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Effect of vancomycin as antibiotic lock technique in prevention of catheter associated infection in stem cell transplantation patients

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Abstract:

Introduction: This trial assessed the efficacy of vancomycin lock solution in reducing catheter-related blood stream infections among bone marrow transplantation patients who were transplanted using tunneled catheters.
Methods and Results: patients randomly received either heparin only (control group) or a mixture of 5 mg/ml vancomycin and 2500 U/ml heparin (antibiotic group) as catheter lock solution. Results: The control group, CRBSIs rates per1000 catheter-days was significantly lower (0.1609 vs 6.214 events; p=0.0265, Hazard ratio 4.924 %95 CI of ratio1.238-31.20) and BSI (Blood Stream Infection) rates per 1000 catheter-days was significantly lower (0.2744vs 3.644events; p=0.0073, Hazard ratio 7.209 %95 CI of ratio (0.03205-0.808)). More over, The cumulative infection-free catheter survival was significantly higher (log rank statistic 4.924 p=0.0265) in the antibiotic group and cumulative infection-free survival was significantly higher (log rank statistic 7.209 p=0.0073) in the antibiotic group compared with the control group. There is no significant difference in catheter removal incidence (27.27% in the antibiotic group vs 15.38% in the control group; p=0.245) between the two group.
Conclusion: Vancomycin containing catheter lock solution is effective in reducing CRBSIs incidence and prolonging central vein catheter survival in Hematopoietic stem cell transplantation (HSCT) patients.

Keywords: Vancomycin, Catheter-Related Infections, Bone Marrow Transplantation

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1. Introduction

Central venous catheter (CVC) use has increased substantially, and associated infections have become a frequent complication of CVC use. An estimated 250,000 catheter-related bloodstream infections (CRBSI) occurred annually in the United States [1-4].
In acute care settings, mortality and morbidity rates have declined by as much as 50 percent from 2008 to 2014 due to initiatives designed to prevent these infections [4]; nonetheless, CRBSIs remains a significant cause of morbidity and mortality among patients receiving chemotherapy, parenteral nutrition, and hemodialysis. Infection rates are dependent on the type of CVC used and are reported as the number of bloodstream infections per 1000 intravascular device days. CVC infection rates are highest with short-term non cuffed, non-tunneled, and non-medicated hemodialysis multi lumen catheters and lowest with subcutaneous central venous ports [1]. The prevention and management of CRBSI is a significant health care challenge. CRBSI occurs at an estimated rate of 41,000 infections in US hospitals annually [5]. This rate varies based on hospital bed size, medical school affiliation of the hospital, and type of unit/facility (e.g., burn critical care unit, inpatient medical ward, rehabilitation facility). In US medical and surgical units of any acuity level, the most recent data from 2012 estimate the mean incidence rate of CRBSI at

0.8 to 0.9 per 1,000 central line days[6]. However, patients in both medical and surgical critical care units have a higher overall risk of developing CRBSI compared with inpatient wards with only 0.15-0.17 [6]. Among critically ill patients, those in burn units or long-term care acute hospitals are at exceptionally high risk of developing CRBSI (mean rates of 3.4 and 1.6 CRBSI per 1,000 central line days, respectively). While overall CRBSI rates appear to have decreased in the last 10-15 years, they remain as a substantial cause of morbidity and mortality in the health care system[7]. Clinical practice guidelines recommend antibiotic lock therapy(ALT) for both prevention and treatment of catheter-related infections (CRI) (8,9). Guidelines from the Centers for Disease Control and Prevention (CDC) recommends ALT as prophylaxis for patients with long-term catheters and a history of multiple CRI despite maximal efforts to follow the aseptic technique [8]. Guidelines from the Infectious Disease Society of America (IDSA) for the diagnosis and management of CRI recommend antibiotic lock as adjunctive therapy specifically for catheter salvage in cases where the catheter is not removed [9].

Intravascular catheters and other implanted medical devices routinely develop microbial biofilms on their inert surfaces. A biofilm is defined as a microbial community with cells attached to a substratum or each other and embedded in a matrix of extracellular polymeric substances (EPS), or glycocalyx. EPS density varies within the biofilm itself, appearing densest in deeper layers immediately surrounding the colonies of microorganisms. Its density decreases in more superficial layers, leading to the formation of water channels in and around the biofilm matrix [10]. Such channels allow for the transfer of nutrients, waste products, quorum-sensing molecules, and other substances (including antibiotics), similar to the function of a circulatory system in a multicellular organism. Biofilms represent a form of adaptive resistance resulting in a significant reduction of antibiotic susceptibility by 10 to 1,000-fold(based on minimal inhibitory concentrations [MIC]). Biofilms may slow the distribution of antibiotics via charge interaction, size exclusion, the viscosity of the matrix, and possible adsorption. EPS may also inactivate antibiotic molecules before reaching biofilm cells [11]. The extent of penetration varies widely (range 0%-100%), being excellent with agents such as fluoroquinolones and rifamycins, variable with beta-lactams and vancomycin, and attenuated with aminoglycosides [11]. In the general antibiotic lock, solutions is combined from a highly concentrated antibiotic (100-1000 times planktonic MIC) with an anticoagulant to allow local instillation into the catheter lumen. The solution is allowed to dwell or is “locked” while the CVC is not used to prevent colonization or sterilize a previously infected catheter. ALT is often utilized in clinical practice in a prophylactic modality to prevent luminal colonization and subsequent CRBSI. This study has demonstrated significant benefit in hemodialysis-dependent patients and those with indwelling CVC for intravenous (IV) chemotherapy and total parenteral nutrition (TPN)[12,13,14]. ALT is also an option in the management of CRBSI as an adjunct to systemic antibiotics, increasing rates of catheter salvage [12, 15]. Although there is wide variability in clinical utilization of ALT among infectious diseases specialists, nearly 40% report attempting catheter salvage with ALT [16].

