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Complications of total implantable access ports and efficacy of Taurolidine-citrate lock solution against catheter-related infections

Emine Ince, Pelin Oğuzkurt, Abdulkerim Temiz, Semire Serin Ezer, Hasan Özkan Gezer, Nalan Yazici[1], Akgün Hiçsönmez

ABSTRACT

Background: Totally, implantable access ports (TIAPs) are used for long standing venous catheterization. This study was designed to present our experiences of the TIAPs applications and efficacy of Taurolidine-citrate lock solution (TCLS) against catheter-related infections. **Materials and Methods:** We evaluated records of the 108 patients implanted with 112 TIAPs, which had been performed using heparin solution or TCLS between 2005 and 2013. **Results:** Duration of exposure to TIAPs was 17-2051 days (median: 411 days). The primary diagnoses were solid tumours (n = 57), lymphoma (n = 23), haematologic diseases (n = 23), nephrotic syndrome (n = 4), Hirschsprung disease (n = 1). The right external jugular vein was most frequently used vascular access route (72.3%). Mechanical complications were observed in four cases. TIAPs were removed due to remission in 19 cases and infection in 19 cases. Median time from implantation and to the development of infection was 60 days. Heparin solution had been used for care in 33 ports, whereas heparin and TCLS had been used in 79 ports. Based on statistical comparison, use of TCLS was considered to be an important factor for preventing infection (P = 0.03). **Conclusion:** We consider that TCLS reduces infection prevalence so TIAPs would be used more extensively and effectively to prevent infections.

Key words: Catheter, infection, malignancy, port, Taurolidine-citrate

INTRODUCTION

A safe central venous access is required in paediatric cases for various purposes, including chemotherapy, prolonged antibiotic therapy, frequent blood sampling, parenteral nutrition, and blood transfusion. Totally, implantable central venous catheters have been preferred rather than external catheters because of patient's comfort and low infection rates.[1,2]

Totally, implantable access ports (TIAPs) can be implanted either by puncture or dissection technique. Despite extreme discussions, there is no consensus on which technique is superior to other yet.[3] Internal jugular, subclavian or femoral veins are preferred when puncture technique is used; whereas, external jugular veins (EJVs) or internal jugular veins are preferred for dissection technique.[3-6]

Totally, implantable access ports lead to certain complications, associated with application and care, in long-term follow-up. The most common mechanical complications are catheter obstruction, venous thrombosis, catheter migration, skin necrosis, pocket infection, and catheter-related infection and hematoma in the pocket. Rare complications are catheter rupture, cardiac tamponade, and catheter separation.[3-10] Repeated access causes intraluminal biofilm formation in TIAPs by leading to local and systemic infections.[11]

Catheter-related bacteraemia (CRB) and biofilm-associated infection require antimicrobial therapy together with catheter removal. However, loss of the vein used and cost of catheter removal and reinsertion have raised the need for catheter rescue as much as the clinical condition allows.[12,13] Combination of antibiotic lock therapy and conventional systemic antibiotherapy provides effective treatment and prevention for CRB in some cases for long-term use. Nevertheless, studies on this issue have demonstrated that infection usually causes removal of infected catheter and reinsertion of a new one in about 45-59% of the patients.[12-17]

However, there are several studies about efficacy of Taurolidine-citrate lock solution (TCLS) in different

Departments of Paediatric Surgery, and [1]Pediatric Oncology, Başkent University, Faculty of Medicine, Ankara, Turkey

Address for correspondence:
Dr. Emine Ince,
Başkent University, Faculty of Medicine, Adana Research and Educational Hospital, Departments of Paediatric Surgery, Seyhan Hospital, Baraj Yolu, 1. Durak, Seyhan, Adana, Turkey.
E-mail: inceemine@yahoo.com

diseases, few articles focused on efficiency of TCLS against TIAP infections in literature.[18-21] We intended to evaluate the preferred vascular access route and surgical method for TIAPs as well as risk factors for complications, and care of TIAPs for prevention of infection.

