Chlorhexidine gel dressing in hematopoietic stem cell transplantation

Curativo gel de clorexidina no transplante de células-tronco hematopoéticas

Vendaje gel de clorhexidina en el trasplante de células madre hematopoyéticas

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Abstract

Objective: Monitor the use of chlorhexidine gel dressing in the central venous catheter of children and adults submitted to hematopoietic stem cell transplantation (HSCT) to check for catheter-related bloodstream infection and skin irritation while using this dressing.

Methods: This is a prospective observational study with 25 patients with central venous catheters (CVC) inserted for hematopoietic stem cell transplantation. Dressing characteristics, skin characteristics, clinical conditions of patients and infection-related characteristics were evaluated daily. Patients were monitored from the first day of CVC insertion until removal, up to 45 days from the CVC insertion date.

Results: Catheter-related bloodstream infection (CRBSI) occurred in 28% of all patients, with an association between febrile neutropenia and infection ($p<0.01$). Skin irritation was identified in 24% of patients. No association was found between catheter-related bloodstream infection and skin irritation ($p=0.51$). A significant association was observed between skin irritation and dressing removal ($p=0.03$). Unscheduled dressing changes corresponded to 50% of all dressing changes identified during the study, and the main reason was presence of blood in the dressing (57.8%).

Conclusion: Using chlorhexidine gel dressing in patients submitted to HSCT proved to be an effective measure to reduce the occurrence of catheter-related infections, when compared to literature data. The cases of CRBSI found in this study were mainly associated with the condition of neutropenia, which is very common in this population. The cases of dressing-related skin irritation and presence of blood as the main reason for unscheduled change highlight the importance of nurses having proper knowledge about how to use this dressing in order to create protocols for safe dressing use and handling.

Resumo

Objetivo: Acompanhar o uso do curativo gel de clorexidina em cateter venoso central de crianças e adultos submetidos ao transplante de células-tronco hematopoéticas para verificar a ocorrência de infecção da corrente sanguínea relacionada ao cateter e irritação cutânea na vigência deste curativo.

Métodos: Estudo observacional e prospectivo, com 25 pacientes com cateter venoso central inserido para realização do transplante de células-tronco hematopoéticas. Diariamente avaliou-se as características do curativo, da pele, clínicas do paciente e relacionadas a infecção. Os pacientes foram acompanhados a partir do primeiro dia da inserção do CVC até a sua remoção, até o limite de 45 dias a partir da data de inserção do CVC.

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Conflict of interest: none to declare.

Resultados: A infecção da corrente sanguínea relacionada ao cateter ocorreu em 28% dos pacientes, houve associação entre neutropenia febril e infecção (p<0,01). A irritação cutânea foi identificada em 24% dos pacientes. Não foi identificada associação entre infecção da corrente sanguínea relacionada ao cateter e a irritação cutânea (p=0,51). Houve associação significativa entre irritação cutânea e suspensão do uso do curativo (p=0,03). As trocas não programadas ocorreram em 50% das trocas identificadas e o principal motivo foi a presença de sangue no curativo (57,8%).

Conclusão: O uso do curativo gel de clorexidina em pacientes submetidos ao TCTH demonstrou ser uma medida eficaz na redução da ocorrência de infecções relacionadas ao cateter, quando comparado aos dados da literatura. Os casos de ICSRC encontrados foram associados, principalmente, à condição de neutropenia, muito comum nesta população. Os casos de irritação cutânea relacionados ao curativo identificados e a presença de sangue como principal motivo de troca não programada salientam a importância do conhecimento relacionado ao uso do curativo por parte dos enfermeiros assistenciais, a fim de criar protocolos que indiquem o uso e manejo do curativo com segurança.

Resumen

Objetivo: Hacer un seguimiento del uso del vendaje gel de clorhexidina en catéter venoso central (CVC) en niños y adultos sometidos al trasplante de células madre hematopoyéticas (TCMH) para verificar los casos de infección del flujo sanguíneo relacionados con el catéter (IFSRC) y la irritación cutánea durante la validez de este vendaje.

Métodos: Estudio observacional y prospectivo, con 25 pacientes con catéter venoso central insertado para realizar el trasplante de células madre hematopoyéticas. Diariamente se evaluaron las características del vendaje y de la piel, las características clínicas del paciente y las relacionadas con la infección. Los pacientes recibieron un seguimiento a partir del primer día de la inserción del CVC hasta su retirada, con un límite de 45 días a partir de la fecha de inserción del CVC.

