LONG TERM VENOUS ACCESS IN PATIENTS WITH ACUTE LEUKEMIA AND HIGH GRADE LYMPHOMAS

(Based on AFMRC Project 1868/91)

Lt Col RAJAT KUMAR*, Lt Col R RANGA RAO+,
Lt Col G RAJAGOPAL#, Lt Col V P SINGH#

ABSTRACT

Twenty Hickman catheters were passed in 19 patients undergoing chemotherapy for acute leukemia (15 patients) and high grade lymphoma (4 patients). The catheters were inserted into the superior vena cava through the cephalic or external jugular vein with subcutaneous tunneling and exit through the anterior chest wall, and were functionally effective in 19 cases. The catheters remained in situ for a mean period of 50.5 days (range 1-266 days). The catheters were well tolerated eliminating the need for repeated venepuncture. The complications encountered were: hemorrhage - 1 case, thrombosis - 1 case, catheter related bacteremia - 2 cases, tunnel infection - 1 case, and exit site infection - 5 cases. Most of the complications were managed conservatively. These catheters ensured safe and reliable venous access in these high risk patients during episodes of severe neutropenia, sepsis and thrombocytopenia.

MJAFI 1995; 51 : 231-236

KEY WORDS : Catheterisation central venous; Leukemia; Lymphoma.

Introduction

The current chemotherapeutic management of acute leukaemias, lymphomas, and a number of malignancies requires ready venous access for blood sampling and for delivery of drugs, fluids, and blood products [1]. The need for a reliable long-term venous access led to the introduction of a silicone-rubber catheter, by Broviac et al [2], suitable for prolonged parenteral alimentation. This was modified by Hickman et al for use in leukemic patients [3].

Multiple peripheral venepunctures, using either scalp vein sets or venflons, is the usual method of providing venous access in India. The repeated needle pricks lead to thrombophlebitis and an eventual exhaustion of sites for venous access. There are two published reports from Indian hospitals evaluating the use of Hickman lines, with varying results [4,5]. The aim of this study was to evaluate

the use of Hickman line catheters in patients of acute leukemia and high grade lymphoma undergoing chemotherapy at Command Hospital (SC) Pune and Armed Forces Medical College, Pune.

Materials and Methods

Patients with acute leukemia and high grade lymphomas with platelet counts more than 50,000/mm³ or those for whom platelet concentrates could be arranged preoperatively were included in the study after obtaining informed consent. All the patients received standard chemotherapy.

All catheters were inserted under aseptic conditions in the operation theater by one of the two oncology surgeons, under general anaesthesia (Fig 1). An incision in the infraclavicular or cervical region was made and the cephalic vein or external jugular vein was identified and exposed. The right side was preferred since it offers a more direct route to

*Reader in Medicine, Armed Forces Medical College, Pune; +Medical Oncologist, #Surgical Oncologist, Command Hospital (SC), Pune.

Fig. 1 : Anatomical position of single lumen Hickman catheter. SVC - superior vena cava, RA - right atrium

the right atrium. A subcutaneous tunnel was developed from this incision to an exit site below the nipple. The Hickman catheter was pulled up from the exit site through the upper incision such that the dacron cuff was positioned 4-5 cm proximal to the exit site. The catheter lumen was filled with heparinised saline (50 units in 5 ml), trimmed to a proper length and inserted through a venotomy in the cephalic or external jugular vein to lie near the junction of superior venacava and right atrium. The catheter patency was tested by withdrawing blood and if there was any difficulty, the catheter was pulled back. The upper incision was closed and a single suture anchored the catheter at the exit site. Fluoroscopy was not used during the procedure as

this facility was not available.

The external surface of the catheter, exit-site wound, and cervical incision site were cleaned with povidone-iodine and sterile alcohol daily. The catheter was flushed with heparinised saline (50 units in 5 ml) at least once a day and also whenever blood was taken for investigation, or blood or fluids were administered. At the time of catheter insertion, cloxacillin and gentamicin were given prophylactically and continued for five days.

