Successful Use of Indwelling Tunneled Catheters for the Management of Effusions in Children With Advanced Cancer

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Background. Malignant pleural effusion (MPE) and ascites (MA) negatively impact quality of life of palliative patients. Treatment options are limited. This study’s purpose is to examine the experience with indwelling tunneled catheters (ITCs) for management of MPE/MA in children with advanced cancer. Methods. Children with MPE/MA who underwent ITC insertion (2007–2012) were retrospectively reviewed. Clinical, procedural, complication and outcome details were analyzed. Results. PleurX® ITCs (n = 12) were inserted in eight patients (5–18 years) with sarcoma (11 MPE, 1 MA), achieving symptom relief and facilitating discharge home post ITC (median 2 days). Median survival following ITC was 51 days. There were two major complications: pain (n = 1), late site infection (n = 1), and five minor complications. Drainage ceased in four patients (pleurodesis/tumor progression). At time of death, six ITCs (five patients) were still in situ. Conclusions. ITC appears to be a safe, effective treatment for MPE/MA in advanced pediatric cancer, achieving symptomatic relief and discharge home. Pediatr Blood Cancer 2014;61:1007–1012. © 2013 Wiley Periodicals, Inc.

INTRODUCTION

Over the last few decades, the cure rate for pediatric patients with cancer has improved considerably, however 20% of pediatric cancer patients still die due to disease or treatment [1]. In the setting of patients receiving palliative care, quality of life optimization is particularly important and the ability to be discharged home is an important goal [2].

Malignant effusions (ME), which includes malignant pleural effusions (MPE) and malignant ascites (MA), can occur at initial diagnosis, during the treatment period and/or when care is focused solely on palliation. Non-resolving or recurrent malignant pleural effusions (MPEs) are associated with a median survival of 3–12 months in adults [3]. Traditional treatment options include repeated needle thoracocentesis, therapeutic pleurodesis and pleuropertitoneal shunt insertion [4]. Thoracentesis is painful, often has to be repeated due to effusion reaccumulation and tends to become more difficult over time due to increasing fluid loculation [4,5]. Therapeutic pleurodesis is associated with prolonged hospitalization, significant pain [4,6] and the formation of loculated effusions [7,8]. Pleuropertitoneal shunt insertion is often complicated by infection and blockage [9].

As a result of these limitations of traditional treatments, there is growing interest in small-bore, cuffed drainage tubes that can be inserted and then managed by the patients and their families on an outpatient basis. In adults, the use of indwelling tunneled catheters (ITCs) has been shown to be effective with a low complication rate in treating malignant effusions [10,11]. While there is experience with ITCs in adults, to our knowledge, there are no published reports in children.

The purpose of the study was to examine if the use of ITC was a safe and an effective outpatient treatment option in the management of effusions in pediatric oncology patients.

METHODS

This retrospective study was approved by the Research Ethics Board at The Hospital for Sick Children (SickKids), Toronto, Canada. The need for individual informed consent was waived due to the minimal risk to study subjects and the potential negative impact on the family related to patient mortality. Patients were identified using the interventional radiology database (Esh-IGT; www.esh.ca). Chart review was performed on all pediatric oncology patients who underwent insertion of a cuffed 15.5 French PleurX® ITC (CareFusion, McGraw Park, IL) to manage ME. Information collected included patient demographics (gender, age) oncologic diagnosis, relapse status, time from initial diagnosis, duration of effusion and previous treatment methods. Technical details, peri-procedural bloodwork, date of drain insertion/removal, complications, hospital discharge information, and date of death were also documented. Complications were categorized as minor and major according to the Society of Interventional Radiology’s (SIR) classification system [12].

Definitions

No distinction was made between paramalignant and malignant effusions [13] as it would not affect clinical management or outcome. An effusion was considered to be symptomatic if respiratory symptoms were documented within 3 days prior to ITC insertion. Respiratory symptoms were defined as increased...
work of breathing, increased shortness of breath, respiratory distress, cough or thoracic pain. Respiratory symptom control was determined within 3 days after catheter insertion and was defined as complete resolution if symptoms were absent and partial resolution if symptoms were still present but improved. An effusion was deemed to be recurrent if it resolved after initial ITC drainage but subsequently re-accumulated. Technical success was defined as the ability to place a catheter into the targeted effusion. Early complications were defined as those that occurred within 30 days of ITC placement. A complication was defined as major if it required hospital treatment for greater than 48 hours [12]. Cessation of drainage secondary to pleurodesis or tumor progression around the ITC was considered an expected outcome, not a complication.

