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EARLY EXPERIENCE WITH TOTALLY IMPLANTABLE VENOUS ACCESS PORT SYSTEM FOR PEDIATRIC CANCER PATIENTS

By
Ashraf M. Shoma, FRCS, MD,* Amany M. Shoma, MD,** Tarek Khatab, MD, Mohamed Sarhan, MD,** Mohamed Elgendy, MD****
*From Department of Surgery, **Mansoura University, Department of Pediatric, ***Mansoura University and Department of Pediatric, Banha University, Egypt.

Background & Aim of work: ***Vascular access in children receiving chemotherapy often poses an important problem. The irritating drugs used destroy peripheral veins, leading to a progressive decrease of available surface vessels. This can delay or prevent the administration of a planned therapy. Several methods of venous access have been developed, from arteriovenous fistula to indwelling right atrial silicon rubber catheters. Totally implanted devices, consisting of a subcutaneous injection port attached to a silicon catheter, have been tried for those children.***
We are reporting here our early experience to assess the efficiency of this device.
Patients & Method: ***Between February 2001 and February 2004, 28 devices were placed in 28 patients with solid neoplasm or haematologic malignancy. All the catheters were inserted by cutdown of the subclavian veins. The age of the patients ranged from 6 months to 12 years old. Follow up period ranged from 4 to 20 months.***
Results: ***We did not have any early complication of insertion. System obstruction was the most frequent late complication. The mean life of the implanted system was 288 days.***
Conclusion: ***Totally implanted devices proved safe & efficient venous access. Implantation should be performed by experienced surgeon. Obstruction is the most common complication & may be prevented by adequate information & training of the users.***

Keywords: *Venous port, Cancer, Pediatric.*

INTRODUCTION

Venous access is a problem for children receiving prolonged courses of cytotoxic therapy for solid tissue or haematologic malignancies. Venous integrity may be compromised by venotoxic antineoplastic agents-induced inflammatory changes and trauma related to repetitive blood sampling. Accordingly, reliable peripheral venous access becomes progressively harder to achieve and even more difficult to maintain over a period of a 6 to 9 month course chemotherapy. This has led to the search for a prolonged venous access for these patients. During the past four decades, several methods of permanent & safe venous access have been developed, from arteriovenous fistula to indwelling right atrial silicon rubber catheters.(1)

Indwelling tunneled, externalized central venous catheters of the Hickman or Broviac types has been advocated to improve venous access reliability, reduce the discomfort and anxiety associated with repetitive venous cannulation, and improve the overall quality of life. Externalized central venous access systems have the advantages of easy implantation and reliable, multilumen venous access but the disadvantage of requiring frequent maintenance to maintain patency, a high incidence of malfunction due to thrombotic occlusion, a high risk of associated infection due to the endogenous skin microflora, and for reasons of safety, a requirement for some activity restriction.(2)

In 1972, Belin et al(3) were the first to use a totally implanted venous access for intermittent hyperalimentation in children. Four years later, Fortner and Pahnke(4) reported a similar system for the cyclic administration of chemotherapeutic agents through the portal vein. Finally, totally implanted devices, consisting of a small-volume subcutaneous injection port attached to an

intravenous silicon rubber catheter, have been developed and successfully used during the past 10 years.[5]

Totally implanted venous access port systems have the same advantages as external indwelling catheter systems plus many others, including reliable venous access, a requirement for only monthly flushing and anticoagulant to maintain patency, fewer restrictions on activities such as bathing and a relatively low incidence of infection and malfunction compared with externalized systems.[6] It is now a common practice to implant theses devices in patients beginning the course of chemotherapy to avoid potential peripheral venous access problems.

Accordingly, we designed and conducted a study to critically examine the safety and efficiency of totally implantable venous access systems in children receiving cytotoxic therapy for solid tissue and haematologic malignancies.

PATIENTS AND METHODS

Between February 2001 and February 2004, 28 totally implanted double way devices (Districath- districlass medical SA, Saint-Etienne, France) were placed at our institution (Mansoura University Hospital). There were 10 females and 18 males with a mean age of 5.9 years (range of ages: 6 months – 12 years). The patients had different solid and haematologic malignancies. All the devices were indicated for administration of prolonged antineoplastic chemotherapy or as a preparation for bone marrow transplantation. No one of those patients was indicated for a second system placement.

