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Original Paper

Complications of an Implantable Venous Access Device (Port-a-Cath®) During Intermittent Continuous Infusion of Chemotherapy

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In 149 patients, treated with intermittent continuous infusion of different chemotherapeutic agents, 169 Port-a-Caths® were implanted by qualified surgeons and residents in training. The peri- and postoperative complications of implantation of the Port-a-Cath® system and the complications during treatment were retrospectively analysed. The Port-a-Cath® was *in situ* for a total of 36247 days (median 181, range 1–1332). Of the 169 catheters, major complications occurred during treatment, with infection in 4 patients (2.4%), occlusion in 3 (1.8%), thrombosis in 8 (4.7%), extravasation in 8 (4.7%) and migration in 3 (1.8%). The peri- and postoperative complication rate was low, although pneumothorax occurred in 6 patients (3.6%). In 25 patients (14.8%) the Port-a-Cath® had to be explanted due to complications. It can be concluded that continuous infusion of chemotherapy via a Port-a-Cath® system is a relatively safe procedure, although major complications do occur. The experience of the surgeon could not be related to the complications. Copyright © 1996 Elsevier Science Ltd

Key words: chemotherapy, continuous infusion, Port-a-Cath®, venous access device

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INTRODUCTION

CONTINUOUS INFUSION of chemotherapy is a relatively new way of administering chemotherapeutic drugs. Recently, ambulant outpatient continuous infusion has been made possible by technological improvements, such as the development of venous access devices [1]. The Port-a-Cath® system (Pharmacia Deltec, St Paul, Minnesota, U.S.A.) is one of the most applied venous access devices. Since the first report on infusion of chemotherapy via the Port-a-Cath® in 1984 [2], several authors have published the peri- and postoperative complications encountered by implanting this venous access device [3–15], but only few data exist on the long-term complications of the Port-a-Cath® during continuous infusion of chemotherapy [3]. In a large group of patients, we retrospectively evaluated the problems encountered during and after the implantation of the Port-a-Cath® system and, in particular, during intermittent continuous infusion of chemotherapy.

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PATIENTS AND METHODS

Patients recruited from different studies using continuous infusion of chemotherapeutic agents were retrospectively analysed for complications of the Port-a-Cath® system (Pharmacia Deltec). The occurrence of complications was studied in three separate periods: peri-operative, postoperative and during treatment. Postoperative complications were defined as being apparent after the implantation until initiation of treatment. Patient characteristics are shown in Table 1.

The Port-a-Cath® system consists of a stainless steel or titanium portal with a silicone catheter that selfseals by means of a slip ring. Implantation of the Port-a-Cath® system was performed by both surgeons and residents in training. Surgery was performed under general anaesthesia and under sterile conditions in the operation theatre. After subcutaneous tunnelling, the catheter was introduced either

Table 1. Patient characteristics

Patients	149
Male	85
Female	64
Tumour	
Colon	54
Pancreas	30
Kidney	25
Stomach	15
Breast	15
Lung	8
Miscellaneous	2
Chemotherapy*	
5-FU	69
5-FU (ECF-schedule)	11
FUdR	26
Ifosfamide	19
Ifosfamide/5-FU	17
Not started	7

* 5-FU, 5-fluorouracil; FUdR, fluorodeoxyuridine; ECF, epirubicin, cisplatin, 5-FU.

percutaneously in the subclavian or jugular vein, or surgically in the jugular vein. The portal was implanted in a subcutaneous pocket in a site not interfering with measurable disease locations. These methods have been described before [1]. During and after the implantation, the catheter position was controlled by fluoroscopy. In general, initiation of treatment was planned 10–14 days after surgery.