Insertion and Removal Technique

Informed consent was obtained by the interventional radiologist. A complete blood count, international normalized ratio (INR) and partial thromboplastin time (PTT) were performed. Coagulopathy or thrombocytopenia was corrected at the discretion of the interventional radiologist and oncologist.

Insertion of the PleurX® catheter was performed under sterile technique, using local or general anesthesia depending on the patient’s age and clinical condition. Prophylactic antibiotics were not administered. Ultrasound was used to identify the entry site—an appropriate access route to the collection and point for insertion of a 16 or 18 gauge needle. For MPEs the needle was guided along the upper margin of a rib, avoiding the intercostal blood vessels. For MA a site was chosen over a deep pocket of fluid, avoiding bowel and any abdominal wall blood vessels. A fluid sample was obtained and sent for laboratory analysis. An 0.035 in. wire was inserted through the entry needle and the needle removed. Local anesthetic was injected in the subcutaneous tissue tract. A second incision was created in the adjacent skin approximately 5–8 cm distant to create the exit site. The catheter was tunneled from the exit site back to the entry site using the supplied device. The intended internal portion was cut to an appropriate length in smaller children. The entry site tract was dilated over the 0.035 in. guide wire, and a 16 French peel-away sheath placed. For most patients, the catheter was then inserted through the peel-away sheath after removal of the wire. If the catheter needed to be oriented in a specific direction or location, it was inserted over a stiff 0.035 in. Amplatz wire (Cook, Bloomington, Indiana). The outer plastic sheath of an angiocatheter was used to protect the internal valve from damage during retrograde passage of the wire. Dissolvable sutures were used to close both entry and exit sites. Dressings were applied. Fluid was evacuated using either a vacuum jar (Denver Biomedical, Colorado) or a Sahara collection device (Teleflex Medical, Research Triangle Park, Pennsylvania) attached to wall suction. Small effusions (<20 ml/kg) were drained completely. Larger effusions were drained intermittently to avoid pulmonary edema or third-spacing effects.

After discharge home the catheters and drainages were managed by the parents and caregivers. The external component of the ITC was covered with a simple dressing, and was discreet under clothing. The patients were mobile and free to lead as normal a life style as their disease permitted, including showering. The dressings were changed after each drainage session or if they became wet. Drainage usually took about 15–30 minutes to perform during which time the plastic vacuum bottle was attached. All necessary supplies for drainage and dressings come in a prepared kit.

Catheters were removed using sterile technique. After administration of local anesthetic, blunt dissection was used to free the subcutaneous cuff and the catheter was removed. Vaseline impregnated gauze was applied to the exit site and covered by an occlusive dressing.

Statistics

Descriptive data analysis was undertaken.

RESULTS

Between July 2007 and January 2012, eight patients (five female, three male) underwent insertion of 12 ITCs (PleurX® catheters) (Fig. 1). The median age of patients at time of first insertion was 16 years (range 5–18). One patient underwent primary insertion of bilateral ITCs. Three patients required placement of a second ipsilateral ITC catheter at 14, 21, and 55 days following their primary insertion, due to local pleurodesis around their initial ITC (n = 1), an unexpected temporary tumor response followed by relapse with recurrent effusion (n = 1) and development of a separate locule without removing the original ITC (n = 1). Tables I and II summarize the results.

Seven patients underwent a variety of conventional treatments for ME prior to ITC insertion (thoracentesis (n = 5), paracentesis (n = 1), temporary non tunneled pleural drains (n = 4)). The median time from diagnosis of effusion to first ITC placement was 74 days (range 3–133 days). At the time of ITC placement, nine were inpatients and three were outpatients. Three patients required administration of blood products (red blood cells (n = 2); platelets (n = 1)) prior to undergoing insertion. None were neutropenic at

