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Evaluation of a Totally Implanted Venous Access Port and Portable Pump in a Continuous Chemotherapy Infusion Schedule on an Outpatient Basis

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Abstract—*In this study we evaluated the feasibility of a totally implanted vascular access port (VAP) and portable infusion pump for cytostatic drug administration on an outpatient basis, in a 21-day continuous infusion schedule with 4-epidoxorubicin (phase I and phase II study) and mitoxantrone (phase I study). Patients were instructed to dissolve their own drugs at home. Fifty patients were treated with 114 cycles (2394 infusion days). The complication rate was low. In one patient thrombosis of the subclavian and superior caval vein resulted in the termination of treatment. One patient developed pulmonary embolism during treatment. Needle dislocation was observed in two patients. No septicaemia and no irreversible catheter occlusion were seen. Pump functioning was efficient and pump arrest (9 ×) never lasted longer than 24 h. We conclude that a VAP and portable pump are a safe and reliable route of administration for cytostatic drugs on an outpatient basis and that patients are capable of preparing their own drugs at home without increase of complications.*

INTRODUCTION

THE TREATMENT of cancer patients with continuous infusion of different chemotherapeutic agents on an outpatient basis has been made possible by the development of improved venous access procedures and the availability of various infusion pumps. Experiences with several catheters, infusion pumps and therapy regimens have been described [1–12]. It is, however, still controversial which central venous catheter is the safest and most suitable for long-term administration. For a phase I and phase II study we chose a totally implantable venous access port and portable pump for administration of 4-epidoxorubicin (4-ED) [13] and mitoxantrone (MX) in a continuous infusion schedule. Patients were treated on an outpatient basis and were instructed to prepare their own drugs, so they would not be dependent on a nurse's help. In this paper the feasibility of continuous infusion administered this way in 50 patients is reported.

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MATERIALS AND METHODS

The patients participated in a phase I and phase II study with continuous infusion of 4-ED and a phase I study with continuous infusion of MX. Patients were accepted if there was histological proof of malignant disease for which no other conventional therapy was available. The Karnofsky performance score at start of therapy had to be >60, the platelet count before therapy was $\geq 100 \times 10^9$/l and leucocyte count $\geq 3 \times 10^9$/l. Only patients who were willing to take an active part in an investigational study were accepted after informed consent was obtained.

Both drugs were administered in cycles of 3 weeks followed by a 3 week period of rest. For the first part of the first cycle, the patients were admitted to the hospital for the implantation of the VAP and they were instructed by the nurse to dissolve their own cytostatic drugs, to fill the syringes and to handle the portable infusion pump [14]. Within 1 week after the VAP implantation the drug treatment was started, while the instructions were continued. The patient was dismissed when capability in preparing the drugs and handling the pump had been shown. Further treatment took place on an out-

patient basis. A responsible physician could be reached by telephone 24 h a day. During the infusion period the patients were seen once a week in the out-patient department for a short evaluation and change of the needle and extension tube. Diluent and drugs for 1 week were given to take home every week during the infusion period. The needle was removed at the end of each cycle. Courses were repeated when no unacceptable toxicity due to the cytostatic drug, no tumour progression, and/or no serious complications with the VAP had occurred. Anticoagulant prophylaxis was not given routinely.

The totally implantable venous access port (Infuse-A-Port®) used consists of a polyether sulfone plastic port with a diameter of 4.76 cm, a height of 1.58 cm and an internal volume of 0.2 ml. It contains a self-sealing silicone rubber septum for percutaneous needle entry and a radiopaque silicone rubber catheter with an internal diameter of 0.63 mm, an external diameter of 2.3 mm and a volume of 0.032 ml/cm length.

The implantation of the VAP was performed under local anaesthesia, preferably on the left side, because of an easier entry into the superior caval vein from that side. In case of tumour on or in the left hemi-thorax or prior surgery or radiotherapy of the left chest-wall or jugular region, which might compromise the implantation, the right side was chosen. The catheter was introduced via the subclavian vein into the superior caval vein by using a Seldinger technique with a pacemaker lead introduction set with peel-a-way sheet. The port was implanted in a subcutaneous pocket on the major pectoral muscle fascia. Catheter position and accidental pneumothorax were checked by fluoroscopy and a plain X-ray picture in the operating room.

Every puncture of the port-membrane was done by one out of six physicians familiar with the procedure under aseptic conditions. When the needle was changed, inserting the needle through the previous puncture was avoided. A standard procedure for connection of the implanted system to the external system was used.