Chemotherapy was administered on an outpatient basis via a portable infusion pump (mainly Pharmacia CADD-Plus®; Pharmacia Deltec). The pump was connected via a syringe and a non-coring needle (Port-a-Cath needle® or Gripper®; Pharmacia Deltec) with the implanted portal. Chemotherapeutic agents used were: 5-fluorouracil (5-FU); 5-FU in combination with bolus epirubicin and cisplatin (ECF-schedule); fluorodeoxyuridine (FUdR); ifosfamide; and the combination of ifosfamide and 5-FU. All chemotherapeutic agents were administered as a 14-day continuous infusion every 4 weeks. Patients visited the outpatient clinic every 14 days at the end and beginning of each chemotherapy course. At the end of each course the Port-a-Cath® system was flushed with heparinised saline to prevent occlusion. Furthermore, every 14 days the medical history of the patient was taken and a physical examination was performed.

RESULTS

From 13 June 1989 until March 1995, 169 Port-a-Caths® were implanted in 149 patients. Of these, 14 patients received two Port-a-Caths® and 3 patients had three devices implanted. Median age of the patients was 57 years (range: 23–77 years). The Port-a-Cath® was *in situ* for a total of 36247 days in 146 patients [median 181 days (range: 1–1332)]. In 3 patients, these data were not available.

52 Port-a-Caths® were inserted by surgeons, and 95 by residents (32 by residents in their first year of training, 19 in the second year of training, 21 in the third, 16 in the fourth and 7 in the fifth) in our centre, whereas 22 Port-a-Caths® were inserted in another hospital. Percutaneous catheter introduction was performed in 77% (130/169) of cases. Open, surgical introduction was used in only 6 cases (4%). No data on the method of catheter introduction were available in 33 Port-a-Caths® (20%). Details concerning the time taken to insert the catheter are given in Table 2. The number of administered chemotherapy courses are shown in Table 3. 7 patients had no treatment at all. In 6 patients this was due to a rapid progression of their disease. One patient had the Port-a-Cath® removed because of a postoperative complication (paraesthesia of the arm), after which the patient refused further therapy.

Table 2. Time for catheter introduction

	Total number of implantations	Mean time (range) (minutes)
Surgeon	50*	54.8 (25–103)
Resident (year 1)	31†	55.4 (20–110)
Resident (year 2)	19	49.9 (30–80)
Resident (year 3)	21	54.4 (30–110)
Resident (year 4)	16	51.2 (25–120)
Resident (year 5)	7	57.9 (35–90)
All	144‡	54 (20–120)

* No data available on 2 patients. † No data available on 1 patient. ‡ Insertion data on the 22 patients operated elsewhere were not available.

All complications are listed in Table 4. Six peri-operative complications were recorded in 6 patients, 14 postoperative in 13 patients and 26 during treatment in 19 patients.

Peri-operative complications

Here, 6 patients had a partial pneumothorax. One patient required chest tube drainage. In the other 5, the pneumothorax was resolved by conservative treatment. Pneumothorax was seen only in resident procedures (three in their second training year and three in the third training year). In one patient, supraventricular extrasystoles were observed, which normalised during the operation. No procedure-related bleeding complications were observed.

Post-operative complications

In 5 patients, a haematoma became apparent. These resolved spontaneously and caused no delay of treatment. One patient developed a purulent infection of the subcutaneous pocket, for which the Port-a-Cath® had to be explanted. Bacterial culture of both the pocket and the catheter tip identified *Staphylococcus aureus*. Migration of the catheter out of the vessel was observed twice. A new catheter had to be inserted. One patient complained of paraesthesia of the left arm. This Port-a-Cath® was inserted by the percutaneous route via the left subclavian vein. After removal of the Port-a-Cath®, the paraesthesia disappeared completely.

Twice, kinking of the catheter caused occlusion leading to surgical repositioning of the Port-a-Cath® in one patient. In the other patient, the kinking could be corrected under local anaesthesia at the outpatient department.

In 2 patients, the catheter tip was placed in the right atrium and had to be pulled back in order to avoid arrhythmia. In one female patient, the portal had to be removed, because no access could be obtained.