At the time of the procedure all patients had more than 50,000 platelets/mm3 and more than 3,000 leucocytes/ mm3. None had ongoing infection. Pre- and intraoperative prophylactic antibiotic was given in all patients in the recommended dose of a third generation broad spectrum cephalosporin. All the procedures were done in the operating room in strict aseptic conditions, with intra operative fluoroscopic control of the correct positioning of the tip of the catheter in the superior vena cava. All cases were done under general anesthesia. Postoperatively, chest x-ray was performed in order to confirm the position of the line and to exclude complication.

All catheters were placed through an ipsilateral infra-clavicular incision with direct puncture of the subclavian vein. Nevertheless, all efforts were made to advance the catheter into the superior vena cava. These included gentle movements of the head of the patient toward the operative side to achieve a more open subclavian venous angle, use of a J-tip flexible guide wire and careful pushing and rotation of the catheter through the vein. The patients had close monitoring of the electrocardiogram (ECG) and blood pressure.

All catheters were made of silicon, with external diameter of 2.5 mm and internal diameter of 1.3 mm. The tissue contact material of the port is polysulphone for the port body and silicon rubber for its septum. The drug contact material was titanium for the port chamber and silicon rubber for the port septum. The ports used had 10.2 mm height, 25 mm base width, 0.25 ml internal volume and 4.5 grams weight.

All ports were placed in a subcutaneous pocket made in the infra-clavicular space over the pectoralis major muscle (Fig. 1). Subcutaneous tissue haemostasis was done with electrocoagulation. The ports were fixed in place by one to two nonabsorbable sutures. The incision in the skin was closed with interrupted or continuous subcuticular 4/0 nonabsorbable suture and covered with sterile gauze. When the procedure ended all systems were flushed with 10 ml. of a solution of normal saline and 5% sodium heparin. Maintenance of the devices was done after each use our every 4-6 weeks if not in use by flushing with 10 ml. of normal saline and 1 % sodium heparin.

All patients were followed either through their records or by telephone. The latest control was done in June 2003 with follow up ranging between 4 and 20 months. No devices had been removed because of complications. Antineoplastic drugs, blood products, parentral nutrition, antibiotic or other intravenous drugs as well as colloid and crystalloid solutions were infused through the devices during that period. We also kept notice in the follow up sheet about the use of a peripheral venous line by medical or paramedical personnel despite of the presence of the central port system.

Infection complication is defined by the presence of any local (at the site of port implantation) or systemic evidence of micro invasion. Even patients with suspected primary bacteremia as presented by fever and shivers were confirmed using blood culture. When bacteremia is proved, they were treated using peripheral endovenous antibiotic therapy (vancomycin) for the first 48 hours, followed by infusion of the same drug via the catheter till the culture became negative.

Any inflow or outflow obstruction was counted as a catheter obstruction. In this case the treatment employed was local fibrinolysis with the use of streptokinase solution at a concentration of 12.500 U/ml. The solution was maintained for one hour and then a catheter function test was performed. The local fibrinolysis was repeated every hour up to the fourth attempt.

The incidence of complication was calculated, as if shown in many literatures[7-12] per one thousand day of catheter use. This is through dividing the number of cases with a specific complication by the total number of day's use of all catheters, multiplied by 1000.

We have not taken into consideration the number of the punctures to the septum because the silicon septum may withstand 1000-2000 entries without tearing if a Huber-type needle is used,[7] significantly exceeding the accesses the patient may receive in the course of treatment.

RESULTS

All 28 systems were successfully inserted. There was only one case (3.6%) of difficult insertion where the puncture was tried on both sides for several times till it was successfully inserted. We did not have any early complication of insertion apart from two cases (7.1%) of subcutaneous pocket haematoma that was successfully treated conservatively. There were no cases of pathway haematoma, thrombophlebitis, pneumothorax, arterial lesions, or catheter emplacement failure. Table 1 shows all patients with complications faced in our study. In two (7.1%) patients more than one complication were observed during the follow up period: one had infection and occlusion while the other had subcutaneous haematoma and occlusion.