A 22 G 90° bent Huber point needle with a length of 19 or 32 mm was used for puncturing the port-membrane. The needle was connected to a Luer lock extension tube (Vygon Lectrocath®) of 50 cm length with an internal diameter of 1 mm and a volume of 0.45 ml. The VAP was flushed with sterile normal saline, before connecting the drug-containing Luer lock syringe. After puncturing the port the needle was secured on the skin with tape strips (Steri-strips®) and a sterile transparent plastic dressing (Tegaderm®, 10 × 11 cm or in case of an allergic skin reaction Opsite®, 10 × 14 cm). At the end of each cycle the VAP was flushed with 10 ml normal saline followed by 10 ml heparinized saline (50 U/ml) before removing the needle. During the period between two courses the system was not flushed.

Table 1. Patient characteristics

Number of patients	50
Mean age (range)	51 (26–72)
	No. of patients
Sex:	
male	39
female	11
Diagnosis:	
colo/rectal carcinoma	19
gastric carcinoma	15
non small cell lung cancer	4
non-seminoma testis	4
prostatic cancer	1
nasopharyngeal carcinoma	1
hypernephroma	1
cervical carcinoma	1
ovarian carcinoma	1
Sertoli Leydig cell carcinoma of the ovary	1
malignant melanoma	1
bladder cancer	1
Previous chemotherapy	17
Previous radiotherapy	6

The Graseby Medical MS 16A syringe driver was used as portable pump. It is a battery powered pump of 17.5 × 8.5 × 2.5 cm including the cap, and a weight of 250 g including the battery. The infusion rate can be adjusted from 0.02 to 33 ml/h using commonly available syringes. Pumps were adjusted to an infusion rate of 0.38 ml/h using 20 ml syringes in this study. Patients had to change the syringe every 48 h. There was some margin because the syringe was filled with enough drug for 52 h. The pump was worn in a cotton shoulder holster, specially made for each patient by the seamstress of the hospital.

RESULTS

A total of 53 patients entered the study. Three patients were excluded during the first week of the study. They proved technically capable of following the procedure but chose not to accept the responsibilities involved. Fifty patients completed a total of 114 cycles over a period of 2394 infusion days which means a total treatment period of 4788 days. Patient characteristics are listed in Table 1. Each of these 50 patients did get at least one complete 21 days cycle. All patients were treated on an outpatient basis and all patients who did enter the studies were capable of dissolving their own drugs. The instruction was usually completed after 3–5 days in most patients. The period in the hospital for the implantation of the VAP and starting the first course was sufficient in almost all the patients.

Table 2. Number of complications due to the VAP, pump, extension tube and needle in 114 cycles.

Complications	Number
Due to the VAP:	7
thrombosis of the subclavian and/or superior caval vein	2
pulmonary embolism	1
needle dislocation with extravasation of 4-ED	1
MX	1
temporary catheter occlusion	1
cellulitis around puncture site	1
septicaemia	0
Due to the pump:	9
temporary pump arrest (<24 hr) due to:	
—mechanical malfunction	0
—wrong placement of the syringe	6
—failure to start the pump	2
—empty battery	1
Due to the needle/extension tube	5
leakage of the needle/extension tube connection	4
fracture of the extension tube	1

The maximum number of cycles for a single patient was nine.

Ultimate tumour progression was the reason for cessation of chemotherapy in 49 patients. In one patient the therapy could not be continued because the catheter had to be removed. Complications due to the VAP, pump, external catheter and Huber point needle are listed in Table 2.

Subclavian vein and superior caval vein thrombosis during treatment was responsible for cessation of the therapy in one patient, who had received prior mediastinal and supraclavicular irradiation. The thrombus was resolved by administration of urokinase through the catheter, but recurred during the following infusion cycle. After resolving the thrombus by urokinase infusion again, the catheter was removed, and the thrombus did not recur.

Other catheter related problems were a pulmonary embolism in one patient. With sufficient anticoagulant therapy, continuous infusion could be continued without further complications. Needle dislocation was observed in two patients. One patient was a very obese women treated with 4-ED and the other patient was a man treated with MX. Drug extravasation occurred in both patients but recovered uneventfully and no skin necrosis was seen. Chemotherapy was discontinued for less than 1 week in both cases. Temporary catheter occlusion at the beginning of a new course was seen in another patient without signs of thrombosis at the tip of the catheter. Continuous infusion could be continued without complications.

The only complication due to infection was cellulitis around the puncture site of the port, observed in one patient at the end of the infusion cycle. It responded well to antibiotic treatment and therapy could be continued after the 3 week rest period according to the schedule. Septicaemia was not seen in this study.

Pump arrest occurred nine times with a maximum duration of 24 h. It was caused by an empty battery (1 ×), wrong position of the syringe on the pump (6 ×) and failure to start the pump (2 ×). Leakage of the connection between the Huber point needle and extension tube occurred four times. In one patient the extension tube fractured due to extreme bending of the tube.