Table 3. Number of courses

Chemotherapeutic agent*	Total number of patients	Total number of courses	Median number of courses (range)
5-FU	62†	388	3 (1–34)
5-FU (ECF)	11	36	3 (1–6)
FUdR	26	181	4 (1–22)
Ifosfamide	19	70	3 (2–4)
Ifosfamide/5-FU	17	56	3 (1–6)
Total	135	731	4 (1–34)

* 5-FU, 5-fluorouracil; ECF, epirubicin, cisplatin, 5-FU; FUdR, fluorodeoxyuridine. † No data available on 7 patients.

Complications during treatment

Infection. 4 patients developed an infection at the site of the implanted portal. All patients presented with local signs of infection. None developed a secondary septicaemia. In all cases, the Port-a-Cath® was removed and bacterial cultures were taken. The patients were treated with an appropriate antibiotic regimen for a short time. In one patient, there was a bacteriaemia with *Bacillus cereus* after 3 months of treatment. In another patient, the Port-a-Cath® was implanted at a previously irradiated site. Wound healing was impaired and led to wound dehiscence and subsequent infection. This complication occurred after two courses. Cultures of the catheter and portal showed *Staphylococcus aureus* and *Pseudomonas aeroginosa.*

One patient had an infection after one month of treatment. This was accompanied by thrombosis in the subclavian and jugular vein. Blood cultures identified *Staphylococcus epidermidis* and cultures from the catheter tip showed *Staphylococcus epidermidis* and *Staphylococcus aureus.* In another patient, the infection was accompanied by both thrombosis and extravasation. Cultures from blood and the catheter tip showed *Staphylococcus epidermidis.* The thrombosis was extensive and localised in the jugular, subclavian, axillary and brachial vein. This complication occurred after 9 months of treatment. Even in those cases in which the infection occurred simultaneously with thrombosis, no late sequelae were observed.

Table 4. Complications

Pre-operative	
Pneumothorax	6 (3.6%)
Postoperative	
Haematoma	5 (3.0%)
Infection	1 (0.6%)
Migration out of the vessel	2 (1.2%)
Arm paraesthesia	1 (0.6%)
Occlusion by kinking	2 (1.2%)
Catheter tip too low	2 (1.2%)
Portal too deep	1 (0.6%)
Total	14 (8.3%)
During treatment	
Infection	4 (2.4%)
Occlusion (by catheter-tip thrombosis)	3 (1.8%)
Thrombosis	8 (4.7%)
Extravasation	8 (4.7%)
Migration	3 (1.8%)
Total	26 (15.4%)

Thrombosis. Thrombosis of the catheter tip caused an occlusion in 3 cases. In all 3 patients, the Port-a-Cath® had to be removed. In addition to the 2 patients mentioned above, who also had an infection or extravasion, thrombosis occurred in 5 patients after a median of 2 months (range 1–16). 3 of these patients developed a superior vena cava syndrome, of which one had initially a thrombosis of the axillary, subclavian and brachiocephalic vein. At a later stage, the contralateral subclavian and brachiocephalic vein also became thrombotic. The patient then developed a superior vena cava syndrome. One patient had thrombosis of the jugular vein, and the other thrombosis of the subclavian and brachiocephalic vein. 2 patients were treated with fibrinolytic agents. In one, symptoms diminished and the Port-a-Cath® became functional again. All patients with thrombosis were treated with heparin and oral anticoagulant drugs.

Extravasation. Extravasation was seen in 8 patients. It occurred after a median of 2.5 months (range 1–9 months). Except for pain during the extravasation, no serious complications were observed. In 3 patients, the site of extravasation was the entrance of the catheter into the vessel, and in one patient at the vessel wall where the catheter tip was located. Three times the catheter migrated out of the vessel. Once the extravastion was due to a disconnection of the slip ring. In all cases, the Port-a-Cath® was removed.