The line was removed after completion of treatment, or earlier in case of a complication. If the line was removed early it could be pulled out by gentle traction whereas the

dacron cuff had to be separated from the subcutaneous tissue surgically in case of catheters removed late.

Catheter function was graded on a 0-2 scale. Grade 0 represented complete lack of function. Grade 1 was considered when blood could not be withdrawn but infusion could be done. Grade 2 was the optimum function when it could be used for both withdrawal and infusion [6].

Significant hemorrhage was defined as that requiring blood transfusions. Mild hemorrhage was defined as presence of local ooze or hematoma.

Infections were studied prospectively and were correlated with degree of neutropenia. Hickman catheters were considered to be the source of infections when one of the following was present :

(a) The exit site cultures and blood cultures revealed the same organisms and there was active inflammation around the catheter.

(b) Cultures of blood from both, the catheter and a peripheral vein grew the same organism and there was no other source of bacteremia.

(c) Blood cultures of samples drawn from the catheter were positive while peripherally drawn blood was sterile.

The control group were patients who refused to undergo Hickman catheter implantation or those who were ineligible for catheterisation. Their infection and neutropenic patterns were noted and analyzed. Previous data from our centre was also used to compare the pattern of infections in patients prior to the use of Hickman catheter [7].

Results

Patient characteristics

Twenty Hickman catheters were passed in 19 patients over a 19 month period from July 92 to Jan 94. Eighteen patients required only one catheter, while one patient required a second catheter as the first catheter was removed due to infection. The patients profile is shown in Table 1.

TABLE 1
Patients characteristic at catheter placement

	Patient	Control
Number	19 *	20
Sex	11M*/9F	17M/3F
Mean age (range)	29 yr (13-50 yr)	29.6 yr (15-46 yr)
Diagnosis		
Acute Myeloid Leukaemia	12 *	14
Acute Lymphoblastic Leukaemia	3	3
Non-Hodgkin's Lymphoma	4	3
Platelet Count		
< 50,000/mm ³	4	5
< 50,000/mm ³	9 *	8
> 100,000/mm ³	6	7
Neutrophil Count		
< 500/mm ³	3	4
500 to 1000/mm ³	5	4
> 1000/mm ³	12	12

* includes the patient who had 2 catheter insertions

Catheter placement and function

The catheter function is shown in Table 2. In one patient of NHL, the cephalic and external jugular veins were thrombosed due to prior therapy and the catheter was threaded into the inferior vena cava via the right saphenous vein. This catheter provided grade 2 function till the time of patient's death.

TABLE 2
Duration of function and complications of Hickman catheters (n=20)

Duration of function	
Mean	50.5 days
Range	1-266 days
Functional status at removal/death	
Grade 2	13
Grade 1	5
Grade 0	2
Antemortem catheter loss/removal	
Thrombosis	1
Mechanical	1
Infection	3

In 3 patients, the catheter placement was incorrect. In 2 patients, the catheter migrated up into the internal jugular vein. One catheter retained grade 2 function and was used for chemotherapy for 60 days being finally removed for suspected, but undocumented,

Fig. 2 : Hickman catheter placed in opposite subclavian vein with partial thrombosis of veins.

catheter infection. The second catheter was non-functional, and attempts to reposition it the next day were ineffective, requiring removal. A third catheter migrated into the subclavian vein of the opposite side. It retained function for 70 days and was removed on account of thrombosis of left subclavian vein (Fig 2).

The catheters with grade 1 function (partial occlusion) were mainly encountered in the earlier part of the study when the nursing and medical staff were not always conversant with the use of the catheters. With increasing experience the later insertions retained grade 2 function. The longest duration that a catheter was kept in situ was 266 days.

One patient was sent home, after induction, with the Hickman catheter in situ. As daily flushing of the line was not feasible, a higher dose of heparin (5000 units in 5 ml) was used to flush the line prior to discharge. On return after three weeks the line still retained grade 2 function.

Complications

One patient of AML-MI had significant hemorrhage after operation. This patient had a post-operative fall in platelet count to below $30,000/\text{mm}^3$ and developed bleeding from the operation site, the subcutaneous tunnel, and chest wall requiring multiple blood transfusions. Finally the bleeding stopped after a unit of platelet concentrate was transfused.