The total catheter use was 8456 days, ranging from 63 to 522 days per patient, with an average of 302 days. of the 28 catheters implanted, 6 (21.4%) presented some type of complications at a later stage Table 1. Despite of complications there were no catheters removed because of them. only 4 (14.3%) catheters were removed electively due to termination of treatment. In 25 (89.3 %) cases, the catheter remained fully functional until the patient's death, elective extraction or end of our follow up period. The remaining three (10.7%) cases were still able to use their catheters for receiving treatment but not for blood sampling.

Catheter obstruction was the major complication observed in our study. Four catheters (14.3%) were obstructed representing an incidence of 0.47 obstructions per 1,000 days of catheter use. However, after duplex ultrasound evaluation, there were no cases of associated deep venous thrombosis. Only in one case, after use of local fibrinolytic treatment, normal catheter function was reestablished. The other three cases showed persistent outflow obstruction with normal catheter inflow. No catheter extraction because of obstruction was required.

Infection occurred in lower number of cases. Two catheters showed infection at a frequency of 0.24 per 1,000 day of catheter use. The children presented with non complicated primary bacteremia (fever and shivers only) and were treated using peripheral endovenous antibiotic therapy (vancomycin) for the first 48 hours, followed by infusion of the same drug via the catheter. Both cases resolved clinically and the catheters were decided to be preserved after negative port aspirate culture. There were no cases of subcutaneous pocket infection or thrombophlebitis.

A very distressing observation during the follow up period was to find these children using or giving a history of use of a peripheral line for blood sampling and or drug infusion despite of having a fully functioning port system. This problem was noticed in 16 cases (57.1%).

Table 1. Patients with complications following insertion.

Type	Number of patients	Percent
Subcutaneous pocket Haematoma	1	3.6 %
Catheter Obstruction	2	7.1 %
Infection	1	3.6 %
Subcutaneous Haematoma + Obstruction	1	3.6 %
Infection + Obstruction	1	3.6 %

Table 2. Infection & Obstruction complications in literature and our data.

	Number of catheters	Infection/1000 day catheter use	Obstruction/1000 day catheter use
Bothe et al.19848	75	1.0/1000	-
Lokich et al. 19859	92	0.6/1000	-
Harvey et al. 19897	198	0.4/1000	-
Freytes et al.199010	134	0.02/1000	0.04/1000
Torramade et al. 199311	234	0.2/1000	0.2/1000
Biffi et al. 199812	178	0.16/1000	-
Wolosker et al. 200413	519	0.23/1000	0.06/1000
Our data	28	0.24/1000	0.47/1000