Explantation. Of the 169 Port-a-Caths® inserted, 25 (14.8%) were removed owing to complications: due to the combination of infection, thrombosis and extravasation in one patient, due to the combination of infection and thrombosis in one, due to extravasation in 7, to dislocation in 5, to thrombosis in 4, to occlusion in 3, to infection in 3, and to paraesthesia of the arm in one.

DISCUSSION

In the last decade, continuous infusion of chemotherapy has become feasible by use of implantable venous access devices such as the Port-a-Cath®. There are advantages of the Port-a-Cath® over external venous catheters especially with regard to an outpatient ambulatory setting: (1) the maintenance of the venous access device is minimal, especially for the patient; (2) the body image with the Port-a-Cath® is better; and (3) the infectious and thrombotic complications are reported to be lower as compared to external venous catheters. As a quality control, we retrospectively evaluated the complications in our patient group using intermittent continuous infusion of chemotherapy and compared the results with published studies.

Insertion of the Port-a-Cath® in our hospital was performed by both surgeons and residents. There was no influence of experience on operation time (Table 2), which is in accordance with other data in the literature [5, 6]. Two other studies have reported the operation time [5, 6] with a mean operation time of 46.3 min (range 15–180) from 50 catheter insertions in one study [5] and 60 min from 50 catheter insertions in the other [6]. In the first study, no data were available on the qualifications of the surgeons [5], and in the second study the insertions were performed by an experienced anaesthetist [6]. The percentage of pneumothorax (3.6%) in our study is comparable to other studies, which, in general, is less than 5% in the literature [1]. In all cases of pneumothorax, the insertion was performed by a resident. This might be an indication of a relationship between complications and the degree of experience. However, since the occurrence of pneumothorax in our study is not higher compared to other studies and the qualification of the surgeon is not known in 17% of the insertions, this conclusion cannot be confirmed from this data.

Two cases of migration were observed in the postoperative period. One patient vomited fiercely after surgery. This might have led to such pressure changes in the thoracic cavity that it could be an important factor or even the cause of migration and extrusion of the catheter [3]. In the other patient, the catheter migrated out of the vessel and had curled around the portal. In a case report, the explanation for this phenomenon was thought to be the excessive length of the catheter in combination with space around the portal and, therefore, increased mobility of the catheter [16]; this might be the same in our patient. One patient complained of paraesthesia that was probably due to an injury or irritation of the brachial plexus. The immediate disappearance of symptoms after explantation strengthens this hypothesis.

The occlusion by kinking, the wrong positioning of the catheter tips and the wrong position of the portal are situations that can be avoided by conscientious surgery. Peri- and postoperative complications have been reported extensively in previous studies [3–15], and have shown approximately the same complication rate as our study. Recently, two randomised trials, both including 100 patients, compared the use of the Port-a-Cath® with an external indwelling central venous catheter [6, 7]. These studies showed conflicting results. In the study by Carde and colleagues, it was concluded that the Port-a-Cath® was more reliable, safer and better tolerated than the classical external catheters [6], whereas the other study of Mueller and colleagues did not find any difference between the two groups between the incidence of documented infections, or mechanical or thrombotic complications [7]. However, in neither of these studies was chemotherapy administered as a continuous infusion.

Table 5. Complications during treatment in studies with continuous infusion of chemotherapy

	Lokich and collagues [3] ($n = 92$)	Current study ($n = 169$)
Infection	6 (7%)	4 (2.4%)
Occlusion	0 (0%)	3 (1.8%)
Thrombosis	15 (16%)	8 (4.7%)
Extravasation	6 (6%)	8 (4.7%)
Migration	7 (8%)	3 (1.8%)
Total	36 (39%)	26 (15.4%)

The complications of the Port-a-Cath® during treatment with continuous infusion of chemotherapy were compared with the only published study that also used continuous infusion of chemotherapy [3] (Table 5). The main difference between the treatment schedules was that we used an intermittent continuous infusion schedule in contrast to Lokich, who used a continuous infusion schedule with a minimal infusion duration of 4 weeks.