The port was not used for blood sampling. As an extra control of the needle position, drawing blood through the catheter right after each puncture was always attempted. These attempts were not always successful despite the possibility of infusion through the catheter.

DISCUSSION

Several groups have described their experience with totally implantable venous access devices in different treatment schedules for intermittent high dose chemotherapy injections as well as for continuous infusion regimens [1–12]. Compared with percutaneous central venous catheters the advantages of a totally implantable venous access device are obvious. There is less risk of infection and septicaemia [6, 7]. No special care is needed in the period between its use, such as dressing changes or flushing of the catheter. There are no restrictions for the patients when the VAP is not in use and the VAP is less visible and therefore more acceptable to the patient.

The major disadvantage compared to other catheters is the risk of drug extravasation due to needle dislocation. Reed *et al.* [11] reported needle dislocation in five out of 10 patients during overnight drug infusions. In our study needle dislocation occurred in two out of 50 patients, fortunately without skin or deep tissue necrosis. Dislocation of the needle can be avoided by adequate fixation of the 90° bent Huber point needle. In obese patients, women with large pendulous breasts and in patients with a port lying deep subcutaneously, a long Huber point needle should be used. The position of the port on the chest-wall is also important in this regard. It should not be implanted in the shoulder joint region or too high below the clavicle because the risk of needle dislocation is increased in active patients [15].

Subclavian vein and superior caval vein thrombosis developed in one of our patients (2%). Lokich *et al.* [1] reported the occurrence of subclavian vein thrombosis in 16% of 92 patients receiving chemotherapy and/or hyperalimentation by a tot-

ally implanted subclavian venous access system. In their studies with open ended, externally sited, tunneled subclavian venous catheters, the rate of thrombosis varied from 0% [2] to 40% [3]. A relationship between the frequency of thrombosis and catheter size was suggested. Subclavian vein thrombosis occurred rarely when catheters with an external diameter less than 2.8 mm were used [1]. This is in agreement with the results of our study where catheters with an external diameter of 2.3 mm were used. Catheter occlusion might be related to internal diameter, as suggested in two reports, where occlusion occurred in seven out of 16 patients with a 0.51 mm lumen catheter [6] and in five out of six patients with a 0.38 mm lumen catheter [4]. In our study using a 0.63 mm lumen catheter no irreversible occlusion developed. These results suggest that a catheter with an external diameter of less than 2.8 mm and a lumen of more than 0.51 mm may be advantageous with regard to the risk of thrombotic complications and occlusion of the lumen.

As infectious complication only cellulitis around the puncture site was seen in one patient in this study. This confirms the results of other groups [4, 5, 7]. Strict aseptic technique in all aspects of care of the VAP, needle change every week and care by a limited group of doctors may account for this result. No septicaemia occurred in our study although patients dissolved their own drugs and connected the syringes with the drug at home. It might be possible to keep the needle inserted for longer than 1 week. In our study we did not want to take the risk on increasing complications in patients treated on an outpatient basis. In the future it certainly may be worth trying to leave the needle in position for longer periods.

Real pump failure, due to mechanical malfunction, did not occur in our study. Pump arrest was mostly due to wrong placement of the syringe on the pump by the patient after changing the syringe and never lasted longer than 24 h. Overall pump functioning was accurate and safe. The advantages of this mechanical portable pump compared to other pumps for continuous infusion are its easily controlable function because the syringe is directly visible and can be easily checked, and its economy, because the price is reasonable and the pump can be used in more than one patient. Compared to a totally implantable pump [8] an advantage of a portable pump is that the pump can easily be disconnected. The need to wear a portable pump is a major disadvantage and a handicap for some patients. It is important to reduce this uncomfortable feeling by a suitable holster fitted for each patient.

Only limited data can be found about the preparations of cytostatics by the patients themselves. In almost every study of continuous infusion of chemotherapy as well as for parenteral nutrition or antibiotics at home, the drug solutions are prepared by the hospital pharmacy or a nurse. In some studies patients had to visit the hospital, or were visited by a nurse every day to prepare and administer their drugs [16–21]. In our institution we found that it is possible to instruct patients adequately to mix every other day their own cytostatic drugs at home, to fill a syringe with the correct amount of fluid and to handle a portable infusion pump [14]. It has proved a safe and reliable method, motivates the patient and it makes him or her less dependent on the hospital department. When patients can prepare their own medication, the short stability of a drug solution does not have to be a contraindication for a continuous infusion regimen on an outpatient basis.

We conclude that for a continuous infusion regimen on an outpatient basis, a totally implantable venous access device is a safe and reliable route for drug administration. For drug infusion the portable pump is accurate, cheap and easy to handle by the patient. The complication rate of this administration technique is low and does not increase when patients prepare their own medication.

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