2. Materials *&* Methods

This randomized prospective clinical trial compared vancomycin-heparin lock with heparin as a central vein catheter lock. This study was conducted at the BMT ward of Talegani Hospital, Shahid Beheshti University of Medical Sciences, between February 2017 and January 2018. All patients whom were Candidate HSCT and recently underwent tunneled CVC (ARROW) insertion through the Internal Jugular vein were included in this study.

Patients were using Permuted Block Randomization assigned to either antibiotic or control group. The exclusion criteria consisted of patients with active infection within one week before entering the study, patients who received other antibiotics, or those with known vancomycin hypersensitivity. The antibiotic group received vancomycin-heparin lock solution. This solution was a mixture of 5 mg/ml vancomycin and 2500 U/ml unfractionated heparin. Patients in the control group received a solution containing only heparin common in the BMT ward of this hospital. When catheter accessibility was allowed, the catheter lumen was flushed with 5 ml of normal saline solution and then was locked for a minimum of 8 hours to 24 hours per day. Ideally, the solution may be locked in situ whenever the CVC is not in use. Catheter access often limits the dwell time, especially when the CVC is used for IV antibiotics and other systemic therapies. The nurse responsible for medication administration should be actively engaged to ensure the replacement of lock solution if interruption of the dwell is required. Catheter capacity described by the manufacturer determined total volume (usually 2 ml for tunneled and 3-5 ml for implanted ports). The nurses were trained to ensure proper profiling of the ALT, and certain factors were considered: 1) the number of lumen for the Specific CVC and 2) IV therapies scheduled for administration through the CVC (especially any continuous IV infusion). In cases of multi-lumen CVC, the optimal scenario is to lock all lumen with the antibiotic solution. If a continuous IV fluid was being administered in a patient with multiple lumens, the nurse was instructed to rotate lumens every 12-24 h. alternating the lock solution

to allow for exposure of each lumen to the ALT. This might be a significant challenge, and proper labeling of CVC lumens would be helpful to identify a rotation schedule. However, if a significant number of scheduled IV therapies are expected, an attempt should be made for co-administration wherever possible (based on known compatibility data).

Alternatively, holding continuous infusions like fluids or TPN for brief (24-36 hours) periods initially or changing the administration to a peripheral IV access may be viable options in select patients [17]. Patients in the antibiotic group were subsequently divided into two subgroups. Both the lumens were locked for 8 hours in one subgroup, and in the other subgroup, the lumens were alternatively locked for 8-24 hours. The patients were observed for 21 days after recent catheterization. Catheters were not used during ALT. The pharmacist prepared Lock solutions every 72 h. Vancomycin-heparin solutions are stable for 72 h at room temperature based on Antibiotic Lock Solution Therapy Guideline [18]. The patients were evaluated for adverse drug reactions and dermatologic complications such as skin rash, pruritus, and other rare adverse effects such as Stevens-Johnson syndrome or erythema multiform during ALT. The patients were followed up for 21 days unless one of the following events occurred: (1) unexpected catheter removal; (2) the patient was expired; or (3) discharge before the end of the study period. The major endpoint of the study was the incidence of CRBSIs between the two comparative groups, based on the classification by the Center for Disease Control (CDC) of the United States has introduced the term laboratory-confirmed bloodstream infection (LCBSI) [19].

Patient has a documented pathogen cultured from one or more blood cultures and organism grown from blood is not associated with an infection at another site or Patient has at least one of the following signs or symptoms: fever (>38 °C), chills, or hypotension and signs and symptoms and positive laboratory results are not linked to an infection at another site and at least one of the following: a. frequent skin contaminant is cultured from two or more blood cultures collected on separate occasions. b. common skin contaminant is cultured from at least one blood culture from a patient with an intravascular line, and the clinician institutes appropriate antibiotic therapy. c. positive antigen test on blood. CRBSI should be suspected when bloodstream infection occurs in a central venous catheter setting with no other apparent source.

