Totally Implantable Venous Access Devices in Children Requiring Long-Term Chemotherapy: Analysis of Outcome in 122 Children from a Single Institution.

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Abstract Children with malignancy require venous access that is reliable, safe and compliant on a long-term basis. There is little data available on utilization of totally implantable venous access devices (TIVAD) for long term chemotherapy in children in an Indian setting [1]. We report our long-term follow-up results of utilization of totally implantable venous access devices for long-term chemotherapy in children. This was a retrospective analysis of 122 children requiring long-term chemotherapy done between January 2008 and December 2013. Data collected included primary disease process, type of port, site of insertion, intraoperative events, early and late postoperative complications, and issues with utilization, maintenance and removal. 127 ports were placed in 122 children. The follow up ranged from 16 to 50 months. Internal jugular vein was accessed in 96.8 % of cases (123/127). Majority of children (61 %) had hematological malignancy. Early complications occurred in 5 children. Late complications occurred in 18 children which included port pocket infection in 3, port site skin issues in 5, catheter related issues in 3, venous thrombosis in 2 and catheter related bacteremia in 5 children respectively. Only 10 children have been lost to follow-up either due to death or discontinuation of treatment and rest are on follow up. Totally implantable venous access devices usage is safe and reliable for access needs in children for long-term chemotherapy. Their low complication and low cost maintenance should increase their utilization in children requiring long-term chemotherapy. Chemoport placement in

children with hematological malignancy can be carried out safely without much impact on complication rates. Though management and compliance of children with malignancy has improved; critical analysis and standardization of port system care through prospective trials are necessary to reduce the morbidity and for cost analysis in these children.

Keywords Chemoport · Paediatric malignancy · Long-term chemotherapy

Introduction

Many children with cancer require long-term central venous access for the safe delivery of chemotherapeutic agents, transfusion of blood and blood products, and for laboratory tests [2]. There are both tunneled catheters and chemoports available for long-term venous access. The choice of the devices is made by the treating physician and the available local resources.

Subcutaneous venous ports are preferred to external catheters, particularly in children who require intermittent long-term infusion therapies, due to low infection rates, high patient comfort, the absence of dressing and external catheters [3].

The purpose of this study was to assess the outcome of chemoport in children requiring long-term chemotherapy in an Indian setting.

Material and Methods

The records of children who were referred to us for placement of chemoport were reviewed. There were 122 children referred to us between 2008 and 2013. These children were identified to require chemotherapy for long-term basis. Most

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had hematological malignancies (61 %). The distribution of the patients according to their demographic profile and primary disease is shown in Table 1. Single lumen ports were used in all patients. All were placed on the anterior chest wall. Platelet counts below 60,000, absolute neutrophil count under 500/mm³ and INR above 1.5 were considered contraindications. Ports produced by 3 different manufacturers were placed with predominant usage of Access devices (98 %) (Access devices, Bard devices, Vygon). Data was collected for primary disease process, type of catheter, technique, site of venous access, intraoperative events, early and late postoperative complications, and issues with utilization and removal.

Technique

All of the procedures were performed in operation theatre under general anesthesia with C-ARM confirmation for the distal tip. Antibiotic prophylaxis was given at induction.

Right internal jugular vein access (IJV) was initially preferred in all patients (Table 2). If the right internal jugular vein was occluded, then the left internal jugular vein was accessed. In cases of bilateral occlusion, subclavian / femoral veins were used. Open-ended catheters of size 5.5 F to 7 F with detachable port were used.

Percutaneous Seldinger's technique was used in 123/127 procedures. Right internal jugular vein was used in 121 children. Open cut down technique was used in 4 children. Open access was used only during our early experience and in children when percutaneous techniques failed.