Resultados: La infección del flujo sanguíneo relacionada con el catéter se presentó en el 28% de los pacientes, hubo relación entre neutropenia febril e infección (p<0,01). Se identificó irritación cutánea en el 24% de los pacientes. No se identificó relación entre la infección del flujo sanguíneo relacionada con el catéter y la irritación cutánea (p=0,51). Hubo relación significativa entre la irritación cutánea y la suspensión del uso del vendaje (p=0,03). Los cambios no programados sucedieron en el 50% de los cambios registrados, y el motivo principal fue la presencia de sangre en el vendaje (57,8%).

Conclusión: El uso del vendaje gel de clorhexidina en pacientes sometidos al TCMH demostró ser una medida eficaz para la reducción de casos de infecciones relacionadas con el catéter, en comparación con los datos de la literatura. Los casos de IFSRC encontrados se relacionaron principalmente con la condición de neutropenia, muy común en esta población. Los casos identificados de irritación cutánea relacionados con el vendaje y la presencia de sangre como principal motivo de cambio no programado resaltan la importancia del conocimiento del uso del vendaje por parte de los enfermeros asistenciales, a fin de crear protocolos que indiquen el uso y manejo seguro del vendaje.

Introduction

Hematopoietic stem cell transplantation (HSCT) is the intravenous infusion of hematopoietic stem cells to restore the bone marrow function, indicated for the treatment of malignant and nonmalignant diseases.[1] To facilitate patient management and ensure safe drug infusion, patients eligible for HSCT require a central venous catheter (CVC) installed before starting the chemotherapy conditioning regimen that precedes HSCT.[2]

During HSCT, permanent or temporary CVCs are used. A permanent CVC is tunneled, for instance, Hickman-type catheter, which is surgically implanted using a subcutaneous tunnel, and a cuff on the distal portion impregnated with antimicrobial.[2,3] A temporary non-tunneled CVC is percutaneously inserted in the central vein through a procedure performed on the patient bed, such as the double-lumen catheter.[3,4]

Despite being an essential device, a CVC involves some complications, including catheter-related bloodstream infection (CRBSI), which is a predictive factor for catheter removal among patients submitted to HSCT,[3,5,6] as well as increased morbidity and mortality rates, longer hospitalization period, and higher hospital costs.[3,7]

Patients undergoing HSCT are potentially more susceptible to CRBSI due to treatment-induced immunological fragility and the underlying disease itself.[8] In addition, severe immunosuppression, long-lasting neutropenia, breakdown of skin integrity for catheter insertion, and delayed healing due to the effects of chemotherapy contribute to infectious complications.[8-10]

The incidence of intravascular catheter-related infections can be reduced with the adoption of preventive measures, such as hand hygiene before handling the catheter and its connections, maximum protection barrier during catheter insertion, skin antisepsis with chlorhexidine, preventing access through the femoral vein, removing catheters when they are no longer needed, changing dressing as recommended, and evaluating the catheter exit site, dressings, and connections at least once a day.[4,11]

One strategy to reduce intravascular catheter-related infection refers to the use of chlorhexidine gel or chlorhexidine-impregnated disk dressing.[7,12] This dressing effectively reduces skin colonization by microorganisms that cause extra-luminal cath-

eter contamination.[9,13] However, protocols for dressing change should be created and observed, since the adhesiveness of any type of dressing that covers the CVC can cause skin injuries as a result of removing the stratum corneum from the skin.[10,14]

Two systematic reviews of the literature showed a positive effect of chlorhexidine gel or chlorhexidine-impregnated disk dressing on preventing colonization and reducing the incidence of catheter-related infection,[7,12] but only few studies describe aspects related to dressing application and daily maintenance,[15,16] particularly in the context of hematology-oncology patients submitted to high-dose chemotherapy followed or not by HSCT.[9,17,18] Chlorhexidine gel dressing (CHXGD) presented more benefits in terms of suppression of bacterial growth,[19,20] including application in a single step, direct contact of 2% chlorhexidine with the skin, and translucent gel allows visualization of the catheter exit site.[15]

This study aimed to monitor the use of CHXGD in the CVC of children and adults submitted to HSCT to check for CRBSI and skin irritation while using this dressing.

Methods

This is a prospective observational study conducted at the bone marrow transplant, hematology and immune therapy inpatient units and at the bone marrow transplant outpatient unit of Hospital de Clínicas at the Medical School of Ribeirão Preto, University of São Paulo.