Fever is the most sensitive clinical manifestation, although the specificity is poor. Inflammation or purulence at the insertion site has great specificity but poor sensitivity [20,21].

Other clinical manifestations include hemodynamic instability, altered mental status, catheter dysfunction (as occurs with intraluminal clot), and clinical signs of sepsis that start abruptly after catheter infusion. Complications related to bloodstream infection (suppurative thrombophlebitis, endocarditis, osteomyelitis, metastatic infection) may also be observed. Based on guidelines, catheter-related infection criteria: Bacteremia or fungemia in a patient who has an intravascular device and >1 positive blood culture result obtained from the peripheral vein, clinical manifestations of infection (e.g., fever, chills, and hypotension), and no apparent source for bloodstream infection (except for the catheter). One of the following should be present: a positive result of semiquantitative (>15 CFU per catheter segment) or quantitative (>102 CFU per catheter segment) catheter culture, Whereby the same organism (species) is isolated from a catheter segment and a peripheral blood culture; simultaneous quantitative cultures of blood with a ratio of >3:1 CFU/ml of blood (catheter versus peripheral blood); differential time to positivity (growth in a culture of blood obtained through a catheter hub is detected by an automated blood culture system at least 2 hours earlier than a culture of simultaneously drawn peripheral blood of equal volume)[22]. Catheter colonization (CC) was defined as the growth ≥ 15 organisms in the lumen of the catheter without any evidence of fever. After diagnosing CRBSIs, infection treatment was the responsibility of related individual physicians, and we had no special responsibility for patient management according to the study protocol.

2.1. Statistical analysis

All analyses were performed on an intention-to-treat using SPSS software (version 20.0). Data are represented as mean ± standard error of the mean (SEM) or as medians (ranges). The normal distribution of quantitative variables was assessed by Kolmogorov- Smirnov test. The student's t-test, Mann-Whitney U-test, chi-square, Fisher Exact, two-way ANOVA test analyses were used. CRBSIs rates (CRBSI events for 1000 catheter-days and BSI events for 1000 catheter-days) were compared using the log-rank test. The cumulative infection-free catheter was determined using the Kaplan-Meier method. P-value<0.05 were considered statistically significant.

3. Results

Baseline characteristics of the patients

Figure 1 shows patients' recruitment in the study. One-year follow-up period was completed by 33 patients in the antibiotic group and 39 patients in the control group. All patients had tunneled CVC (Arrow) internal jugular vein. All relevant baseline characteristic of the patients in the antibiotic and control groups have been shown in Table 1.

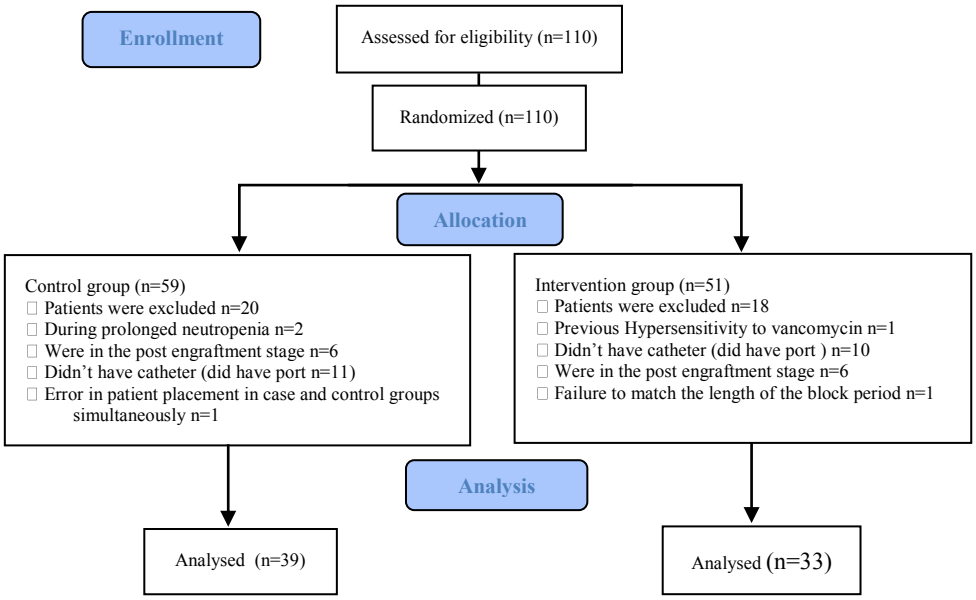

Figure 1. Trial Profile

Table 1. Demographic, clinical and laboratory characteristics of the patients at the initiation of the study.