MATERIALS AND METHODS

Cases who admitted to our department between January 2005 and December 2013 for TIAP implantation were retrospectively evaluated in terms of indications, demographic and surgical characteristics and route of venous access, mechanical complications during follow-up period, time elapsed to infection development and isolation of microorganisms from catheter and peripheral blood culture. All cases underwent elective surgery in the same hospital. Hemoglobin (Hb), platelet (Plt) counts and absolute neutrophil count (ANC) levels were preoperatively analysed. Patients with Hb <8 g/dL received erythrocyte suspension, and patients with Plt <50,000/mm^3 underwent thrombocyte transfusion prior to the surgery. Diluted heparin solution (100 IU/mL) was used for care of TIAPs. TCLS which has properties of anticoagulation and prevention of bacterial and fungal growth was used for care of TIAPs after 2007. Efficacy of TCLS (standard solution containing 1.35% Taurolidine and 4% sodium citrate) was also retrospectively evaluated in this study.

The definition of infection was made as follows: Two isolations of coagulase-negative staphylococci or any other positive blood culture from catheter and/or peripheral blood except coagulase-negative staphylococci were defined as CRB stream infection in case of fever and no evidence of other focal infection. Infections were also classified as two groups according to time they were detected; early infections (within the first 8 weeks) and late infections (after the eighth week).

Mono-lumen TIAPs were implanted in all patients under fluoroscopy in operating operation setting. All TIAPs were implanted on the fascia of pectoralis major muscle in the anterior chest wall. All catheters were implanted with standard surgical procedure in to the EJVs or internal jugular veins. Puncture technique was used only for subclavian vein. Deltec (SIMS Deltec, St. Paul, MN, ABD) or Polysite (Perouse Laboratories, Ivry-Le-Temple, France) brand TIAPs were used.

SPSS package program (version 17.0; SPSS Inc., Chicago, IL, USA) was used for the statistical analyses of data. Categorical variables were summarized as number and percentage, whereas continuous variables were summarized as mean and standard deviation (median and minimum-maximum when required). Categorical variables were compared using Chi-square or Fisher's test. Intergroup comparison of continuous measurements was done by Mann-Whitney U-test when the parameters were not distributed normally. Kruskal-Wallis test was used for the comparison of more than two variables. Level of statistical significance was considered to be 0.05 for all tests.

RESULTS

A total of 112 TIAPs were implanted into 108 patients. Sixty-five of the cases who underwent TIAP implantation were male. Median age was 3 years (range 1 month-17years). The diagnosis was solid tumour in 52.7% (n = 57), lymphoma in 20.5% (n = 23), hematologic disease in 20.5% (n = 23), nephrotic syndrome in 3.6% (n = 4), and Hirschsprung disease in 0.9% (n = 1) of the patients [Table 1]. The most common vascular route used for catheter implantation was right EJV in 81 (72.3%) patients. The catheter routes used in patients are shown in Table 2. Four cases (3.6%) developed mechanical complication (skin necrosis), and required re-implantation. The implant was removed due to remission in 19 cases (16.9%) and due to infection 19 cases (16.9%). Thirteen cases died during follow-up due to primary disease [Table 3].

Median duration of TIAPs was 411 days (range 17-2051 days). Catheter infection was detected in

Table 1: Clinical characteristics of patients

Primary diagnosis		*n*	%
Hematologic diseases	ALL	15	13.4
	AML	3	2.7
	Thalasemia	2	1.8
	Hemophagositic Syndrome	3	2.7
Lymphomas	Non-Hodgkin	22	19.6
	Hodgkin	1	0.9
Solid tumors	Neuroblastoma	22	19.6
	Hepatoblastoma	2	2.7
	Rhabdomyosarcoma	6	5.4
	Wilms tumor	6	5.4
	Ewing sarcoma	3	2.7
	Osteosarcoma	2	1.8
	PNET	2	1.8
	Meduloblastoma	8	7.1
	Teratoma	4	3.6
	Pulmoneroblastoma	1	0.9
	Ovarian JG tumor	1	0.9
Others	Nephrotic syndrome	4	3.6
	Hirschsprung	1	0.9
Total		108	100