Two other patients had minor local ooze and swelling, at the incision site, which subsided with local pressure.

These patients had one or more disease-related or chemotherapy-induced episodes of severe neutropenia during the period of catheter use. Majority of the catheter related infections developed in patients who entered early in the study. Exit site infections were seen in 5 cases which subsided with local care and antibiotics. These did not spread along the subcutaneous tunnel. Tunnel infection developed in only 1 case requiring line removal. Bacteremia was documented in 7 cases either ante-mortem (5 cases) or post mortem (multiple microabscesses - 2 cases). Of these, 2 were catheter related while 5 were not catheter related (Tables 3,4).

TABLE 3

Neutropenic duration and infective episodes

	Hickman catheter group (n=19)	Control group (n=20)
Neutropenic period		
Mean duration	29 days	30 days
Range	11-150 days	4-60 days
Number of venepunctures	3 per week	28 per week
Infections		
Exit site infection	5	NA
Tunnel infection	1	NA
Thrombophlebitis	Nil	8
Bacteremia/Sepsis on autopsy*		
Total Number	7	11
Catheter related	2	NA
Non-catheter related	5	NA
Organisms isolated**		
Blood culture		
Staphylococci	1	3
Pseudomonas	3	2
E. coli	2	1
Klebsiella	—	1
Other sites		
(Skin, abscess, urine etc.)		
Staphylococci	2	3
Klebsiella	—	1
Fungus	—	3

*Sepsis on autopsy => disseminated bacterial colonies or microabscesses, NA-Not applicable, **More than one organism isolated in 3 patients.

Controls

The characteristics of controls are as given in Table 1. These patients had one or more episodes of neutropenia, the mean duration of each neutropenic period being 30 days (Table 3). During neutropenia they required repeated venepunctures for blood sampling, and antibiotic and blood administration. The mean number of venepunctures per week was 28, aggravating patients discomfort. They had a high incidence of thrombophlebitis and in 3 patients the venous access was exhausted. Their infection patterns show that staphylococcal infections were commonly attributable to the frequent thrombophlebitis.

TABLE 4
Catheter related infections in early and late patient groups

	Catheter serial number	
	1-10	11-20
Total catheter days	371	639
Exit site infection	3	2
Tunnel infection	1	—
Catheter related bacteremia	1	1
Catheter infection rate per 100 functioning day	1.35	0.47

Discussion

This study shows that the use of Hickman catheters was successful in minimising the need for venepunctures. This resulted in increasing patient comfort, reduction in thrombophlebitis and, consequently, in potential sources of infection. Patients with acute leukemia and other hematological malignancies often develop severe neutropenia [1]. These neutropenic patients invariably get infected often developing bacteremia and septic shock. It is a common experience that peripheral venous access is exhausted in the middle of a treatment schedule when intravenous antibiotic administration is of critical importance. This is often a nightmarish situation for the patient and resident doctors [5]. This situation was avoided in all our cases.

Infections are common in neutropenic patients [1,8]. All our patients had varying periods of severe neutropenia and many developed infections. Indwelling intravenous silastic catheters are associated with an increased risk of bacteremia [8]. Exit-site infections are usually caused by *Staphylococcus epidermidis* or other skin bacteria; tunnel and catheter tip infections are most often due to *S.epidermidis* or *S.aureus* and less frequently due to gram negative rods or other organisms [1]. Gram-negative bacteremias were more common in our Hickman line patients, suggesting a gastrointestinal source. More over these gram-negative bacteremias did not fulfill the criteria for catheter infections. The catheter related infections were more common in the early part of the study. In the latter 10 patients, the catheter related infection rate was 0.46/100 catheter days. This compares favourably with the reported rate (0.30 to 0.49 per 100 catheter days) in other centres abroad [5,6]. This is especially significant as most of these centres use vancomycin or teicoplanin to reduce catheter related staphylococcal infections [9,10]. We could not use these drugs as they are not routinely available. The lower infection rates in the latter part of our study may be attributed to the increasing experience of the paramedical staff in handling the catheters.