Variable	Case	control	P value
Age(years)	44.11±14.23	41.97±13.37	0.2
Sex(male)n(%)	18(41.9%)	25(58.1%)	0.4
Sex(female)n(%)	15(51.7%)	14(48.3%)	0.4
BMI(Kg/m^2)	24.31±0.9152	26.61±0.9450	0.0868
Type of disease			
MM	17(51.51%)	15(38.46%)	
HD	6(18.18%)	9(23.08%)	
AML	3(9.09%)	18(20.51%)	
ALL	4(12.12%)	3(7.69%)	0.086
NHD	2(6.06%)	3(7.69%)	
GCT	1(3.03%)	0	
AA	0	1(2.56%)	
Type of Transplant			
Autologous	28(84.85%)	26(66.66%)	0.08
Allogen	5(15.15%)	13(33.33%)	
Blood type			
O	13(41.9%)	11(3.06%)	
A	9(29%)	11(3.06%)	0.5
B	8(25.8%)	10(27.8%)	
AB	1(3.2%)	4(11.1%	

No statistically significant differences were found between the two groups in terms of demographic data (age, sex), underlying type of disease, type of blood group, and type of transplant. Data including type of central venous catheter, date of catheter insertion, start date of the block, peripheral blood culture, Catheter culture, Day's fever number, Number of days to receive systemic antibiotic and their type, the number of days the GCSF ainjection? received on neutropenic days, Duration of hospitalization were collected to be compared between the group. In the patients, the catheter placement and volume of lumen were identical. Redness and infection around the catheter were checked and reported by nurses. During the study period 110 consecutive cases were evaluated. 38 cases were excluded for ALT: 1 due to Previous Hypersensitivity to vancomycin, 21 Didn't have catheter (did have port), 2 were prolonged neutropenia (>10 days), 12 Were in the post engraftment stage, 1 Error in patient placement in case and control groups simultaneously, and 1 failure to match the length of the block period. 72 patients were analyzed (Figure 1). We included 72 HSCT patients with a newly inserted jugular internal CVC. Each patient was obseveed for 21 days from new catheterization by pharmacists. A total of 1512 catheter-days were analyzed. 693 catheter-days in the antibiotic group and 819 catheter days in the control group. CRBSI developed in 6 patients (15.38%)in control group but in antibiotic group, no case was observed. CRBSIs rates per 1000 catheter-days were 0.1609 events in the antibiotic group versus 6.214 events in the control group (p=0.0265). CRBSIs rates per 1000 was significantly lower (p=0.0265). BSI rates per 1000 catheter-days were 0.2744 events in the antibiotic group versus 3.644 events in the control group (p=0.0073).

BSI occurred in 17 patients (43.59%) in control group and 4 patients (12.12%). BSI s rate per 1000 catheter-days was significantly lower (0.274 vs 3.644; p=0.0085). Colonization catheter occurred in 1(3/03%) in 1 patient in case group and 6 (15.38%) patients in control group (p=0.115). In 3 cases , two culture of both blood and catheter's tip contained Staphylococcus epidermidis and in 2 cases Pseudomonas were isolated. In one case Staphylococcus epidermidis was isolated from catheter's tip and isolated E.coli from blood culture. we divided case group to sub group.one group were blocked for 8 hours two lumens. Another group blocked for 24 hours

one lumen. We observed two groups. BSI occurred in 4(25%) patient whom the dwell-time was shorter and the one didn't occurred BSI (p=0.0445). Duration of hospitality in case group was s significantly lower than control group (26.30±0.6735 vs 31.17±1.216, p=0.001). mortality didn't occurred in case group but occurred in 4 patients in control group (p=0.1197), although the cause of death was not CRBSI. The hospitalization days in patients whom received systemic antibiotic and vancomycin in case group was significantly lower than one? (135 vs 221, 95%CI 1.147-1.673, RR=1.385,P=0.0001) and systemic vancomycin (RR=2.162,1.007-4.673, P=0.0484). The difference in catheter removal between two groups didn't reach statistical significance (p=0.245).

Catheter survival analysis

Cumulative infection-free catheter survival was significantly higher in the antibiotic group compared with the control group (log-rank statistic 4.924; p = 0.0265) that was comparable to the reported (log-rank statistic 4.95; p=0.026)(36) (Table2&Figure 2). The microorganism causing CRBSI, and BSI are displayed in Table 3.

Table 2. Comparing catheter-related blood stream infections

variable	case	control	pvalue
CRBSIs rate per 1000catheter-day	0.1609	6.214	0.0265
BSIs rate per 1000 catheters day	0.2744	3.644	0.0073
Catheter Colonization	3.03	6(15.38)	0.115
Duration of hospitality	26.30±0.6735	31.17±1.216	0.001
Death	0	4	0.1197
Systemic antibiotic in 21-days(day)	135/693	221/819	0.0007
Systemic vancomycin	9/693	23/819	0.0484
Systemic Gram-positive	19/693	60/819	<0.0001
Systemic Gram-negative	61/693	148/819	<0.0001
Catheter-removal	27.27	15.38	0.245
Fever(in 21 days)	37.03±0.05108	37.22±0.07288	0.0411
Neutropenia_days	163/693	210/819	0.3692
WBC in engraftment-day	1774±2157	37469±3838	0.1908
Hb	9.530±0.2119	10.05±0.2409	0.1133
plt	31697±2157	37469±3834	0.1908