ALL: Acute lymphoblastic leukemia; NHL: Non-Hodkin lymphoma; AML: Acute myolocytic leukemia; PNET: Primary neuroectodermal

33 patients during follow-up. Early infection (8-56 days, median = 19 days) occurred in 13 TIAPs and late infection (63-430 days, median = 150 days) was detected in 20 TIAPs. Isolated microorganisms from peripheral blood and catheter cultures were summarized in Table 4. Re-infection was detected in 12 patients. The infection rate in whole group was 0.82/1000 catheter days antibiotic therapy was successful for eradication of re-infections. In these cases, TIAPs were not removed due to re-infections. Despite antibiogram-based antibiotic therapy, 19 of TIAPs had to be removed due to treatment failure of early infection in 5 and late infection in 14 patients [Table 4]. In removed TIAPs, heparin and TCLS were used in 13 and 6 patients, respectively.

Age, gender, diagnosis, re-implantation, Hb level, Plt count, ANC, preferred vascular configuration, and diameter of TIAPs were analyzed as risk factors for infection and no statistically significant difference was determined [Table 5]. For the care of TIAPs, heparin solution was used in 33 patients, whereas both heparin solution and TCLS were used in 79 cases [Table 6].

Table 2: Preferred route of venous access

Vein	*n*	%
Right EJV	81	72.3
Right IJV	17	15.2
Left EJV	10	8.9
Left IJV	3	2.7
Left subclavian vein	1	0.9
Total	112	100

EJV : External juguler vein; IJV:= Internal juguler vein

Table 3: Duration of catheters and causes of catheter removal

Maintenance period	Median 411 days (range 17-2051 days)	
Cumulative	62581 days	
Mechanical complication	Skin necrosis over the port	4 (3.6%)
Causes of Explantation	Termination of use	19 (16.9%)
	Death	13 (11.6%)
	infection	Early (≤8 weeks):5
		Late (>8 weeks):14

Table 4: Distribution of blood culture isolates

	Heparin solution (*n* = 33) (%)	Taurolidine-citrate lock (*n* = 79) (%)
Candida albicans	15 (48.2)	6
Coagulase-negative staphylococcus	2(5.9%)	7 (9)
Serratia marcescens	2(5.9)	2 (2.6)
Klebsiella oxytoca	—	2 (2.6)
Acinetobacter	—	1 (1.3)
Total	19 (57.6)	18 (22.8)

*Total infection episodes in 28 patients

Statistical comparison of these solutions revealed that TCLS is a significant factor for the prevention of infections ($P = 0.03$). It was also observed that duration of TIAP use had been significantly increased after infection prevention.

DISCUSSION

Paediatric cases have limited venous accessibility, and cannulation of suitable peripheral veins may be a very painful and terrifying experience to them. Therefore, central venous access is a better option for long-term therapy in children who require long-term intravenous drug administration, chemotherapy, frequent blood sampling, total parenteral nutrition, and regular transfusion.[1,2,22,23] External catheters carry the risk for accidental displacement, injury of outer part, and susceptibility to infections.[1] TIAPs were developed to improve quality-of-life, and unlike external catheters, they have advantages such as lack of dressing, no restriction of patient's daily activities, and relatively low infection rates.[1,2]

Totally, implantable access ports can be implanted either by puncture or dissection. Despite comprehensive discussion regarding best technique for catheter implantation (dissection vs. puncture), no consensus has been reached so far.[3,4] Recently, however, EJV cut-down catheterisation is preferred because of relatively high risk of various post- and intra-operative complications as well as low success rate of first puncture in paediatric cases.[5] EJV can be easily detected among superficial peripheral thick vessels and are located close to the palpable central veins. We as well, primarily preferred the right EJV (72.3%). Other vessels are used when EJV was not available for catheterisation.

The mechanical complications including catheter obstruction, vein thrombosis, pocket hematoma, migrating catheter, catheter rupture, skin necrosis, and cardiac tamponade are observed in 4.5-5.1% of the patients reported in different series.[3-6] We observed skin necrosis over TIAPs reservoir in 4 (3.6%) patients. These patients underwent re-implantation. We eliminated this complication in subsequent years by avoiding extreme subcutaneous dissection and using smaller TIAP reservoir. We did not encounter any other mechanical complication.