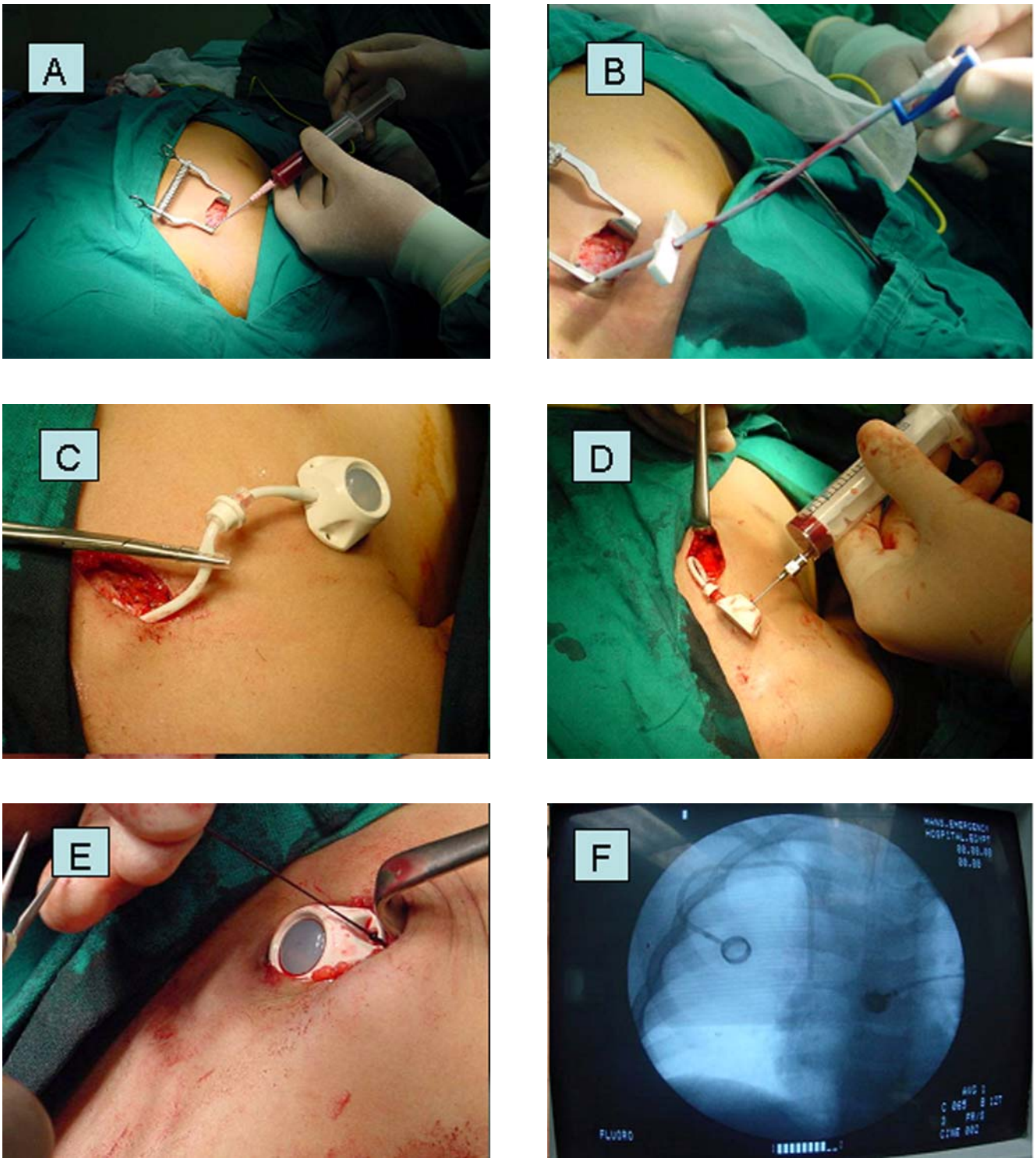

Fig 1. Technique of subcutaneous port system implantation. A: Subclavian vein puncture, B: Subclavian vein cannulation, C: Complete Port system connected, D: Port final testing before implantation, E: Fixing & implanting the port, F: Postoperative Chest x-ray.

DISCUSSION

Since the introduction of totally implantable catheters, the treatment of oncological patients has become much better because such venous access allows the safe infusion of chemotherapy over long period.[14] In addition to this such devices foster improved quality of life for patients, with an absence of restrictions on their activities[15] which is very important for children. The increased indication for these devices reflects their acceptance in the day-by-day routine of oncology centers. However, despite the great usefulness of these catheters, their insertion and maintenance is not free of complication.

Our preferred access route for implanting such catheters was direct puncture of the subclavian vein through a small subclavicular incision. Despite of having a case of difficult insertion where puncture was tried repeatedly on both sides, all catheters were successfully implanted. We believe that puncture of the subclavian vein is a safe fast route. It requires minimal tissue manipulation and no vein dissection. It has been also proven to be safe in relation to complications, considering that we did not have any case of pneumothorax, haemothorax, arterial lesion or pinching of the catheter between the first costal arch and the clavicle.

General anesthesia was used in all cases because of their young age. It was required to provide greater comfort for the children and reassurance for the surgical team when dealing with the possible complications inherited in the operation.