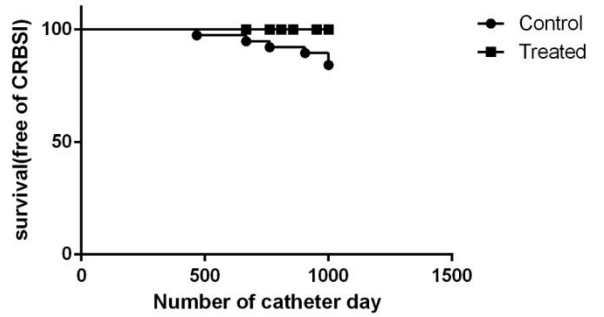

Figure 2. Comparing patients free of catheter-related blood stream infections between the two groups

Table 3. Microorganism isolated in catheter-related blood stream infection.

Type of MO	Blood culture		Catheter's Tip culture		Both blood and catheter's Tip culture	
	case	control	case	control	case	control
Staphylococcus aureus	2	0	0	0	0	0
Staphylococcus non-hemolytic	1	1	0	0	0	0
Staphylococcus epidermidis	1	9	1	2	0	3
Escherichia coli	0	2	0	0	0	2
Acinetobacter	0	2	0	0	0	0
Klebsiella	0	1	0	0	0	0
Pseudomonas aeruginosa	0	2	0	2	0	0

According to the study group, Kaplan- Meier curves show survival on time to the first Episode of infection (figure 3). In figure 4, patients free of bloodstream infections between the two groups of the study were compared.

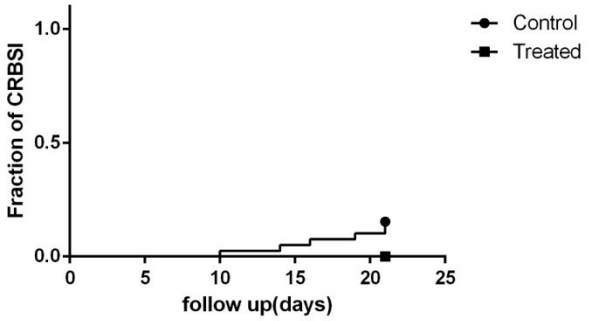

Figure 3. Kaplan-Meier curves for the time to a first Episode of infection according to study Group

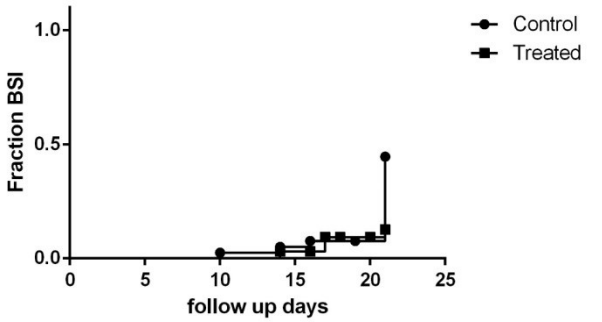

Figure 4. Comparing patients free of blood stream infections between the two groups of study

4. Discussion

in this study, vancomycin lock solution was introduced as an option to prevent CRBSI in HSCT patients. This study showed that an antimicrobial-lock solution containing vancomycin- heparin reduces the rate of CRBSIs and BSI. although vancomycin lock solution reduced the incidence of catheter colonization, the difference didn't reach statistical significance (p=0.115). This result may be due to the limitation of sample size. The optimal dwell time for ALT is unclear; however, most clinical studies have proposed a minimum of 8 hours per day, with targets of >12 per to achieve optimal sterilization [23,24]. The study results showed that the longer dwell time is more effective in reducing BSI (P=0.0445). Bloodstream infection associated with the central venous catheter (CVCs) can be attributed to four primary sources: colonization from the skin, intraluminal or hub contamination, secondary seeding from a bloodstream infection, and, rarely, contamination of the infusate.

