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Acknowledgements—We thank Dr Chwetzoff of Janssen Laboratories for her advice on the protocol and for providing itraconazole, Dr Levron and Dr Le Moing of Janssen for information on the itraconazole assay and P. Bourret-Casarosa for technical assistance.

Eur J Cancer, Vol. 28A, No. 4/5, pp. 841–844, 1992.
Printed in Great Britain

0964–1947/92 $5.00 + 0.00

Comparison of Totally Implanted and External Catheters in Paediatric Oncology Patients

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From June 1982 until December 1989, 93 permanent central venous catheters [59 external catheters (ECs) and 34 implanted catheters (ICs)] were placed in 69 patients. The median age of these patients at placement was 5.6 years for ECs and 8.8 years for ICs ($P < 0.05$). Follow-up evaluation was possible on 86 catheters (58 ECs and 28 ICs). The median time of insertion was 236 days and 316 days for ECs and ICs, respectively ($P < 0.05$). The median number of open days was 58 for ECs and 66 for ICs (not significant). 17 catheters (6 ECs and 11 ICs) were transiently obstructed ($P < 0.005$). 30 episodes of bacteraemia were documented in 20 patients. The incidence of catheter sepsis and bacteraemia of unknown source was one in 278 and 283 open days for ECs and ICs, respectively (not significant). In this retrospective study, ECs appeared to be as safe as ICs when infection was correlated with use of the catheter, but this finding should be confirmed in a randomised design.
Eur J Cancer, Vol. 28A, No. 4/5, pp. 841–844, 1992.

INTRODUCTION

CHILDREN WITH cancer require repeated intravenous infusions and blood sampling for chemotherapy, as well as intravenous supportive care such as blood product transfusions, antibiotics and parenteral nutrition. To improve the administration of medications, and the quality of life of these children, permanent central venous catheters have been developed. Broviac *et al.* and Hickman *et al.*, in 1973 and 1979 respectively, introduced silicone rubber catheters [1, 2]. External catheters (ECs) and totally implantable catheters (ICs) are available [3].

Published series have found different rates of complications (i.e. obstruction and catheter-related sepsis) between ECs and ICs, related to the duration of insertion [4–6]. We have analysed retrospectively the complication rate in relation to the number of days the catheters were opened, with particular emphasis on infections.

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Revised 14 Nov. 1991; accepted 15 Nov. 1991.

PATIENTS AND METHODS

From June 1982 to December 1989, children with malignant diseases followed at the Pediatric Hemato-Oncology Unit were offered the placement of a permanent central venous catheter early in the treatment of their disease. Two different types of catheters were used: Broviac® (Davol, Cranston, USA) and Port-A-Cath® (Pharmacia Nu Tech, Walpole, USA) for ECs and ICs, respectively. The choice of the type of catheter was based on expected frequency of use, age of the child, and the ability of the child and his/her family to handle an EC. The catheters were used for blood drawing, administration of medications, blood products, intravenous hydration and parenteral nutrition.

The catheters were placed in the operating room by an experienced paediatric surgeon, using either a venous cut down technique [7] or a percutaneous approach [8]. Catheter patency was maintained with a heparinised solution (10 ml with 100 U/ml heparin), three times weekly (ECs), monthly (ICs), daily when the catheter was open, or after each blood transfusion. The iodine dressing was changed once a week (ECs). No occlusive dressing was used.

Mask, gloves and sterile dressing were mandatory for catheter opening (IC or EC). Catheter manipulations (infusion change or blood sampling) were made from an extension set that was connected to the luer (EC) or to a non-coring needle (IC).

An infectious work-up was done at each episode of fever and granulocytopenia and/or when sepsis was suspected. Blood cultures were drawn through the catheter. When possible, paired qualitative blood cultures (Isolator®, Merk, Darmstadt, Germany) were simultaneously drawn from the catheter and from a peripheral vein. For patients already on antibiotics, cultures on Isolator® were mandatory. Local identified organ infections with secondary bacteraemia were excluded from the study. Different types of bacteraemia were defined as follows.

Catheter sepsis. Sepsis or bacteraemia originating from an infected catheter, documented by differences (> 1log) in paired quantitative blood cultures and/or subcutaneous infection of the tunnel or site of the reservoir [9].