In our study, staphylococcal infections were more common in the control group as compared to Hickman line patients. In our previous experience from the centre (July 1990 to January 1992), the commonest single organism that was isolated was also *Staphylococcus* [7]. There was a high incidence of thrombophlebitis in controls and in patients studied in our previous series [7], suggesting that the skin is a common sources of infection in neutropenic patients subjected to multiple venepunctures. Hickman lines helped to reduce this infection.

Nevertheless, these catheters are prone to complications. A uniform technique for catheter insertion and strict adherence to catheter-care guidelines is mandatory [1,6]. Ideally, these should be placed under fluoros-

copy but, our experience suggests that, even without this facility functionally effective lines can be placed in most cases. It should be ensured that platelet counts are adequate and standby donors available, to avoid bleeding complications. Thrombotic catheter obstruction should be prevented by regular flushing with heparin and can be overcome with low-dose fibrinolytic therapy [11].

The present study is our initial experience and it involved concomitant training of the resident doctors, and nursing and paramedical staff. With the experience gained we anticipate a marked reduction in catheter related complications, and the ability to provide our patients with a reliable and safe venous access. These catheters can also be used in patients requiring parenteral nutrition where a subclavian venous catheter must be left in place for several weeks or even longer [12].

REFERENCES

1. Schimpff SC. Infections in the leukemic patient. Diagnosis, therapy and prevention. In : Henderson ES, Lister TA, editors, *Leukemia*, 5th ed, Philadelphia : WB Saunders 1990; 687-709.
2. Broviac JW, Cole JJ, Scribner BH. A silicone rubber atrial catheter for prolonged parenteral alimentation. *Surg Gynecol Obstet* 1973; 136 : 602-6.
3. Hickman RO, Buckner CD, Clift RA et al. A modified right atrial catheter for access to the venous system in marrow transplant recipients. *Surg Gynecol Obstet* 1979; 148 : 871-5.
4. Mehboob B, George M, Rufen I, Advani SH. Right atrial catheters in long term use. An Indian experience. *Indian Journal of Haematology* 1993; 11 : 4-76 (abstract).
5. Hariharan J, Muralidharan, Korula R, Chandy M. Hickman catheter implantation in the treatment of acute leukemia. *J Assoc Physicians India* 1991; 39 : 168-70.
6. Reed WP, Newman KA, de Jongh CA, et al. Prolonged venous access for chemotherapy by means of the Hickman catheter. *Cancer* 1983 ; 52 : 185-92.
7. Kumar Rajat, Srivastava AK, Jaiprakash MP, Anand KP, Akhtar M, Lazar AL. Clinico-etiological spectrum of febrile and infective episodes in acute leukemia. Proceedings of 33rd Annual Conference of Indian Society of Hematology and Blood transfusion, 1992; 54 (abstract).
8. Pizzo PA. Management of fever in patients with cancer and treatment-induced neutropenia. *N Engl J Med* 1993; 328 : 1323-32.
9. Lim SH, Smith MP, Machin SJ, Goldstone AH. A prospective randomised study of prophylactic teicoplanin to prevent early Hickman catheter-related sepsis in patients receiving intensive chemotherapy for hematological malignancies. *Eur J Haematol* 1993; 54 (Suppl) : 10-3.
10. Al-Sibai MB, Harder EJ, Faskin RW, Johnson GW, Padmos MA. The value of prophylactic antibiotics during the insertion of long-term indwelling silastic right atrial catheter in cancer patients. *Cancer* 1987; 60 : 1891-5.
11. Haire WD, Lieberman RP, Edney J. Hickman catheter induced thoracic vein thrombosis : Frequency and longterm sequelae in patients receiving high dose chemotherapy and marrow transplantation. *Cancer* 1990; 66 : 900-8.
12. Haire WD, Lieberman RP. Defining the risks of subclavian vein catheterisation. *N Engl J Med* 1994; 331 : 1769-70.