The most common source of CVC-related infections is the colonization of the intracutaneous and intravascular portions of the catheter by microorganisms from the patient's skin and occasionally the hands of the healthcare worker (on insertion or as a result of manipulation) [25-27]. Furthermore, many studies have found a strong correlation between heavy skin colonization and catheter colonization and subsequent catheter-related infection, especially with short-term intravascular devices [26,28-30]. Microorganisms gain access to the catheter wound and migrate along the catheter-subcutaneous tract into the fibrin sheath surrounding intravascular catheters (31). The deposition of biofilm on vascular catheters' external and internal surfaces is thought to play an important role in colonization. A combination of host factors produces the biofilm (e.g., fibrinogen and fibrin) and microbial products (e.g., glycocalyx or "slim"). Thus, it is not surprising that common skin commensals such as S.aureus and coagulase-negative staphylococci are often isolated from colonized catheters and patients with primary bloodstream infections. Intraluminal and/or hub contamination is an essential source of bloodstream infection in patients with centrally inserted CVCs that are in place for more than two weeks or in patients with surgically implanted devices [32-35]. We undertook this study to determine whether the use of vancomycin-heparin lock for HSCT patients with CVC could provide an effective way to reduce complications such as infection, duration of hospitalization, catheter colonization, fever, treatment cost, morbidity, and mortality. these complications limit their long-time use in developing countries such as Iran, and we performed vancomycin-heparin lock as a long-term and low-cost alternative means of reducing the CRBSIs rate. Moghaddas et al., in 2015, during a study for prevention of hemodialysis catheter-related bloodstream infection, used Trimethoprim/ Sulfamethoxazole lock. Their study was conducted at HD wards of three hospitals. Forty-six patients in the antibiotic group and 41 patients in the control group were followed for six months. All dialyzed patients by tunneled cuffed HD catheter three times a week for four hours in each dialysis session were included. After each HD session, the lumen of the dialysis catheter was flushed by 10 ml of normal saline solution and then was locked for the whole inter-dialytic period. Their study showed a reduction of CRBSI rate per 1000 catheter-days in the antibiotic group (0.58 vs. 4.4; p=0.002) [36]. In this study, the CRBSIs rate per 1000 catheter-days was 6.214 in the control group, which is comparable to the reported rate of 6.8 events by another epidemiologic research. The reported pooled incidence of central line-associated BSI across 422 ICUs in 36 countries in Latin America, Asia, Africa, and Europe from 2004 to 2009 was substantially higher, 6.8 events per 1000 central line days [45]. Many of these sites are resource-limited areas, and the high incidence is related to a lack of official regulations regarding catheter care. In the present study, the application of vancomycin-heparin lock solution reduction in CRBSIs rate and CRBSIs-free survival. Weijmer et al., during a well-designed study in 2005, using a catheter-lock solution containing trisodium citrate 30% as an antimicrobial agent in 291 catheters (33.7% tunneled), reported a 75% reduction in CRBSIs episodes [37]. In this study, 72 catheters (newly inserted) resulted in an 82% reduction in BSIs episodes and a considerable reduction in CRBSIs rate and CRBSIs-free survival. O'Horo JC in 2011 in a meta-analysis of five observational studies and the randomized trial above, a smaller proportion of patients treated with ALT plus systemic antibiotics required catheter replacement (10 versus 33 percent with systemic antibiotics alone, odds ratio 0.20, 95% CI 0.10-0.39) [39]. Andris et al suggested the possibility of using various types of antibiotics in antibiotic-lock technique in an in vitro model of TPN catheter and found a significant reduction in intraluminal bacterial colonization after several known antibiotic installations [38]. Data on the efficacy of antibiotic lock therapy are limited mainly to small observational studies that are generally supportive of ALT for catheter-related bloodstream infection (CRBSI) in various patient populations (hemodialysis, total parenteral nutrition, and oncology) [40]. The critical point is that any reduction in CRBSI rate is associated with less antibiotic exposure to patients. This study showed the reduction of CRBSI, CC, BSI, thereby decreasing the overall need for systemic antibiotics (RR=1.385, %95 CI 1.147-1.673, p=0.0007). Vancomycin combination with heparin has been evaluated in several in vitro and clinical studies. Compatibility with heparin has been consistently demonstrated at vancomycin concentration <10 mg/ml.

As previously described, vancomycin activity against established biofilms is concentration dependent. In this study Staphylococcus aureus and Staphylococcus epidermidis were the most isolated microorganisms, and vancomycin is a glycopeptide antibiotic and effective on them.

In this study, there were no reported vancomycin-resistant microorganisms, but low-level antibiotic exposure may potentially increase the risk of resistance [41,42].

However, we should weigh this concern against findings that routine prophylactic use of ALT may reduce the general rate of CRBSI, thereby decreasing the overall need for systemic antibiotic therapy [43,44]. Many antibiotics have been evaluated for clinical use, with the largest body of data available for vancomycin and gentamicin. To ensure optimal clinical outcomes with ALT, clinicians should consider common technical questions and logistical challenges in advance. These include lock preparation procedures, additives (e.g., heparin, citrate, or EDTA), the timing of initiation and therapy duration, dwell time and catheter accessibility, and risks associated with ALT. This study suffers several limitations. Although there were no adverse reactions due to vancomycin toxicity, drug level monitoring to identify systemic exposure to antibiotics was not carried out in this study. The second limitation is the absence of a control group. The control group in our study received heparin with a low concentration based on a routine in the BMT ward. Without a doubt, a multicenter design would have enabled the inclusion of larger sample size and lent more strength to the conclusion.