Fig. 1. Chest X-ray of an 18-year-old male with Ewing sarcoma, showing a right sided mediastinal mass, a portocath in situ with its catheter in the right internal jugular vein and a large right pleural effusion occupying approximately the lower 2/3 of the right hemithorax.
<table>
<thead>
<tr>
<th>Patient</th>
<th>ITC</th>
<th>Gender/age</th>
<th>Oncologic diagnosis</th>
<th>Relapse</th>
<th>Location ME</th>
<th>Recurrent ME</th>
<th>Symptomatic ME</th>
<th>Prior intervention</th>
<th>Complications</th>
<th>SIR grade</th>
<th>Reason for removal</th>
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<tr>
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<td>Yes</td>
<td>Temporary drain × 1</td>
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<td>NA</td>
<td>Pleurodesis</td>
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<td>Yes</td>
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<td>Thoracentesis × 3, ITC × 1</td>
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<td>No</td>
<td>Temporary drain × 1</td>
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<td>Major D</td>
<td>Treatment response</td>
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time of ITC insertion. Eight patients had respiratory symptoms at the time of ITC placement and four did not. ITC placement in the four patients without respiratory symptoms were performed for the following reasons: in two patients because of ongoing large volume outputs which were being controlled though temporary percutaneous chest drains, in one patient with an existing ITC who had developed partial pleurodesis and a separate large collection, prompting placement of a second ipsilateral ITC, and lastly in one patient with a massive pleural effusion causing superior vena cava compression symptoms and abdominal symptoms from diaphragmatic inversion, but without respiratory symptoms.

Seven catheters were placed under anesthesiologist administered sedation or general anesthesia and five were placed using local anesthesia only. Three insertions were labeled as technically difficult by the operator due to the presence of extensive pleural tumor (n = 1) and prominent venous collaterals in the chest wall (two ITCs in one patient). All insertions were technically successful.

At the time of ITC placement, the fluid obtained was described as sanguineous (n = 4), serosanguineous (n = 5) or serous (n = 2), and not specified on one. The volume drained at ITC insertion ranged from 120 to 1,610 ml (median 700 ml), achieving complete evacuation of fluid in 1, partial in 9 and not documented in 2 (Fig. 2). Cytologic analysis was undertaken in six cases (five MPE, one MA), one was positive and five were negative for malignant cells.

**Post-Procedure Outcomes**

In those patients with respiratory symptoms at the time of insertion (n = 8), improvement was complete (n = 3) and partial (n = 5). Minimal transient leakage (<24 hours) of pleural fluid occurred at the insertion site in two cases. Median time to discharge home after ITC placement was 2 days (range 0–8 days). Post procedure pain was noted with three catheters, the symptoms of which were completely controlled with opioids. However one was hospitalized was for >48 hours for his ITC associated pain. Other reasons for prolonged hospitalization were non-ITC related, mainly for other aspects of the management of their malignancy.

Multidisciplinary outpatient care of the ITCs was provided by a combination of the family, community care and hospital services. Six ITCs (n = 5 patients) were in situ at time of the patient’s death (median 32 days following insertion). Six catheters were removed 14–41 days (median 22 days) after insertion. Two of the six catheters were replaced as previously described (local pleurodesis in 1, temporary response with subsequent recurrence in 1). The remaining four catheters were removed when drainage stopped due to tumor progression (n = 2), treatment response (n = 1) and a combination of both tumor progression and pleurodesis (n = 1).

There were no immediate procedure related complications. ITC associated complications are summarized in Table I. A pneumothorax (n = 1) developed the day after insertion, which resolved spontaneously within 24 hours without further intervention. The
pneumothorax was not evident at the time of the drainage procedure.

According to the SIR complication classification system, there were two major complications of pain (n = 1) and infection (n = 1). The first patient’s pain was treated successfully but he was hospitalized for >48 hours. The second was a late site infection, which developed in a patient 10 weeks after removal of the catheter. The clinical appearance of the dark eschar at the catheter removal site and a positive growth of *Pseudomonas aeruginosa* in blood cultures taken from her portacath, indicated a pseudomonas site infection. The infection was successfully treated with admission, frequent dressing changes and intravenous antibiotics, resulting in the classification as a major complication. There were five minor complications (transient self limiting pneumothorax (n = 1), transient leakage at site (n = 2), pain (n = 2)). There were no deaths related to ITC insertion.

**Survival**

At the time of analysis, one patient was alive. The remaining seven patients died outside of hospital. The median survival time from ME diagnosis was 101 days (range 54–201 days). The median survival time following all ITC insertions was 51 days (range 14–90 days), and 41 days (range 14–57 days) following a patient’s last ITC insertion (Table II). A formal patient/family satisfaction or quality of life survey was not performed. However, all patients were able to be discharged and their ITC drainage was managed without difficulty by parents and caregivers. Informal non-structured feedback from families and health care staff was very positive.