The sample had 25 patients, including children and adults with a CVC inserted for HSCT to treat autoimmune diseases, benign hematologic disorders or oncological-hematological diseases. The inclusion of children in the study was due to the fact that the institution's care protocol defines the use of transparent dressings for all patients undergoing HSCT.

Exclusion criteria were the history of chlorhexidine allergy and having received CVC insertion before hospital admission. Data were collected from September 23, 2013 to February 23, 2014. After meeting the selection criteria, patients themselves or family members in charge of child patients received explanations about the study and were invited by the researcher to participate in the study. All eligible patients met the selection criteria and accepted the invitation to be included in the study. Figure 1 shows the study protocol.

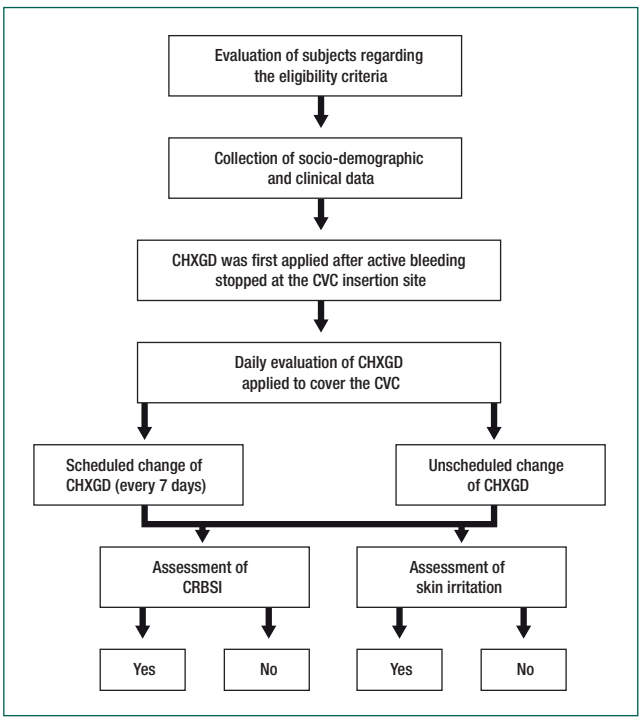

Figure 1. Flowchart of study protocol steps.

According to the institutional protocol of inpatient units, CHXGD (Tegaderm CHG, 3M, Brazil) was applied after active bleeding stopped at the CVC exit site, usually within 48 hours of catheter insertion.

Twenty-one nurses of the inpatient units changed the CVC dressings. Before data collection, the researcher trained all 21 nurses of the inpatient units to standardize the dressing change procedure. The training consisted of a presentation about CHXGD and dressing change technique, preceded by a pre-test and followed by a post-test with 20 assertive questions to identify the prior knowledge of nurses and how much the training added to their knowledge.

Data were collected by a team of researchers comprised of the main researcher and two research assistants who received the same training as the nurses, plus guidance about filling out the data collection instrument used in this study.

A 45-day follow-up was defined considering the results of a prior study conducted in one of the in-

patient units, which identified the catheter remains in place for 45 days on average.[5]

An instrument validated by five judges for its content and appearance was used for data collection. Analyses were performed using SAS 9.2 and Statistical Package for Social Science (SPSS) version 25.0; a significance level of 5% was adopted. Absolute and percentage frequency, mean, standard deviation, and median (minimum and maximum) values, and simple and multiple log-binomial regression models were used to estimate the relative risk (RR) of CRBSI and skin irritation. Mann-Whitney test was used to compare CRBSI to the quantitative variables of interest. Association measurements were made by Fisher's exact test.

This study was approved by the Research Ethics Committee of the Ribeirão Preto College of Nursing, University of São Paulo, registered under CAAE number 12055813.7.0000.539. Patients and nurses signed an informed consent form. A child consent form was used with literate children and their parents also signed an informed consent form.

The evaluated dressing was already used at the study sites, according to the institutional protocol, but these units did not have enough dressing for all patients submitted to HSCT. Then, the researchers bought an amount of dressings with resources from CAPES (Coordination for the Improvement of Higher Education Personnel) to ensure the study would be performed. No conflict of interest of any study researcher/author was reported.

The primary outcomes of this study were: occurrence of CRBSI (yes or no) and presence of skin irritation related to CHXGD (yes or no).

CRBSI was defined as bacteremia or fungemia during CVC use with one or more positive peripheral blood cultures, clinical manifestations of infection (fever, tremor and/or hypotension) in the absence of any other identified source of infection besides the catheter, and growth of microorganism in blood culture obtained from the catheter hub, detected two hours before peripheral blood culture positivity.[21] This is the definition adopted by the Hospital Infection Control Committee (CCIH) as a criterion for the microbiological diagnosis of infection, also used in this study as data related to CRBSI were obtained from the CCIH.