5. Conclusion

This study suggests that vancomycin-heparin lock is highly effective in reducing CRBSIs incidence and Catheter colonization, BSIs incidence among HSCT patients with central vein catheter (CVC). Further studies are required to determine the optimal drug regimen and concentrations for vancomycin antibiotic lock technique.

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Conflict of interest

None.

Ethics

The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (SBMU).
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References

1. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with differernt intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc 2006;81;1159.
2. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52:e162.
3. Berenholtz SM, Lubomski LH, Weeks K,et al. Eliminating central line-associated bloodstream infections: a national patient safety imperative. Infect Control Hosp Epidemiol 2014;35:56.
4. Centers for Disease Control and Prevention. Helathcare-associated Infections (HAI) Progress Report. http://www.cdc.gov/hai/progress-report/index.html(Accessed on January 03,2018).
5. Centers for Disease Control and Prevention(CDC). Vital Signs. Making Health Care Safer: Reducing Bloodstream Infections. Available from: http://www.cdc.gov/VitalSigns/pdf/2011-03-vitalsigns.pdf. Accessed May 10,2014.
6. Dudeck MA, Weiner LM, Allen-Bridson K, et al. National Helathcare Safety Network (NHSN) report, data summary for 2012, Device-associated module. Am J Infect Control.2013;41(12):1148-1166.
7. Centers for Disease Control and Prevention(CDC). Vital Signs: Central line-associated bloodstream infections-United States,2001,2008,and 2009.MM20WR Morb Mortal Wkly Rep.2011;60(8):243-248.
8. Centers for Disease Control and Prevention(CDC), Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011. Atlanta,GA: Centers for Disease Control and Prevention; 2011. Available from:http://wwww.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf. Accessed May 10, 2014.
9. Mermel LA, Allin M, Bouza E,et al. Clinical practice guidlines for the diagnosis and managment of intravascular catheter-related infection:2009 Update by the Infections Diseases Society of America. Clin Infect Dis.2009;49(1):1-45.
10. Costerton JW, Lewandowski Z, Debeer D, Caldwall D, Korber D, James G. Biofilms,the customized microniche.J Bacteriol 1994;176(8):2137-2142.
11. Jefferson KK, Goldmann DA, Pier GB. Use of confocal microscopy to analyze the rate of vancomycin penetration through Staphylococcus aureus biofilms. Antimicrob Agents Chemother, 2005;49(6): 2467-2473.
12. Mermel LA, Allon M, Bouza E,et al. Clinical practice guidlines for the diagnosis and managment of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis.2009;49(1):1-45.
13. Maiefski M, Rupp ME, Hermsen ED.Ethanol lock technique: review of the literature. Infect Control Hosp Epidemiol. 2009;30(11):1096-1108.
14. Jaffer Y,Selby NM, Taal MW, Fluck RJ, McIntyre CW. A meta-analysis of hemodialysis catheter locking solutions in the prevention of catheter-related infection. AM J Kidney Dis. 2008;51(2):223-241.
15. O'Horo JC, Sliva GL, Safdar N. Anti-infective locks for treatment of central line-associated bloodstream infection: a systematic review and meta-analysis. Am J Nephrol.2011;34(5):415-422.
16. Polgreen PM, Beekmann SE, Dickema DJ, Sheretz RJ. Wide variability in the use of antimicrobial lock therapy and prophylaxis