La Quaglia et al., 1992,[16] defined age less than seven years as a significant predictor of device related septicemia. Ross et al., 1989,[17] reported that prematurity, total parentral nutrition, continuous catheter use but not duration of catheter placement increased the risk of thrombosis. In our study we failed to identify any difference in the group with and without complications. Specially, there were no significant differences in age, sex, number of courses of antibiotic per year, steroid therapy, duration of insertion and death in the groups with and without complications. Duration of catheter insertion in this study also did not predict complications.

Considering the immune compromised state of our cases, we utilized prophylactic antibiotic therapy in all cases. This may explain the lower rate of infection in our cases compared to that in literature (see Table 2) however this needs further evaluation in a prospective study.

With the improvement of implantation techniques and equipment, complication rates have been diminishing. However recent series in literature show significant complication rates, with up to 2 % incidence of pneumothorax, 14 % cardiac arrhythmia, 3 % arterial puncture, 3 % bending of the guide wire, 3 % kinking of the introductory sheath and 1 % serious bleeding[14,18,19]. In our series we tried to shorten the time of general anesthesia for those critically ill children so we used direct puncture of the subclavian vein without much dissection. This may be why we did not observe such complications. We had only one case of difficult insertion & one case of subcutaneous pocket haematoma. Our incidence of pneumothorax & serious bleeding was nil. The small number of complications during the operations can be attributed to preoperative care (pre-anesthesia evaluation), the utilization of radioscopy equipment, standard surgical techniques and the trained team.

Late complications are of fundamental importance, since they are the main causes of catheter removal.[19] In our series they occurred in 6 cases (21.4 %) however none of them leads to catheter extraction. The catheters remain fully functional in 89.3 % of cases, while in the remaining cases we were only unable to use the catheters for blood sampling. Catheter obstruction was the most common late complication in our series in contrast to many other studies where infection continues to be the main late complication.[11,13]

Obstruction is divided into obstruction of the distal extremity of the catheter and deep vein thrombosis. The prophylactic use of low dose oral anti-coagulant for diminishing the incidence of deep venous thrombosis is discussed in literature.[14] We did not have any case of deep vein thrombosis although we did not use any oral anticoagulant prophylaxis.

Distal extremity catheter obstruction is the major complication observed in our study representing 14.3 % of cases with an incidence of 0.47 obstructions per 1000 days of catheter use. In literature the rates range from 7 to 50%.[20,21,22] We used local fibirinolysis to treat distal end catheter obstruction. This was successful in resolving 25 % of cases while the remaining cases showed persistent outflow obstruction with normal catheter inflow. Although this was satisfactory, other series reported up to 72.7 % preservation rate.[13]

Infection continues to be, just like other series, one of the main complications. We can subdivide the infection into subcutaneous pocket infection and bacteremia related to manipulation of the catheter.[23,24] The diagnosis of infection is routinely based on the clinical condition. When cutaneous hyperemia occurs along the catheter pathway or the incision, the diagnosis is clear. We have no case of pocket infection. In only 7.2 % of cases we observed fever without a determinate focus which is considered as a catheter related bacteremia. When there is such clinical suspicion, peripheral blood and catheter culture were performed. Immediately after this, antibiotic therapy is

begun for a period of 48 hours via a peripheral vein followed by infusion via the catheter for a period of 14 to 21 days. The antibiotic we utilized empirically was vancomycin, because of high incidence of infection by coagulase-negative staphylococcus.[25] In the literature, the catheter preservation rate is between 60 and 80 %,[24] while in our study we obtained success in all cases (two cases). This may be related to our small number of studied cases.

Although there were trained personnel on port access at the inpatient and outpatient cancer services, it was frequently more convenient by many to use peripheral access. Similarly venous access procedures during off hours often required the services of health care provider who were less familiar with the central venous accessing and tended to use peripheral rather than port system. It is still a great role of the pediatric oncology team to educate and train those who provide health services to those children. This is expected to reduce the rate of catheter complication.

From our study we confirm that the routine use of totally implanted venous access port system in pediatric oncology patients facilitate the care of these patients. With appropriate insertion technique and catheter maintenance routine, the catheter can stay patent for long periods, during which intravenous infusions and blood sample can be performed without discomfort to the child. This considerably improves the quality of life for these children.

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