pulmonary arterial shunt insertion, aortic reparative surgery, and repair of left-to-right shunts. The total volume of chyle output, however, did not differ among the different types of operations. The duration and total volume of chyle output correlated with duration of hospital stay, but not with age and onset of chylothorax after operation. For the four deaths, the median duration and total volume of chylous drainage were, respectively, 11.5 days (range, 5 to 89) and 744 mL/kg (range, 119 to 6,476).

Evolution of Management Strategy

Twenty-one patients were identified between
1981 and 1999 before octreotide was available to our institution. All but one of the patients received a medium chain triglyceride diet, while the remaining patients had complete enteric rest with total parenteral nutrition. Two patients required surgical interventions to achieve complete cessation of chyle leak. One of the patients had pleural cauterization on day 33 of chyle leak with complete resolution achieved in 5 days, while the other required ligation of the right lymphatic duct on day 15 and the left thoracic duct on day 19 of chylothorax. The latter patient, however, eventually died of uncontrolled sepsis 3 weeks after complete cessation of chyle leak. Another death occurred in a patient who died of heart failure after insertion of a right modified Blalock-Taussig shunt, although his chyle leak lasted for only 7 days and resolved with medium-chain triglycerides.

Thirty patients were identified between 2000 and 2013. In 12 of the 30 patients, chylothorax resolved completely at a median of 10 days (range, 3 to 16) after institution of a medium-chain triglyceride diet, but one died of pulmonary hypertensive crisis on day 24 after correction of total anomalous pulmonary venous drainage. Four patients required surgical interventions. The latter patient, suspected to have lymphatic injury at the time of operation, underwent ligation of the thoracic duct on day 1 post operation. The persistent chyle leak, despite surgery, responded to 17 days of octreotide treatment. In 2 patients, respective ligation of the thoracic duct and resection of a large seroma that complicated a left modified Blalock-Taussig shunt insertion resulted in complete resolution of chylothorax. The remaining patient had intractable chyle leak despite surgical interventions and eventually died of uncontrolled sepsis and multiorgan failure 3 months after operation.

A total of 18 patients received octreotide treatment, which was started at a median of 19.5 days (range, 7 to 35) after the onset of chylothorax. Eighty-three per cent (15 of 18) of patients responded with complete resolution of their chylothorax and none developed side effects from octreotide therapy.

The demographic and clinical variables of these patients, those of contemporary patients (2000 to 2013 period) who did not require octreotide treatment, and those in the earlier period (1981 to 1999) are summarized in Table II. The chyle leak in patients requiring octreotide therapy was more severe than the other two cohorts as evidenced by the significantly greater total volume and longer duration of chyle leak and prevalence of hypoalbuminemia and sepsis. Nonetheless, the duration of hospital stay, the mortality, and the duration of chyle leak after the start of octreotide therapy of these patients were similar to those of the earlier 1981 to 1999 cohort.

As alluded to earlier, of the 18 patients who received octreotide therapy, 4 required surgical interventions. The median daily output, in terms of the percentage of baseline output just prior to the start of octreotide, reduced to less than 50% at about 6 days of the treatment. The total duration of chyle output in these 14 patients correlated with the interval between onset of chylothorax and time of starting octreotide. However, regardless of the timing of initiation of octreotide, the duration of chyle leak from the start of octreotide was similar and lasted for a mean (±SD) duration of 15.3 (±5.5) days.

DISCUSSION

The prevalence of chylothorax in our institution has shown a significant increase over the past decades, which concur with the findings of previous reports\(^4,7,8\). The changes in prevalence have been attributed to the increased complexity of the surgery being performed and possibly earlier reintroduction of feeding after surgery\(^7,8\). The mortality rate of our patients is similar to that reported previously, which varied from 6% to 21%\(^1,4,6,9,34\). The cause of death is likely to be multifactorial, due to unfavorable hemodynamics, sepsis, and multiorgan dysfunction.
While chylothorax may develop in virtually all types of intrathoracic procedures, several congenital heart operations have been shown to be prone to this complication\textsuperscript{1,4,7}. In particular, bidirectional cavopulmonary shunt operation, Fontan-type procedures, and right ventricular dysfunction after repair of tetralogy of Fallot, which may predispose to increased systemic venous pressure and thus risk of postoperative chylothorax\textsuperscript{4,7}. The present study also showed that the duration of chylothorax after the Fontan-type procedures was significantly longer, which corroborates the findings of Chan and colleagues\textsuperscript{7}. Closed heart procedures performed in the vicinity of the thoracic duct, such as systemic-to-pulmonary arterial shunt insertion, repair of aortic coarctation, and ligation of arterial duct, likewise predispose to the development of chylothorax as
evidenced in this and previous studies\textsuperscript{4,6}.

A higher incidence of chylothorax has been observed in heart transplantation and Fontan procedures. Conceptually, heart transplantation is associated with increased trauma to the chest cavity and Fontan or cavopulmonary anastomosis procedures will elevate superior vena cava pressure, both resulting in higher risk for chylothorax. The systemic venous hypertension can cause a backup of pressure into the thoracic duct, resulting in increased chyle loss. This loss is consistent with our observations of longer duration of chylous drainage after these procedures. Knowing that cavopulmonary anastomosis procedures have a higher risk of prolonged pleural drainage may indicate that earlier, more aggressive therapy is indicated for these patients.