A majority of the patients in our study with infectious complications had an infection with *Staphylococcus aureus* or *Staphylococcus epidermidis*. This is in accordance with other studies, which also reported these micro-organisms in the majority of cases [3–5, 11]. In none of the 4 patients in our study with a documented infection were antibiotics used to save the Port-a-Cath®. In 3 patients, the Port-a-Cath® was not used any further and was explanted. In the other patient, the infection was accompanied by an extensive thrombosis and extravasation, which was the reason for removal. Most authors [1] advocate, in case of infection, sterilising the catheter by antibiotics, but this is not used in all studies. In the study of Lokich and colleagues, 1 out of 6 patients with infectious complications needed removal of the Port-a-Cath®, despite antibiotic therapy [3].

Thrombosis occurred eight times in our study. In Lokich's study, thrombosis occurred more often than in ours (16% versus 4.7%) [3]. This difference can be partly explained by the difference in chemotherapeutic agents; beside 5-FU and FUdR, Lokich also used doxorubicin, which caused 4.4% of the thrombosis. Another explanation may be the longer infusion duration, causing a higher risk of injury to the vascular endothelium, both chemical and mechanical. It has also been suggested that the position of the catheter is a risk factor for thrombosis [17]. Patients in whom catheters are inserted in the left side and with the tip in the upper caval vein would be particularly at risk. Of the 8 patients with thrombosis in our study, 4 had the catheter inserted at the right side.

In 2 patients, fibrinolytic therapy was given in order to try to dissolve the thrombus. In one patient, who presented with early symptoms, the symptoms diminished and the Port-a-Cath® became functional again. In the other patient, no access through the catheter was possible and fibrinolytic agents were administered via a peripheral vein without success. In the other patients with thrombosis in our study the infusion of fibrinolytic agents was not possible due to blockage of the catheter. No fibrinolytic therapy was given via a peripheral vein because of our earlier experience. Treatment with fibrinolytic agents in acute onset is advised in the literature [1], but no indication is given of the time after the initiation of complaints after which fibrinolytic therapy is still useful. In our study, the patients presented with a long duration of complaints. Because of this relatively long time span between complaints and presentation, we decided to treat the patients with heparin and oral anticoagulant drugs. We also removed the Port-a-Cath®. Commonly, the Port-a-Cath® is removed in order to prevent progression of the thrombus, especially in case of the superior vena cava syndrome. Other reasons are persistent pain, despite anticoagulant therapy, and the combination with a documented infection or extravasation. In other studies, the Port-a-

Cath® was removed in approximately 40% of patients with thrombosis [3–5, 11, 15]. In 3 patients, extravasation occurred at the entrance of the catheter into the vessel. Most probably, a clot at the catheter tip caused backtracking of the drug along the catheter to the entrance place into the vessel, where extravasation occurred after the accumulation and damaging effect of the drug on the endothelium. In another 3 patients, the extravasation was due to migration of the catheter out of the vessel. The disconnecton of the slip ring, causing extravasation in one of the patients, has been reported before [3, 18], and is probably caused by a surgical error.

In total, 25 Port-a-Cath® systems (14.8%) were removed owing to complications. Although the exact number of catheters removed in the study of Lokich was not given, it seems approximately the same as in our study [3]. In general, indications for removal of the Port-a-Cath® are: failure of antibiotics, documented septic venous thrombosis, catheter thrombosis refractory to fibrinolytic therapy, catheter or port exposure, extravasation of infusate, and other problematic malfunctions [1].

It can be concluded from this retrospective analysis that long-term continuous infusion of chemotherapy via a Port-a-Cath® system is a relatively safe procedure, even though major complications occur. The major complications were infection (2.4%), occlusion (1.8%), thrombosis (4.7%), extravasation (4.7%) and migration (1.8%). The experience of the surgeon could not be related to the complications. However, it has to be kept in mind that a retrospective design, as executed in our study, has disadvantages that can influence the conclusions of the study.

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