

1 Use of Chemoports in a comprehensive cancer care center, a Retrospective study

3 Abstract

4 **Aim of The Study:** Treatment protocols that use intravenous cytotoxic agents need long term
5 access to peripheral or central veins, but use of these devices have their own own set of **problems**,
6 starting from difficulties in cannulation to safely maintaining the access for a prolonged period of time
7 in a sterile way. The patient population that undergo these treatments are mostly immunosuppressed
8 and prone to systemic infections making the care of any implanted device for Venous Access more
9 difficult. The present study evaluates the experience of using chemoports in a tertiary care center.

10 **Subjects and Methods:** We retrospectively reviewed our experience in handling chemoports at
11 our Center over a period of three years, as regards to difficulties during insertion and handling of such
12 devices during administration of venotoxic agents. All patients who were advised more than 4 cycles
13 of cytotoxic drugs were included and approval of the university research and ethics committee was
14 taken prior to data analysis. **Results:** A total of 120 chemoports were inserted, most commonly in

15 patients with breast cancer, with the commonest chemotherapeutic regimen being
16 Adriamycin/Epirubicin and Cyclophosphamide followed by Taxanes. The preferred site of insertion
17 was right subclavian vein in 52.5 % of cases. The average time taken for the procedure ranged from
18 25 mins to 2 hrs. Procedural difficulties were documented in 48 [40%] insertions , the most common
19 being multiple punctures for venous access. 3 patients developed haematoma during the procedure
20 and, one patient had puncture of carotid artery. Passage of the catheter to the opposite jugular vein
21 was an interesting happening and occurred in 3 patients . None of the patients who had subclavian
22 vessel cannulation had pneumothorax. All the complications were managed conservatively. The
23 median days of catheter life was 265 days. In the follow up period 30 patients [25%] had events
24 related to difficulty of use and port related infection, 12 patients had difficulties in canulation of the
25 chemoport reservoir and 6 Ports could not be used for further chemotherapy and were
26 removed. Infectious complications were seen in 12 ports , the commonest being pocket site infection.

27 We had a policy of recommending removal of the chemoport 6 months after completion of the
28 planned chemotherapy protocol or 2 years after placement of the port, whichever is earlier. At the end
29 of the study period, 47 of the patients had their chemoports removed, 10 patients were lost to follow
30 up and hopefully got the devices removed elsewhere. **Conclusion:** The present day chemoports are
31 simple to insert , and easy to manage with proper asepsis expected in an immunosuppressed patient.
32 However, a dedicated team of trained personnel viz. surgeons, anaesthesiologists, clinical oncologists
33 and nursing staff, are necessary so that complications related to these devices are kept to a
34 minimum. This is also important in resource poor countries where these costly devices are difficult to
35 prescribe , so that once inserted , they can last till the end of chemotherapy.

38 INTRODUCTION

40 The last few decades **have** seen a lot of changes in how we treat patients with cancer. From radical
41 surgeries and radiation regimens, the oncologists now explore newer ways to preserve organs and
42 avoid mutilation wherever possible. Addition of chemotherapeutic agents to existing treatment
43 protocols, either to increase **the** efficacy of Radiation or to downsize tumours to make surgeries less
44 mutilating is the order of the day. More and more evidence is coming up to incorporate these
45 recommendations to existing treatment protocols.

46 Treatment protocols that use intravenous cytotoxic agents need **long term** access to peripheral or
47 central veins. This creates its own set of problems, starting from difficulties in cannulation to safely
48 maintaining the access for a prolonged period of time in a sterile way. The patient population that
49 **undergo** these treatments are mostly immunosuppressed and prone to systemic infections making the
50 care of any implanted device for Venous Access more difficult. Various devices for intravenous
51 delivery of chemotherapeutic agents have come into vogue over the years, from simple IV canulas to
52 totally implantable Venous Access devices. Along with knowledge about the drugs, oncologists and
53 nursing personnel dealing with intravenous chemotherapy also need to learn about the safe
54 placement and handling of such devices. Failure to get adequate training about these devices may
55 result in a broad spectrum of problems in these already compromised patients, ranging from the

simple annoyance of multiple punctures to access the reservoir to a much more dangerous life threatening sepsis due to catheter infections. A totally implantable Venous Access port reduces these problems to a large extent and has become the most preferred device for long term venous access in patients undergoing multiple cycles of chemotherapy [1, 2].

A Totally Implantable Device is a subcutaneous port or reservoir with self-sealing septum that is tunneled beneath the skin and is accessed by a needle through intact skin. Popularly called a chemoport, TIVAPS have gained acceptance as a standard clinical practice, in particular for patients with solid cancers, hematologic malignancies and chronic digestive diseases improving patient quality of life and reducing risk of infection [3].