**DISCUSSION**

This retrospective study described the placement of ITCs for the management of ME in pediatric patients with advanced cancer. The development of ME has a detrimental impact on quality of life [14]. Life expectancy of adult patients with ME is limited [11,15,16]. The major goal of ITC insertion in these children was to enable treatment of ME as an outpatient while decreasing their respiratory difficulty by parents and caregivers. Informal non-structured feedback from families and health care staff was very positive.

All children in this study with respiratory symptoms demonstrated improvement in their symptoms post-ITC insertion. This result parallels the 91–95.4% response rate reported in previous studies [17,18]. All patients in this study were discharged home for outpatient treatment of ME. In comparison, only 70% of pediatric cancer patients treated with pleurodesis by Hoffer et al. [19] were able to return home.

The overall complication rate (16.5% major and 41.5% minor), in this study is high when compared to that reported in adults, which range from 4.8% to 16% [11,15,17]. Most of the complications were minor, and some were expected (e.g., transient pain). We categorized two complications as major. One was the unusual development of a late site infection related to *Pseudomonas aeruginosa* septicemia 10 weeks following an ITC removal, described above. The other was a patient hospitalized >48 hours with pain. It was unclear from the retrospective review of the patient’s chart if the focal ITC site pain was the main reason for prolonged hospitalization in the second patient. However, we erred on the side of overcall and categorized this latter issue as a major complication.

The cause of pneumothorax identified incidentally on a chest X-ray in one patient is unclear. Air can enter the pleural space at the time of ITC insertion. However it was not evident on imaging at completion of the ITC insertion. Alternatively, it may have been patient or disease related or secondary to an improper connection of the catheter drainage system allowing ingress of air. The asymptomatic pneumothorax resolved with continued drainage without further intervention.

Pleurodesis is an expected (and even desirable) outcome of ITC drainage that occurs in approximately 50% of adult patients [17]. In this series drainage ceased in four ITCs, due to pleurodesis (n = 1), tumor progression (n = 2) and both (n = 1) and was not considered a complication. Other reported complications including hemotherax, empyema, tube dislodgment, and tumor dissemination were not found in this study [10,11,17,18,20].

In contrast to adults where carcinomatous malignancies such as breast, lung, and gynecologic are the most common cause of ME [3,4,16,17,21–23], all of our patients had sarcomatous tumors. This finding reflects the inherent differences in cancer types between adult and pediatric patients. In addition, it underscores the poor prognosis of the pediatric patients in our study who received an ITC—-the median survival time was 101 days from diagnosis of ME, while in adult studies reported survival times were 3–12 months [3]. The fact that two patients underwent catheter removal for an unexpected treatment response of their malignancy (Table I) illustrates the difficulty in predicting outcomes in advanced care.

The size of the catheter (15.5 French) may be an issue in very small patients. However, the catheter is made of silicone making it soft despite its large diameter. The development of a similar, smaller bore catheter may be of benefit for the small patient.

Placement of an ITC might initially be considered unsuitable for pediatric patients with ME given their short survival times, young age and small size, combined with the large diameter of the ITC catheter. However this report describes the successful use and excellent tolerance of ITC in this pediatric patient population, and suggest clinicians should not be deterred from considering their use as a valuable option for pediatric patients with ME. With respect to costs, outpatient management costs of a ME are far less than managing a patient as an inpatient or with repeated ME aspirations. The approximate estimate for the insertion kit is in the order of $425 Canadian dollars, and for subsequent management in the home care setting, the full drainage kit is in the order of $75 Canadian dollars (includes the 500 or 1,000 cc plastic vacuum bottle, drainage line, valve cap, and materials for a dressing change).

Limitations of this study include retrospective data acquisition and the small number of subjects. Prospective studies to better determine patient outcomes, a formal quality of life assessment, cost analysis and patient or family satisfaction will help further define the role of ITC in pediatric malignancy. It is also not known whether ITCs may be useful in the non-palliative pediatric cancer setting.

In conclusion, this study represents the first reported use of ITCs in pediatric oncology patients. ITC resulted in symptomatic relief and allowed all patients to be discharged home with relatively minor improvement.
complications. These findings support the use of ITCs as an effective and safe palliative treatment.

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REFERENCES