Bacteraemia of unknown source. Sepsis or bacteraemia without a defined focus of infection.

Contamination. Positive blood culture with < 0.1 colonies per ml on Isolator® and disappearance of the fever without antibiotic therapy.

Obstruction of the catheter was suspected when blood drawing and/or injection were difficult. The child was first repositioned to rule out extrinsic compression or fold of the catheter. A chest radiography was taken to confirm the correct position of the catheter tip. The catheter was then flushed with heparin up to three times daily. If unsuccessful or in the case of total obstruction, 2 ml of urokinase (2500 U/ml) were injected into the catheter, and left in place for 20 min before attempting blood sampling. Urokinase could be used up to three times consecutively in cases of persistent obstruction.

The reasons for catheter removal were: (a) catheter infection resistant to appropriate antibiotic therapy; (b) tunnel or port site infection; (c) fungal catheter infection; (d) permanent thrombosis of the catheter; (e) home accidental section of the catheter.

In this study, the two types of catheters (ECs and ICs) were analysed according to the duration of insertion (number of days from placement of a catheter to its removal or death of the child), the number of open days (any day the catheter was opened for any infusion, except heparinisation), number of days of intravenous chemotherapy, and number of blood product units transfused (packed red cells, platelets and plasma). Catheters were not opened more than once daily. Complications such as haemorrhage, infections (catheter sepsis and bacteraemias of unknown source), catheter obstructions and accidental dislodgements were compared between the two types of catheters.

The Student t-, χ^2- and Mann–Whitney U-tests were used for statistical analysis, significance being assumed for P values < 0.05.

Table 1. Patients' characteristics

	IC	EC	P value
Number of catheters	34	59	
Number of patients*	33	44	
Sex (M:F ratio)	22/11	28/16	
Diseases			
Leukaemia	7	29	< 0.001
Solid tumour	26	15	
Age at placement (years)			
Median	8.8	5.6	< 0.05
Range	1.2–17.2	0.5–15.8	

* 8 children (5 male and 3 female) had an EC and an IC.

RESULTS

General characteristics

93 permanent central venous catheters were placed in 69 patients (45 boys and 24 girls). 50 patients (72%) had one catheter, 19 patients had more than one catheter (15 patients had 2 catheters, 3 patients had 3 catheters and 1 patient had 4 catheters). There were 59 ECs in 44 patients and 34 ICs in 33 patients (Table 1). At placement the median age of the patients was 5.6 years and 8.8 years for ECs and ICs, respectively ($P < 0.05$). ECs were inserted more frequently in leukaemic children (29/44) whereas ICs were placed mainly in solid tumour patients (26/33; $P < 0.001$). Chemotherapy (80 catheters), bone marrow transplantation [12] and parenteral nutrition [1] justified the catheter placement.

90 catheters in 66 patients were placed under general anaesthesia, and in three patients hypnosis and/or local anaesthesia were used. The percutaneous technique was introduced in 1986, and has been used since in 37 of 57 placements.

Right-sided veins were catheterised in 76 of 93 placements. These included the external jugular (28), the subclavian (21), the cephalic (12), the internal jugular (5) and other veins (10). Left-sided catheters (17) were placed in the following veins: sub-clavian (10) and external jugular (7).

86 catheters (58 ECs and 28 ICs) in 63 patients could be studied for follow-up evaluation (Table 2). These catheters were in place for a total of 25 601 days with a median time of insertion of 236 days for ECs and 316 days for ICs ($P < 0.05$). The median number of open days was 58 and 66 for ECs and ICs, respectively (N.S.). The ratio of open days over duration of insertion was significantly larger for ECs than for ICs (27.2% vs. 16.4%; $P < 0.01$).

82 catheters (54 ECs and 28 ICs) were used for chemotherapy and the mean number of days with intravenous chemotherapy were 22.5 and 23.0 for ICs and ECs respectively (N.S.).