We retrospectively reviewed our experience in the use of chemoport devices inserted at our institute over a period of three years, in reference to difficulties during insertion and handling of such devices during administration of cytotoxic agents.

MATERIAL & METHODS

This is a retrospective observational study conducted at the Cancer Research Institute of Himalayan Institute of Medical Sciences. Approval of the University Research Committee and ethics committee was taken prior to the enrollment of patients [Reference no. : SRHU /HIMS/RC/2017/560 and SRHU /HIMS/ETHICS/2018/55]. We included all patients who were advised for chemoport insertion and planned for treatment with more than four cycles of chemotherapy for any malignant tumour in the previous three years, from Jan 2015 to Dec 2017 .All patients who had chemoports implanted from any outside centers or patients who chose to undergo chemotherapy at any other Center after getting the device implanted were excluded from the study. Retrospective data was collected from the medical records division and Hospital Information System as per format approved by the university research committee. Data entry was made in MS Excel 2010 spreadsheet after anonymisation and analysis was done by appropriate statistical tools.

Procedure and Technique of Implantation

The Stimimplant 9.6 F Vygon chemoport device with a silicone catheter and titanium reservoir was implanted in all patients, and access to the reservoir was done by Bards huber needle.

The site and side of insertion was decided prior to the procedure by the surgical team. Under local anaesthesia with 2% plain xylocaine, the anaesthesiologist inserted the chemoport catheter into the vein by Seldinger technique and fluoroscopic guidance [4,5]. A subcutaneous pocket was made on the anterior chest wall for the titanium reservoir and the silicone catheter was tunneled and connected to it. Position of the tip of the catheter was confirmed by fluoroscopy and patency checked by insertion of the Huber needle that came with the chemoport kit. The port was allowed to be used for chemotherapy after 12-24 hrs of insertion.

FOLLOW UP

Post insertion, the patient was advised for ensuring heparinisation of the port at every chemotherapy cycle and every six weeks after completion of chemo. Insertion of Huber needle and heparinisation was done by resident doctors and senior nursing staff in the day care ward under all available aseptic precautions, and documentation of difficulties in handling and nonfunctional Ports was done.

The surgical team remained the same over the period of three years, however the anaesthesiologists and nursing staff handling the devices after insertion were on rotation basis and had different levels of expertise.

We used the Infectious Diseases Society of America (IDSA) guidelines [6] to classify the complication of port site infections and defined them as follows

1. Exit site infection - Clinical signs of infection (erythema, induration, tenderness, and/or pus formation) developing in the skin after the needle puncture or microbiological evidence of a micro-organism.
2. Tunnel infection- Clinical signs of infection along the subcutaneous tract of a catheter.
3. Pocket infection- Infected fluid collection in the subcutaneous pocket of a totally implanted intravascular device, often associated with clinical signs of infection with or without spontaneous rupture or drainage.
4. Blood stream infection- Catheter-related bacteremia or fungemia in a patient who has an intravascular device and more than one positive result of culture of blood samples obtained from the peripheral vein, clinical manifestations of infection (e.g., fever, chills, and/or

hypotension), and no apparent source for bloodstream infection (with the exception of the catheter)

Results

A total of 120 chemoports were inserted in the period of study, for patients undergoing more than four cycles of chemotherapy for solid tumours. The patient and disease profile is described in Table 1. The most common malignancy for which chemoports was advised was breast cancer, considering that chemotherapy traditionally was not given in the veins of the operated side, leaving only one side for use. Colorectal malignancies formed the next major group because of the prolonged duration of chemo (4-5 days continuous) and the 2 weekly regimen. The commonest chemotherapeutic regimen followed for breast cancer was Adriamycin/ Epirubicin and Cyclophosphamide followed by Taxanes. The preferred site of insertion was right subclavian vein in 52.5 % of cases[Table 2]. Left subclavian vein was chosen in patients who had breast surgery on the right side or where right subclavian vein could not be cannulated after multiple attempts. The average time taken for the procedure ranged from 25 minutes to 2 hrs. Procedural difficulties were documented in 48 [40%] insertions , the most common being multiple punctures for venous access. 3 patients developed haematoma during the procedure and, one patient had puncture of carotid artery. Passage of the catheter to the opposite jugular vein was an interesting happening and occurred in 3 patients. None of the patients who had subclavian vessel cannulation had pneumothorax. All the complications were managed conservatively.