To identify skin irritation at the dressing adhesion site, skin in contact with CHXGD was evaluated at each dressing change seeking signs defined by the International Contact Dermatitis Research Group (ICDRG): normal skin; mild erythema; erythema and slightly thickened skin or intense erythema with edema and vesicles.[22] Scheduled changes occurred at day 7 of dressing use[4] and unscheduled changes before this period.[7,14,16] CHXGD was suspended in patients who presented skin irritation – they were monitored until the last day of dressing use. Patients whose dressing was temporarily removed due to active bleeding at the CVC exit site were monitored until catheter removal – CHXGD was applied again as soon as bleeding stopped. In cases of suspended use of CHXGD, dressing with sterile gauze and tape was used instead. In order to avoid confusion in the assessment of skin irritation related to dressing adhesiveness, the researchers inspected it daily for signs and symptoms of acute skin Graft-versus-Host Disease (GvHD) according to the following stages of severity: grade 0 absence of skin rash; grade 1 presence of skin rash affecting body surface area <25%; grade 2 presence of rash affecting body surface area 25-50%; grade 3 presence of skin rash affecting body surface area >50%; and grade 4 erythroderma affecting body surface area >50% associated with blistering and peeling of body surface area <5%.[23]

Secondary outcomes related to CVC and dressing change were: catheter type; how many days CVC remained in place during the data collection period (0-45 days); site; reason for removal; type of microorganism related to the occurrence of CRBSI; time elapsed between CVC insertion and beginning of dressing use; number of dressing changes per patient; number of scheduled and unscheduled changes; reasons for dressing change; dressing suspension; and dressing detachment at the catheter exit site. Other secondary outcomes were: sociodemographic and clinical data of patients (age, sex, days of hospitalization, underlying disease, type of HSCT, type of chemotherapy conditioning regimen, days to start chemotherapy after CVC insertion, days to bone marrow graft, neutropenia at hospital admission, and febrile neutropenia).

The chemotherapy conditioning regimen was classified as high, medium and low intensity according to the following criteria: high intensity – myeloablative conditioning regimen with irreversible pancytopenia; medium intensity – nonmyeloablative conditioning regimen with mild pancytopenia; and low intensity – conditioning regimen that cannot be classified as high or medium intensity.[24]

Bone marrow graft was considered when the patient presented three consecutive days with an absolute neutrophil count above 500/mm^3 after HSCT.[25]

The variable of neutropenia at hospital admission indicates that, when starting HSCT, the patient already had neutropenia (absolute neutrophil count below 1,000/mm^3).[26] Febrile neutropenia was defined as absolute neutrophil count below 1,000/mm^3 and a single temperature measurement above 38.3°C or temperature greater than or equal to 38°C sustained for more than one hour.[27]

Results

The sample consisted of 25 patients. Table 1 describes the sociodemographic and clinical characteristics of the patients, as well as catheter and dressing change information.

For 32% (n=8) of all patients, conditioning regimens started one day after CVC insertion and for four (16%) patients, seven or more days after CVC insertion.

CRBSI was identified in 28% (n=7) of all patients, and in two cases it was treated, not leading to catheter removal. Microbiological analysis of the samples identified five Gram-negative bacteria (*Chryseobacterium indologenes, Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae* and *Comamonas testosteroni)* and two Gram-positive bacteria (*Staphylococcus epidermidis* and *Corynebacterium jk*).

The mean time between catheter insertion and CHXGD start was two days (60%, n=15), ranging from one to seven days. CHXGD applied four days after catheter insertion remained in place for seven days, that is, as scheduled.

Dressings were changed 90 times, 50% (n=45) scheduled and 50% unscheduled dressing changes. The main reason for unscheduled dressing change was that the dressing became dirty (57.8%, n=26), followed by detached dressing (31.1%, n=14), catheter not in good conditions (6.7%, n=3), and skin irritation (4.4%, n=2).