Table 1 Patient disease profile

Malignancy	No.
ALL	56
Neuroblastoma	13
Wilms	12
AML	11
Lymphoma	7
Medulloblastoma	3
Ependymoma	2
Clear cell carcinoma, kidney	2
Rhabdoid tumor kidney	2
PNET	2
Retinoblastoma	2
RMS	2
SCT	2
Hepatoblastoma	2
GCT	2
Histiocytosis	1
Angiomyolipoma kidney	1

Table 2 Access characteristics

Site of venous access	Number
Internal jugular vein	123(96.85 %)
Right IJV	121(95.25 %)
Left IJV	2(1.57 %)
Subclavian	2(1.57 %)
Femoral	2(1.57 %)

After needle puncture a guide wire was passed into the vein. Peel away sheath was passed over the guide wire. Catheter was passed through the sheath and the position of the tip confirmed by C-ARM. The free end of the catheter was threaded to the tunneller. Incision of 2–3 cm was placed on the anterior chest wall, inframammary region. The pocket was deepened to accommodate the port. Once the pocket was created, the catheter was tunneled over the anterior chest wall in subcutaneous plane using the tunneller to the port site. The port was then connected to the catheter. The port was aspirated to confirm the free flow of blood and flushed. This was followed by placement of the port in the pocket created. The port base was fixed to the chest wall. Using a Huber needle, the port was accessed for functioning with easy aspiration of blood and the reservoir was flushed with 100 U/ml of heparin solution while carefully observing for any leakage at the connection site. The incision was closed in layers with resorbable 4–0 vicryl interrupted, subcutaneously, and the skin was closed with a running subcuticular stitch. The venous puncture site incision was closed in the same manner. Transparent occlusive dressing was placed on the incision site. Children received intravenous antibiotic for 24–48 h based on oncologists recommendation and all the patients were called back after 1-week for routine follow-up. The port was accessed for chemotherapy from the 3rd post insertion day unless dictated by local condition. Data from the follow-up of these patients were entered into the form.

Maintenance was done at the regional cancer center by nursing staff trained in care of venous access. Ports were flushed with heparin solution of concentration 100 units/ml each time after access or every 4 weeks during maintenance period.

Complications

Were evaluated as early and late complications.

Early complications were defined occurring up-to 3 weeks post implantation and late complications thereafter. The occurrence of port site infection, cutaneous infection, thrombosis, bacteremia, catheter malfunction or breakage and time to removal were documented.

Results

A total of 127 chemoports were placed in 122 children over 4-year period. There were no port related deaths in this series. There was one procedure related complication seen. This child developed pneumo-hemothorax requiring thoracotomy. This was managed conservatively with no obvious vascular injury. Complications are summarized in Table 3. Early complications occurred in five children (3.93 %). This included port site hematoma in one patient (0.79 %), catheter migration in two patients (1.58 %), early blood stream infection (BSI) in one patient and catheter dysfunction in one patient (0.79 %).

Port site hematoma was managed conservatively and chemotherapy was delayed till resolution of hematoma.

Catheter tip reposition was done in 2(1.58 %) patients. This was due to catheter tip migration. In one the tip was seen in distal internal jugular vein and in the second child the tip was seen lying in brachiocephalic vein. This was identified on negative aspiration and confirmed with X-ray. Catheter reposition was done without removal of the port.

Catheter dysfunction was seen in one child. This resolved with heparin flushing after confirming there was no thrombus formation.

Early blood stream infection (BSI) occurred was managed conservatively without removal of port.

Late complications were seen in 18 children (14.17 %).

Late Infection related complications occurred in 8 children. Five had CBSI (catheter related blood stream infection) and three had port related infection.

5 children developed late BSI 30 days after port insertion. This was seen after a mean duration of 174 days. 3 patients had hematological malignancies and 2 had solid tumors. Organisms causing late BSI were both Gram positive and Gram negative, including; Klebsiella (1), Enterobacter (1), Methicillin sensitive staphylococcus aureus (2), Methicillin resistant staphylococcus aureus (1).

Of 5 late BSI, 2 required removal of ports. All patients recovered promptly after removal of the ports.

Port pocket infection (Fig. 1) occurred in 3 patients (2.3 %). Of the three port pocket infection there was a predominance of Gram positive organisms; staphylococcus aureus (3), co-infection with proteus mirabilis (1). 2 patients had hematologic malignancies and 1 had solid tumor. One was managed conservatively and two required removal of the port.

Port reposition was done in 5 patients (3.9 %). This was needed due to thinning of skin over the port (Fig. 2). This was probably due to drug extravasation. This was done without removal of the port.