Table 1. Demographics of the study population [n = 120]

Characteristics	Value	Percentage
Male/Female	25/97	20.8/ 80.8
Median age (years)	55	
Age range (years)	22–73	
Less than 40 yrs of age	21	17.5
40-49 yrs	25	20.8
50-59 yrs	37	30.8
60-69 yrs	23	19.1
More than 70 yrs	14	11.6
Diagnosis		
Breast cancer	84	70
Colorectal	24	20
Ovary	4	3.3
Sarcomas	3	2.5
Others	5	4.1
Follow-up period, days		
Median days of the catheter	265, (11- 763,	

Characteristics	Value	Percentage
use	SD)	

Table 2. Stage at insertion

Stage	Value	Percentage
I	12	10.0
II	32	26.6
III	41	34.1
IV	35	29.1

Table 3. Type of Chemotherapy Regimen

Chemo Protocol	Value	Percentage
AC + T	33	27.5
Trastuzumab based	16	13.3
TEC	20	16.6
FEC	7	5.8
FOLFOX	19	15.8
FOLFIRI	5	4.1
CapOx	6	5.0
Others	14	11.6

Abbreviations: **AC +T** : Adriamicin(Doxorubicin) + Cyclophosphamide + Taxol, **TEC** : Taxol + Epirubicin + Cyclophosphamide, **FEC** : Fluorouracil + Epirubicin + Cyclophosphamide, **FOLFOX**: Folinic acid(leucovorin) + Fluorouracil + Oxaliplatin, **FOLFIRI** : Folinic acid(leucovorin) + Fluorouracil + Irinotecan, **CapOx** : Capcitabine + Oxaliplatin, **Others** :Gemcitabine + Cisplatin, Ifosphamide + Adriamicin, Cyclophosphamide + doxorubicin + vincristine +Prednisone + Rituximab (**R-CHOP**), Ifosphamide + Carboplatin + Etoposide (**ICE**)

Table 4. Site of Insertion

	Right side (%)	Left side (%)	Total (%)
Subclavian	52.5	11.6	64.16
Internal Jugular	23.4	12.4	35.84

In the follow up period of chemoport use for chemotherapy, a total of 30 patients [25%] had events related to difficulty of use and port related infection [Table 3]. 12 patients had difficulties in canulation of the chemoport reservoir, manifested by inability to heparinise or loss of backflow. 6 out of these ports could still be used for chemotherapy after reinsertion of needle. Position of these ports was checked by chest X Ray in all cases. 6 Ports could not be used for further chemotherapy and were removed. In 4 patients, a change of position of the patient helped in better flow rates. Infectious complications were seen in 12 ports , the commonest being pocket site infection. Extravasation of prechemo medications were found in one patient which was managed conservatively

by stopping immediately. One patient had extravasation of chemotherapy and skin necrosis, requiring debridement and removal of the port. Exit site infections were found in 3 patients who also had Tunnel infection. One patient had features of systemic sepsis(fever) after flushing of the Port , requiring removal. The days of use in these patients where the port had to be removed due to infections ranged from 25 to 265 days. We had a policy of recommending removal of the chemoport 6 months after completion of the planned chemotherapy protocol or 2 years after placement of the port, whichever is earlier. At the end of the study period, 47 of the patients had their chemoports removed, 10 patients were lost to follow up and hopefully got the devices removed elsewhere.

Table 5 . Difficulties during chemotherapy

Loss of Backflow but usable	6	5 %
Loss of backflow and removed	6	5 %
Positional flow	4	3.3 %
Extravasation	2	1.6 %
Exit site infection	3	2.5 %
Tunnel infection	4	3.3 %
Pocket infection	4	3.3 %
Systemic sepsis	1	0.8 %
Total	30	25%

DISCUSSION

Long term Venous access devices or chemoports , as they are popularly called, have revolutionised drug delivery in patients undergoing cytotoxic chemotherapy [7].They are easy to use, concealed, easy to maintain, and convenient to the patient. Various studies have evaluated the efficacy of the totally implantable devices.[8, 9, 10]

Practical difficulties during the process of insertion of chemoports can easily be minimised by simple attention to details and training of the surgical and anaesthetic team. Although USG guided cannulation of preferred vein for puncture has been reported to have lesser complications than blind punctures in a number of studies [11, 12] we did not have facilities available for the same in our operation theater. The number of attempts during blind punctures were observed to be lesser with more experienced anaesthesiologists. Documentation of this could not be possible because the study used Retrospective data analysis and the point was not always mentioned in the patient files. The Cancer Institute being a part of the University Medical College setup, younger members of the anaesthesia team were allowed to take part in course of their training [13,15,18].

The other reported procedural difficulties in available literature include cardiac arrhythmias and hematomas [10,14]. We used the ECG changes on the digital monitor as a guide for the proper site of placement of the guide wire. Minor hematomas observed in patients with multiple attempts of puncture were managed by simple application of pressure. One patient who had an inadvertent puncture of the common carotid artery during access of the Internal Jugular vein of the same side was also managed conservatively and the procedure was abandoned. We noticed an interesting event where the guide wire travelled from the initial site of entry in the subclavian vein to the opposite IJV instead of the ipsilateral SVC.