Leading causes for catheter removal, other than mechanical complications, include infection and thrombus formation.[24,25] Infection develops due not only to surgical complications, but also to intrinsic

Table 5: The analysis for risk factors in catheter related infections

Variabes	Infection (-) (n = 75)	Infection (+) (n = 37)	P-value
Sex			0.002
Female	39	8	
Male	36	29	
Age	Mean	Mean	0.215
	4.40±4.18 years	4.79±3.83 years	
Diagnosis			0.338
Hematologic disease	16	7	
Lymphoma	13	10	
Solid malignancy	41	16	
Others	5	—	
Diameter of TIAPs			0.278
4.5 Fr	4	2	
5 Fr	30	14	
6.5 Fr	5	4	
7 Fr	31	12	
8 Fr	5	5	
Vein			0.337
Right EJV	58	23	
Right IJV	8	9	
Left EJV	6	4	
Left IJV	2	1	
Left subclavian	1	—	
Hb level	Mean	Mean	0.546
	10.66±1.45	10.43±1.44	
Plt count	Mean	Mean	0.548
	340.74±203.74/mm^3	320.48±21078/mm^3	
ANC	Mean	Mean	0.872
	3.79±3.67/mm^3	2.39±2.82/mm^3	
Re-implantation	4	—	0.454
TIAPs use (days)	Mean	Mean	0.012
	635.69±483.12	402.81±418.32	

P values assessed by Mann–Whitney U test, EJV: External juguler vein; IJV: Internal juguler vein, Hb: Hemoglobin, Plt: Platelet, ANC: Absolute neutrophil count

Table 6: The effectiveness of care solutions

		Heparin solution (n = 33) (%)	Taurolidine-citrate lock (n = 79) (%)	P (Chi square)
Infection	No	17 (51.5)	61 (77.2)	0.03
	Yes	16 (48.5)	18 (22.8)	
Removal due to infection		13 (81.2)	6 (33.3)	0,05

bacteraemia.[12-17] In our series, infection rate of all group (0.8/1000 catheter days) was lower than a study from our country which had been reported as 1.96/1000 catheter days.[26] Besides, no statistically significant relation was observed between infection and age, gender, preferred vascular configuration, diameter of TIAPs, re-implantation, low Hb, ANC, and thrombocyte counts.

In addition to treatment of catheter-related infections, antibiotic lock technique is also used for prophylaxis. This procedure is based upon washing catheter lumen with antibiotic solution and leaving this solution in the lumen. Studies on permanent venous catheters have emphasized the importance of application of this method in neutropenic patients.[11-17] Although, there are reports about efficacy of vancomycin, ciprofloxacin, heparin, linezolid, gentamycin or ciprofloxacin against catheter-related infections, a few studies focused on efficacy of TCLS.[11-21] Simon *et al*. determined that, prevalence of primary TIAP-related infections caused by coagulase-negative *Staphylococcus* and methicillin-resistant *Staphylococcus aureus* had been substantially decreased in paediatric cancer patients with TCLS.[20] TCLS has a broad spectrum antimicrobial activity. In present study, the rate of catheter removal due to infection was 47.4% in heparin used catheters and 7.6% in Taurolidine-citrate used catheters. Statistical comparison revealed that TCLS is an important factor for prevention of infection (P = 0.03). We consider that infection rate is lower in Taurolidine-citrate used group than heparin used group, because of antifungal efficacy of Taurolidine-citrate. In our study, it was also detected that duration of catheter use had been significantly prolonged when infection had been prevented.

In conclusion, use of TIAPs in paediatric cases enhances patient comfort. We consider that TCLS reduces infection prevalence and development, so TIAPs would be used long-term.

CONCLUSION

Catheter-related infection is a very serious complication in paediatric patients. This may lead to catheter removal in some patients. Our study demonstrated the benefit of TCLS which had reduced catheter infection rate and removal due to infection.

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