There were 2(1.5 %) thrombosis events related to the catheter. One occurred in the internal jugular vein and another in the inferior vena cava (IVC). The child with inferior vena cava (IVC) thrombus had ipsilateral limb swelling. This required removal of the port.

There were 3 catheter related issues (2.3 %).

In the first child the catheter had detached from the port. This child presented with bulge in the chest wall following infusion. Chest x-ray with contrast confirmed the same. The catheter was lying in the chest wall. This was reconnected to the port.

In the second child there was breakage with migration of catheter into the pulmonary vein (Fig. 3). This child required retrieval by endovascular route using snare. She underwent second chemoport placement subsequently.

In the third child the catheter was incorporated into the wall of internal jugular vein vein and the catheter could not be removed. This child had come for port removal following completion of chemotherapy. This required vascular surgery

Table 3 Results

a	
Early complications	4(122)
Hematoma	1 (0.79 %)
Catheter tip migration	2 (1.58 %)
Catheter dysfunction	1 (0.79 %)
Early blood stream infection(BSI)	1 (0.79 %)
Total	5 (3.93 %)
b	
Late complications	
Port pocket infection	3 (2.3 %)
CBSI	5 (3.9 %)
Port reposition	5 (3.9 %)
Thrombosis	2 (1.5 %)
Catheter related events	3 (2.3 %)
A. Disconnection	A. 1 (0.79 %)
B. Fracture with migration	B. 1 (0.79 %)
C. Incorporation into vein wall	C. 1 (0.79 %)
Total	18 (14.17 %)

Fig. 1 Port site infection

Fig. 2 Thinning of the skin over the port

with excision of the involved vein segment and removal of catheter.

15 (11.81 %) of the 127 ports were removed due to end of treatment, 10(7.9 %) patients were lost to follow-up.

Discussion

Subcutaneous venous access devices are gaining major importance in the care of children with cancer by providing reliable vascular access. They have added advantages over tunneled catheters in having low infection rates, long life, and patient comfort [1–3].

In our retrospective series, the most common site of venous access was the right internal jugular vein. This was done through percutaneous technique. At the beginning of our experience, the surgical cut down technique of internal jugular vein was used in initial few cases and subsequently percutaneous technique was adopted.

The site of venous access has been in debate with few preferring subclavian and others preferring internal jugular vein.

A recent prospective randomized trial noted that insertion modality and site had no impact on the early or late complications [4].

We have not used ultrasound in localizing the vein. This has definitely shown to reduce the complication rate by reducing the number of inserts, operative time and overall outcome [5].

We had one access related complication in form of suspected vascular puncture. This child developed hemo-pneumothorax requiring thoracotomy. There was no obvious vascular injury, as the bleeding had stopped. Nothing further was done and an ICD was left insitu.

In our analysis, the overall complication rate was comparable to that reported by several studies [12–14].

Infection is the most common complication of venous access catheters and the leading reason for their removal. According to the literature, the rate of catheter-related infections in long-term central venous access catheters ranges from 0.6 to 27 % depending on the catheter type and location and the patient's constitution [6]. Immunosuppressed patients with port systems were found to have a median of 0.2 infections per 1000 catheter-days (range 0–2.7 per 1000 catheter-days) [7].

Device-related morbidity from the literature is difficult to compare because of varying definitions and dissimilar patient populations.

However, in a randomized study of infectious morbidity in patients with solid tumors, chemoports were shown to be associated with fewer infections than other catheters [8]. Compared with catheters, chemoports are irrigated less frequently,

Fig. 3 Plain X-ray chest showing the migrated catheter

require no home care, and are less prone to environmental or cutaneous contamination when not accessed. All these factors may contribute to the reduced incidence of infections associated with TIAVD.

Majority of children undergoing chemoport placement in our series were children with hematological malignancy. The main concern has been these children being more prone for catheter related infection and port site hematoma. This is related to the degree of neutropenia and thrombocytopenia seen in these children prior to induction chemotherapy. Many investigators have evaluated the utility of TIVAD in children with hematological malignancy [9–11]. In our series 61 % of our cases had hematological malignancy. There was no significant increase in the incidence of infection compared to solid malignancy. The complication of port site infection and hematoma were noted in children with hematological malignancy (2 / 77 v/s 1 / 49). Similar findings were reported by in these series [9–11].