among infectious diseases consultants. Infect Control Hosp Epidemiol.2010;31(5):554-557.
17. Messing B, Man F, Colimon R, Thuillier F, Beliah M. Antibiotic-lock technique in affective treatment of bacterial catheter-related sepsis during parenteral nutrition. Clin Nutr. 1990;9(4):220-225.
18. Stand ford Hospital and Clinics,Pharmacy Department Policies and Procedures /Antibiotic Lock Therapy Guideline. Issue date:06/2011. Review/Revise Date:01/2015
19. National Healthcare Safety Network. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-Central Line-Associated Blood stream Infection). http://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf(Accessed on November 16,2015).
20. Maki, DG, Mermel, LA. Infections due to infusion therapy. In: Hospital infections, Bennett JV, Brachman PS(EDS), Lippincott-Raven, Philadelphia, PA 1998. P.689-724.
21. Safdar N, Maki DG. Inflammtion at the Insertion site is not predictive of catheter-related bloodstream infection with short-term, noncuffed central venous catheters. Crit Care Med 2002; 30:2632.
22. Pearson ML. Guidline for prevention of intravascular device-related infections. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1996; 17:438-73. Reporduced with permission from: Mermel, LA, Allon, M, Bouza, E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 uptodate by the Infectious Disease Society of America. Clin Infect Dis 2009;49:1.
23. Segarra-Newmham M, Martin-Cooper EM. Antibiotic locktechnique: a review of the literature.Ann pharmacother. 2005;39(2):311-318.
24. Fernandez-Hidalgo N, Almirante B, Calleja R, et al. Antibiotic-lock therapy for long-term intravascular catheter-related bacteraemia: results of an open, non-comparative study. J Antimicrob Chemother. 2006;57(6):1172-1180.
25. Snydman DR, Gorbea HF, Pober BR, et al. Predictive value of surveillance skin culturs in total –parenteral-nutrition-related infection. Lancet 1982;2:1385.
26. Bjornson HS, Colley R, Bower RH, et al. Association between microorganism growth at the catheter insertion site and colonization of the catheter in patients receiving total parenteral nutrition. Surgery 1982; 92:720.
27. Cooper GL, Hopkins CC. Rapid diagnosis of the intravascular catheter-associated infection by direct Gram staining of catheter segments. N Engl J Med 1985; 312:1142.
28. Raad II, Baba M, Bodey GP. Diagnosis of catheter-related infections: the role of surveillance and targeted quantitative skin cultures. Clin Infect Dis 1995; 20:593.
29. Guidet B, Nicola I, Barakett V, et al. Skin versus hub cultures to predict colonization and infection of central venous catheter in tensive care patients. Infection 1994;22:43.
30. Armstrong CW, Mayhall CG, Miller KB, et al. Clinical perdictors of infection of central venous catheter used for total parenteral nutrition. Infect Control Hosp Epidemiol 1990;11:71.
31. Raad I, Costerton W, Sabharwal U, et al. Ultrastrutural analysis of indwelling vascular catheters: a quantitive relationship between luminal colonization and duration of placement. J Infect Dis 1993; 168:400.
32. Liñares J, Sitges-Serra A, Garau J, et al. Pathogenesis of catheter sepsis: a prospective study with quantitative and semiquentitative cultures of catheter hub and segments. J Clin Microbiol 1985:21:357.
33. Tenney JH, Moody MR, Newman KA, et al. Adherent microorganisms on luminal surfaces of long-term intravenous catheters. Importance of Staphylococcus epidermidis in patients with cancer. Arch Intern Med 1986; 146:1949.
34. Miller JJ, Venus B, Mathru M. Comparison of the sterility of long-term central venous catheterization using single lumen, triple lumen, and pulmonary artery catheters. Crit Care Med 1984; 12:634.
35. Salzman MB, Isenberg HD, Shapiro JF, et al. A prospective study of the catheter hub as the portal of entry for microorganisms causing catheter-related sepsis in neonates. J Infect Dis 1993; 167:487.
36. Moghaddas A, Abbasi MR, Gharekhani A, Dashti-Khavidaki S, Razeghi E, Jafari A, Khalili H. Prevention of hemodialysis catheter-related blood stream infections using a cotrimoxazole-lock technique. Future Microbiol. 2015;10(2):169-78. doi: 10.2217/fmb.14.116.
37. weijmer mc ,van den Dorpel Ma,Van de VenPJetal.Randomized,clinical trial comparison of trisodium citrate30 %and heparin as catheter-lock solution in hemodialysis patients.J.Am.Soc.Nephrol.16(9),2769-2777(2005
38. AndrisDA,Krzywda EA,Edmiston CE,Krepel CJ,GohrCM,Elimination of intraluminal colonization by antibiotic lock in silicone vascular catheter,Nutrition 14(5),427-432(1998).
39. O'Horo JC, Silva GL,Safadr N. Anti-infective locj for treatment of central line-associated bloodstream infection: a systematic review and meta-analysis. Am J Nephrol 2011; 34:415.
40. Messing B, Peitra-Cohen S, Debure A, et al. Antibiotic-lock technique: a new approach to optimal therapy for catheter-related sepsis in home-parenteral nutrition patients. JPEN J Parenter Enteral Nutr 1988; 12:185.
41. Chatzinikolaou I, Zipf TF, Hanna H,et al. Minocycline-ethylene-diaminetetraacetate lock solution for the prevention of implantable port infection in children with cancer. Clin Infect Dis. 2003;36(1):116-119.
42. Feely T, Copley A, Bleyer AJ. Catheter lock solutions to prevent blood stream infections in high-risk hemodialysis patients. Am J Nephrol.2007;27(1):24-29.
43. Abbas SA, Haloob IA, Taylor SL,et al.Effect of antimicrobial locks for tuuneled hemodialysis catheters on blood stream infection and bacterial resistance: a quality improvement report. Am J Kidney Dis. 2009;53(3):492-502.
44. Landry DL, Braden GL, Gobeille SL,Haessler SD, Vaidya CK, Sweet SJ. Emergence of gentamycin-resistant bacteremia in hemodialysis patients receiving gentamycin lock catheter prophylaxis. Clin J Am Soc Nephrol.2010;5(10):1799-1804.
45. Rosenthal VD, Bijie H, Maki DG, et al. International Nosocominal Infection Control Consortium (INICC) report, data summary of 36 countries for 2004-2009. Am J Infect Control 2012; 40:396.