Although chest tube drainage and nutritional support, albeit non-standardized in terms of the type of nutritional replacement\textsuperscript{8}, is probably the general consensus for the initial management of postoperative chylothorax in children, the next steps in the management algorithm for nonresponders remain elusive. Conservative management for several weeks appears justified as resolution of chylothorax has been reported in up to 77\% of patients after giving either medium chain triglycerides or total parenteral nutrition for up to 45 days with an average of about 12 days\textsuperscript{1,8,33}. Previous studies suggested that persistence of chyle output for more than 3 weeks\textsuperscript{1} and lesions associated with elevated systemic venous pressure\textsuperscript{5,7} are risk factors for failure of conservative management. While 90\% (19 of 21) of our 1981 to 1999 cohort of patients survived and responded to conservative management, the risk of prolonged chylothorax, the need for prolonged hospital stay, and the need for total parenteral nutrition in some of the patients have to be taken into account in the evaluation of the cost-effectiveness of such an approach. The duration of conservative management varies among institutions, and surgical intervention has been recommended for drainage that lasts for more than 1 to 4 weeks\textsuperscript{11,33,36}. Nonetheless, surgical interventions are invasive and not always effective\textsuperscript{2,32,33}, which may be due to diffuse chyle leak after extensive surgical dissection or anatomic variations of the thoracic duct. Indeed, one of our patients required further octreotide therapy despite ligation of the thoracic duct.

Our initial success of the use of octreotide\textsuperscript{12} has prompted a change in the management strategy of postoperative chylothorax in our institution since 2000. Indeed, such change has been included in a recently proposed algorithm (Fig II), in which a trial of octreotide therapy is suggested prior to surgical interventions for prolonged chylous drainage not responding to conservative management\textsuperscript{7}. Octreotide may reduce lymph fluid excretion directly by acting on the vascular somatostatin receptors\textsuperscript{37} and indirectly to decrease lymph flow by reducing splanchnic, hepatic, and portal blood flow and inhibiting intestinal motility\textsuperscript{38}. A recent systematic review revealed marked variations of the treatment regimens\textsuperscript{13}, with the octreotide given either subcutaneously at a median of 40 g/kg/day (range, 2 to 68) or as continuous intravenous infusion at a median of 2.8 g/kg/hour (range, 0.3 to 10).

Adverse effects of octreotide in children are infrequent and usually mild.\textsuperscript{13} Indeed, none of our patients developed any significant side effects while on octreotide, although transient glucose disturbance\textsuperscript{28} and abdominal distension\textsuperscript{25} have been reported. Whether octreotide contributes to a higher prevalence of hypoalbuminemia and sepsis (Table II) is uncertain. While severe chyle leak is probably an important predisposing risk factor, the gastrointestinal side effects and the regulatory, mainly inhibitory role in the immune response of somatostatin are well-documented.\textsuperscript{39} Mohseni-Bod and colleagues\textsuperscript{15} reported a case of necrotizing enterocolitis in a term neonate after repair of aortic coarctation while on octreotide for postoperative chylothorax, although the potential contribution of the complicated preoperative and postoperative course could not completely be excluded.
FIGURE II: RECOMMENDATION FOR THE MANAGEMENT OF CHYLOTHORAX. POSSIBLY TREATABLE CAUSES FOR CHYLOTHORAX SHOULD BE Ruled OUT OR TREATED BEFORE SYMPTOMATIC THERAPY IS STARTED. BEFORE MORE INVASIVE AND LONG-LASTING THERAPIES ARE STARTED, ONE ATTEMPT TO TREAT CHYLOTHORAX WITH MCT-DIET SHOULD BE DONE (EFFICACY TO TREAT CHYLOTHORAX IS 70% WITHIN ACCEPTABLE TREATMENT PERIOD). ABBR.: MCT = FATTY ACID-FREE MCT-ENRICHED DIET; TPN = TOTAL PARENTERAL NUTRITION (40)
The limitations inherent to the retrospective nature of the present study are inevitable. Furthermore, comparisons of patient cohorts in the different eras are likely to be confounded by the differences in the complexity of operations, perioperative management, treatment regimens, and severity of chylothorax. Hence, our data as shown in Table II could perhaps only reflect the more severe chyle loss in patients requiring octreotide. It is encouraging though that these patients, albeit having more severe chyle leak, had similar mortality and duration of hospitalization as those of the 1981 to 1999 cohort. Given the small number of patients, we were unable to identify predictors of failure of response to octreotide.

In conclusion, Chylothorax after repair of congenital heart defects is an infrequent complication, but one that can cause significant morbidity. One of the challenges of managing this complication, especially in neonates and small infants, is to maintain fluid, electrolyte, and nutritional homeostasis while trying to eliminate the lymphatic leak using therapies that are often lengthy. A definitive treatment strategy for postoperative chylothorax is currently elusive. The therapeutic modalities include drainage of the pleural space, diets low in long chain triglycerides and enriched with medium chain triglycerides, or complete abstinence from enteral nutrition opting for parenteral calorie delivery. Surgical ligation of the thoracic duct, and recently octreotide administration, have been used when dietary restrictions fail. The principle of early diagnosis and expeditious resolution of chylothorax, should be followed.

REFERENCES