Parenteral nutrition was administered more frequently

Table 2. Catheter use

	IC	EC	*P* value
Number of catheters	28	58	
Duration of insertion (days)			
Total	10356	15245	< 0.05
Median	316	236	
Range	12–1294	15–806	
Open days (days)			
Total	1700	4153	N.S.
Median	66	58	
Range	4–151	1–217	
Number of chemotherapy (days)			
Mean	22.5	23	N.S.
S.D.	21.5	22	
Number of transfusions (Units)			
Mean	10	34	< 0.005
S.D.	14	39	

Units: units of packed red cells, platelets and plasma.

through EC (25/58) than through IC (7/28; $P < 0.01$), with a mean (S.D.) of 42.5 (39) days per catheter.

Blood product transfusions (number of units) were given more often through EC [34 (39) units] than through IC [10 (14) units; $P < 0.005$].

Infectious complications

Following septic work-up, 30 episodes of bacteraemia were documented in 20 patients. Of these, 9 in 6 ECs were diagnosed as contaminations with *Staphylococcus epidermidis* (7), *Acinetobacter* spp. (1), *Pseudomonas maltophilia* (1), alpha haemolytic streptococcus (1) and multiple organisms (1).

10 cases of catheter sepsis were identified (5 ECs and 5 ICs). In 3 children, the blood cultures were taken only through the catheter. The organisms were *Staph. epidermidis* (5), *Staph. aureus* (1), *Escherichia coli* (1), *Ps. aeruginosas* (1), *Candida lusitaniae* (1) and unspecified (1) (Table 3).

11 cases of bacteraemia of unknown source were diagnosed in 10 ECs and 1 IC ($P = 0.03$), with the following organisms involved: *Staph. epidermidis* (4), *Staph. aureus* (1), *Streptococcus sanguis* (2), *Corynebacterium* spp. (1), *Morganella morganii* (1) and *Ps. aeruginosa* (2).

For catheter sepsis and bacteraemia of unknown source, antibiotic treatment lasted 12.4 (S.D. 7.7) days and allowed the saving of 11 of 21 catheters. 10 catheters (6 ECs and 4 ICs) had to be removed for infectious reasons: 2 tunnel and 4 port site infections, 1 sepsis due to *C. lusitaniae* and 3 infections resistant to systemic antibiotherapy.

Table 3. Complications

	IC	EC	*P* value
Number of catheters	28	58	
Number of CS	5	5	
Number of BUS	1	10	= 0.03
CS and BUS rate per open day	1/283	1/278	N.S.
Obstruction (*n*)	11	6	< 0.005
Catheters removed			
For infection	4	6	
For any reason	5	13	N.S.

CS: catheter sepsis; BUS: bacteraemia of unknown source.

There were 15 cases of catheter sepsis and bacteraemia of unknown source for 58 ECs, and 6 for 28 ICs. These accounted for an infection rate of 1:1016 vs. 1:1772 insertion days (N.S.), and 1:278 vs. 1:283 open days (N.S.) for ECs and ICs, respectively. Infected ECs were opened more frequently [mean 93 (S.D. 41) days] than non-infected EC [67 (50); $P < 0.05$]. The interval between placement and infection varied widely [median 91 (range 5–498) days].

Children with catheter sepsis and bacteraemia of unknown source were younger [mean 4.9 (S.D. 3.6 years)] than children without infection [7.08 (4.5); $P < 0.05$].

No significant correlation was found between catheter sepsis or bacteraemia of unknown source and underlying disease or the technique of insertion.

Obstructive complications

ICs were more frequently obstructed than ECs (11/28 and 6/58, respectively, $P < 0.005$). Concentrated heparin infusions were used in all cases and urokinase in 5. An EC catheter was repermeabilised with a wire. All catheters were in use afterwards. External catheter obstructions were not associated with subsequent infection but in ICs 4 out of 5 cases of catheter sepsis were preceded by obstructions ($P = 0.05$). Obstruction was not correlated with the use of the catheter (open days) or with the number of blood transfusions.

Other complications

Postoperative haematomas necessitating red blood cell and platelet transfusions were observed in six patients in whom ECs had been placed prior to 1985. One of these patients required surgical haemostasis. Two children had a pneumothorax following percutaneous EC placement, and pleural drainage was necessary. The ECs of 2 patients were cut at home during the dressing changes and were removed to prevent catheter colonisation. In an obese child, the IC slipped out of the vein and was surgically repositioned with subcutaneous sutures. In 5 children, the dacron cuff of their EC slipped out without obvious signs of local infection. 1 child with malnutrition had a skin ulcer over the port, and 2 children with ICs were unusually frightened before each manipulation of their catheter.