Catheter occlusion during chemotherapy happens commonly because of improper heparinisation of the reservoir at the end of chemotherapy that results in the formation of a small blood clot which in some cases may cause a ball valve effect that allows fluid to be pushed in, but not aspirated. An occlusion rate of 3.2–21.5% has been reported in various studies.[16] Biffi et al. in a randomized study of 376 patients noted the inability to draw blood in 2% cases where a standard open-ended catheter was used.[17] We noted that in 5 % of our patients, the port had to be removed because neither fluid/blood can be pushed nor aspirated . Jie et al in their center infused 10,000 IU heparin over 24 hours into the port system for 3 days via a perfusion system, after which they were able to use it again.[16] Apart from changing the Hubers needle and personnel concerned, we did not try any other measures but were able to continue using the ports in 5 % of cases.

We noted that a change in position(lying down/ sitting up/lifting the shoulder) facilitates the flow in a group of patients who otherwise had a partial occlusion of the catheter. This was noted more in obese female patients where the catheter tip was placed in the subclavian vein and the chest wall reservoir was pulled down by the sagging breast tissue. This possibly causes the catheter to be trapped between the clavicle and the first rib causing a "pinch -off effect"[10,16]. Jie et al reported 3 patients out of 492 [0.61%] to have this complication. In order to prevent this complication, more lateral access of the subclavian vein is recommended.[19]

The pinch-off effect has also been reported to cause catheter fracture.We had a single case of catheter fracture in our study, and because no other cause was found for this to happen, we attributed it to a manufacturing defect in the catheter itself.

We also observed a single case of catheter migration in our study that was detected only while planned removal of the chemoport. The patient had the port in place for 257 days and had completed chemotherapy 10 months back. The reservoir was removed under local anaesthesia and the migrated catheter was removed by the cardiologist under fluoroscopic control. This rare but potentially serious complication has been seen in 1.22 % to 2.1% of cases in literature [16, 19, 20-24] which also mentions that more than 50% of fractured ports were clinically asymptomatic, and present as accidental findings during scheduled port removal. The authors opine that the natural history of the catheter damage cannot be adequately predicted, and the risk that these asymptomatic fractures might lead to more severe events cannot be excluded [20,21]

Infectious complications in chemoports in the range of 4.8–8.8% have been reported in the literature.[25,26] In a prospective study of 680 patients between June 1987 and May 1989 at Memorial Sloan-Kettering Cancer Center, followed up until port removal, death, or a maximum of 1960 days, infectious complications were noted in 8.8% of patients, half of which were surgical site infections and rest were systemic sepsis.[25] Biffi et al. in a study of 376 patients found 3 patients who suffered from port-related bacteremia (0.8%, 0.016/1000

39 days of use)[17] In our study, 12 patients (10%) had infectious complications leading to removal of the port. Two of these patients had a documented incidence of extravasations leading to subsequent infection of the chest wall pocket.

As chemoports are completely subcutaneous, the risk of extraluminal colonization is low and mostly occurs during insertion. Once the device is inserted, contamination may occur during repeated punctures with Huber needles, if the skin has not been completely cleaned, therefore leading to intraluminal colonization that can spread from the port to the catheter tip. Since frequency of TIVAP handling is one of the major risk factor identified for port infections, it is not surprising to observe that coagulase-negative staphylococci (CoNS), which are frequent colonizers of the human skin, is one of the leading pathogens responsible[26] In an article from the Pasteur Institute of Paris , the authors found that out of 29 cases, 57% were caused by CoNS, 20 % by Gram-negative rods (GNR), 7% by *S. aureus* and 3 % by *C. albicans* [26] As part of protocol, we sent the catheter tips of all patients who required removal of Chemoports during the study period for aerobic culture and sensitivity. The most common organism isolated was *Staph aureus*.

At the end of the study period, 63 patients had their chemoports in place and the devices are being used for chemotherapy.

CONCLUSION

Totally implantable Venous Access devices or chemoports have changed the landscape of intravenous chemotherapy drastically and in a good way. Both patients and physicians now have an alternative to reduce and escape the annoyance of trying multiple Venous punctures in the day care and the morbidities of extravasation of toxic drugs. The present day devices are simple to insert , and easy to manage with proper asepsis expected in an immunosuppressed patient. However, a dedicated team of trained personnel viz.surgeons, anaesthesiologists,clinical oncologists and nursing staff, are necessary so that complications related to these devices are kept to a minimum. This is also important in resource poor countries where these costly devices are difficult to prescribe , so that once inserted , they can last till the end of chemotherapy.

CONSENT

Written consent for the procedure was taken from all patients. University approval for auditing data retrospectively was taken [REF. NO. : SRHU /HIMS/RC/2017/560]

ETHICAL APPROVAL

Taken from University Ethics committee

REF. NO. : SRHU /HIMS/ETHICS/2018/55

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