The infection of the port pocket was the most frequent late complications noted in our series 3 (2.3 %). Similarly, in the series described by Koch et al., this complication occurred in around 5 % of all cases [12].

The port infection rate in the related literature ranges from 2.6 to 9 % [12]. There was one procedure-related early (within the first 3 weeks) infections in our study group. Port pocket infection occurred in 3 patients (2.3 %). In one child this was managed conservatively with local and systemic antibiotics. In the other two there was necrosis of the skin overlying port requiring port removal. Two of those patients underwent a second port placement. The port was positioned in the infraclavicular region. Again right internal jugular vein was accessed in both these children.

Thinning of skin over the port was one of most common complication encountered in our series. This occurred in 5 children. This was related probably to drug extravasation. This was managed by repositioning of the port without removal.

Another major long-term problem of catheter use in cancer patients is thromboembolic complications. The incidence of catheter-related symptomatic venous thrombosis has been very low in our study (1.5 %).

Few prospective studies [13, 14] of catheter-associated thrombosis in patients with solid tumors and hematological malignancies report rates of thromboembolic events between 37 and 66 %. The maintenance used in our series was the use of heparin solution (100 units/ml). Ports were flushed with 10 ml heparinized solution and locked with 4–8 ml of heparinized saline (100 IU/ml) each time after access and every 4 weeks interval during maintenance period. There have been studies regarding the use of low molecular weight heparin or warfarin to prevent thrombotic events [15].

All these recent studies fail to support the routine use of prophylactic anticoagulation in cancer patients with venous catheters to prevent catheter-induced thrombosis. Institutions

should assess their rates of catheter-associated thrombosis and the indication for prophylaxis should be individualized for each patient accordingly.

Catheter embolization is a well-recognized complication and does not appear to be related to any particular port system. In the present study, 1 (0.78 %) of the 127 port insertions resulted in embolization of the catheter to the pulmonary artery (Fig. 3). Although comparisons between patient groups are difficult, the 0.78 % incidence of catheter embolization seen in our study is consistent with the fracture and embolization rate of 0.1 to 2.1 % reported in other series [16, 17]. Similar to patients described in other studies, our patient was asymptomatic after catheter fracture, and embolization. This was discovered only after infusion of the port resulting in pain and resistance to infusion. This led to chest radiographs that identified the location of the embolized catheter. This was successfully removed by intervention cardiologist [18].

Despite embolization frequently being asymptomatic, catheter fragments have been associated with a number of complications such as arrhythmias, pulmonary embolism, thrombosis, sepsis, and cardiac perforation [19, 20]. Given the potential for such complications, patients should be referred to interventional cardiology or radiology, and the embolized catheters retrieved by using interventional endovascular techniques as was done in our study [18].

As our experience in insertion, use, and care of these systems has increased we have encountered fewer problems. Although the initial cost of a tunnelled line is less than that of an implanted system, the higher maintenance costs of the tunnelled line make it equally expensive [2].

The main benefits of implantable systems compared with long tunnelled lines are their low infection rate and the minimal care that is required. This also takes away the requirement of daily flushing as in long tunnelled catheters. This is important where parents or caregivers are not able to understand or provide the necessary daily care as in tunnelled catheters. Children can go about their routine daily activities with no interference as unlike in tunnelled catheters. There is also risk of accidental pulling out of the tunnelled catheter in small children [3].

We were not able to compare the cost benefits between totally implantable versus long tunnelled catheters as the children were primarily referred for chemoport placement.

Conclusion

In summary totally implantable venous access devices usage are safe and reliable for access needs in children for long-term chemotherapy. Their low complication and low cost maintenance should increase their utilization in children requiring long-term chemotherapy. Chemoport placement in children with hematological malignancy can be carried out safely

without much impact on complication rates. Though management and compliance of children with malignancy has improved due to port system; critical analysis and standardization of port system care through prospective trials are necessary to reduce the morbidity and for cost analysis in these children.

Compliance with Ethical Standards

Conflict Interest None.

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