DISCUSSION

Since their first description by Broviac *et al.* [1], permanent central venous catheters (ECs or ICs) have become widely used in different subspecialities [10]. In oncology patients, a reliable vascular access is needed for frequent blood sampling, chemotherapy, transfusions and intravenous nutrition.

In our institution, until 1986, all catheters were placed using the cut down technique. Since then, with increasing surgical skills, the majority of catheters have been placed percutaneously. With this technique, the operation time is shortened and the complication rate is low [11].

The choice of catheter (EC or IC) was essentially made according to the underlying disease. Differences in chemotherapy regimen for leukaemia and for tumours can explain this choice. In the presence of a high-risk leukaemia, ECs were preferred by the staff in the anticipation of an intensive chemotherapy and its expected side-effects. The children with ICs were significantly older than children with ECs. In adolescents with leukaemia or solid tumour, ICs were preferred because of their minimal maintenance, and their cosmetic aspect, allowing a better quality of life.

Catheter infection is a fearful complication in neutropenic patients [12]. Bacterial adherence to indwelling catheters and production of extracellular matrix protein contribute to catheter colonisation with organisms such as *Staph. epidermidis* [13–16]. Silicone catheters, such as those used by us, appear to offer less adherence to bacteria than polyvinyl catheters [17]. When related to the duration of insertion, significant differences in the rates of catheter infections are generally reported in the literature [6]. But in our opinion, the duration of insertion is an unreliable parameter with which to evaluate the incidence of infection and to compare infection rate between ECs and ICs. Catheter use differs greatly between centres because in some hospitals, including ours, the catheters (especially ICs) remain in place several months after the end of chemotherapy, which artificially increases the duration of insertion and lowers the infection rate. Catheter sepsis and bacteraemia of unknown origin should therefore be correlated with the number of days the catheter is opened. In this study the number of catheter sepsis and bacteraemia of unknown origin per open day were very similar between ECs and ICs.

On the other hand, bacteraemia of unknown origin appeared to involve ECs more frequently than ICs. Many cases of bacteraemia of unknown origin in ECs may have represented catheter colonisation at the luer end rather than true CS. The ECs were used more frequently than ICs for blood product transfusions and parenteral alimentation. Infected ECs were more frequently opened than non-infected ECs, emphasising the potential colonisation associated with manipulations of the catheters. In this respect, capillary blood sampling for routine analysis should be encouraged. Half of the catheter sepsis and bacteraemia of unknown origin cases could be treated with antibiotics alone (52%) compared with a 70% catheter salvage published in other studies [18, 19]. This apparently low percentage of successful antibiotherapy can be explained by the exclusion of the group of patients with positive blood cultures diagnosed as contamination in our study.

Transient difficulties in blood drawing and incomplete occlusions were relatively frequent. True obstructions occurred at least once in approximately 40% of ICs, and happened more often with ICs than with ECs. This could be explained by the difference in heparin flushing frequency between the two types of catheters. Catheter obstructions were successfully treated with urokinase injections, but as these procedures were well tolerated, the question of possible pulmonary embolisation remains unsolved [20].

Permanent catheters were well tolerated by children. A few children experienced needle phobia before IC puncture. With local anaesthetic ointment, these children became quickly accustomed to the procedure [21].

Children with cancer or chronic disease necessitating frequent intravenous infusions can greatly benefit from permanent central venous catheters (ECs or ICs). Their placement should be performed at the time of diagnosis, simultaneously with the initial oncologic work-up (biopsies, bone marrow aspiration). In contrast with other studies [6], ECs and ICs appeared equally reliable and safe with respect to infection, when correlated with the number of days the catheters were opened. However, this study was retrospective and several differences existed between the two groups of patients (e.g. age, underlying disease, number of transfusions, use of parenteral nutrition and ratio of open days over duration of insertion). Therefore definite conclusions cannot be drawn and a prospective study should be undertaken to confirm our results.

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