Only one patient (4%) developed grade 1 acute-skin GvHD during the data collection period, starting 30 days after transplantation, at day 43 after CVC insertion. The patient had pruritus and rash on the chest,

Table 1. Sociodemographic and clinical characteristics of patients and catheter and dressing change information (n=25)

Characteristics	n(%)
Age (years)	
Median (min;max)	32(4;66)
Sex	
Female	13(52)
Male	12(48)
Hospitalization (days), mean (SD)	34(15.1)
Median (min; max)	34(12;81)
Underlying disease	
Leukemia	7(28)
Multiple myeloma	5(20)
Lymphoma	4(16)
Other*	9(36)
Days to graft, mean (SD)	16(5.3)
Median (min; max)	14(11;30)
Type d	
Autologous	16(64)
Allogeneic	9(36)
Intensity of conditioning regime	
High intensity	12(48)
Medium intensity	5(20)
Low intensity	8(32)
Start of conditioning regimen, mean (SD)	2(2,56)
Median (min; max)	1(0;10)
Neutropenia at hospital admission	
Yes	7(28)
No	18(72)
Febrile neutropenia	
Yes	13(52)
No	12(48)
CVC type	
Double-lumen	14(56)
Hickman	11(44)
CVC in place, mean (SD)	26(14.3)
Median (min; max)	19(10;45)
Access site	
Internal jugular vein	20(80)
Subclavian vein	5(20)
Reason for CVC removal	
End of treatment	9(36)
Suspected catheter-related infection	8(32)
Catheter not in good conditions	2(8)
Involuntary removal of catheter	1(4)
Catheter not removed (in place for over 45 days)	5(20)
Dressing change per patient, mean (SD)	3(1.9)
Median (min; max)	3(1;7)

SD – standard deviation; min – minimum value; max – maximum value; *Other – systemic lupus erythematosus (n=1), systemic sclerosis (n=2), Poems syndrome (n=1), aplastic/sickle cell anemia (n=3), myelodysplastic syndrome (n=1), myelofibrosis (n=1),

which disappeared in a few days after starting the GvHD treatment and did not result in CHXGD removal.

Of all patients analyzed in this study, 24% (n=6) had irritation on the skin in contact with CHXGD. Of these, three had their dressings permanently removed. Two other patients had their dressing removed due to active bleeding at the catheter exit site, with subsequent dressing reapplication. In the skin evaluation during the dressing change procedures, mild erythema was observed in 88% (n=22) of the patients in some dressing changes.

Tables 2 and 3 show the relative risk of CRBSI and skin irritation, respectively, according to the study variables.

Table 2. Relative risk (RR) of catheter-related bloodstream infection

Variable	CRBSI		Total n(%)	Relative risk (95% CI)	*p-value*
	Yes n(%)	No n(%)			
Febrile neutropenia					
Yes	7(54)	6(46)	13(100)	-	<0.01*
No	0	12(100)	12(100)		
Neutropenia at admission, n (%)					
Yes	2(29)	5(71)	7(100)	1.03 (0.26 - 4.12)	0.97**
No	5(28)	13(72)	18(100)	1	
CVC type					
Hickman	3(27)	8(73)	11(100)	0.95 (0.27 - 3.40)	0.94**
Double-lumen	4(29)	10(71)	14(100)	1	
Chemotherapy conditioning regimen					
High intensity	4(33)	8(67)	12(100)	2.67 (0.36 - 19.71)	0.34**
Medium intensity	2(40)	3(60)	5(100)	3.20 (0.38 - 26.78)	0.28**
Low intensity	1(13)	7(87)	8(100)	1	
Skin irritation					
Yes	1(17)	5(83)	6(100)	0.53 (0.08 - 3.56)	0.51**
No	6(32)	13(68)	19(100)	1	
Type of HSCT					
Allogeneic	2(22)	7(78)	9(100)	1	
Autologous	5(31)	11(69)	16(100)	1.41 (0.34 - 5.83)	0.64**
Days for graft, mean (SD)	18.6(5.8)	15.6(4.9)	25(100)	1.06 (0.98 - 1.15)	0.17***
Unscheduled change, mean (SD)	1.3(1.2)	2.0(1.2)	25(100)	0.68 (0.39 -1.19)	0.18***

CRBSI – catheter-related bloodstream infection; SD – standard deviation; *Unable to calculate relative risk. *p-value* refers to Fisher's exact test; ***p-value* refers to Fisher's exact test; ****p-value* refers to Mann-Whitney test.

Table 3. Relative risk (RR) of skin irritation

Variable	Skin irritation		Total n(%)	Relative risk (95% CI)	*p-value**
	Yes n(%)	No n(%)			
Febrile neutropenia					
Yes	3(23)	10(77)	13(100)	0.92 (0.23 - 3.72)	0.91
No	3(25)	9(75)	12(100)	1	
Neutropenia at admission					
Yes	3(43)	4(57)	7(100)	2.57 (0.67 - 9.83)	0.17
No	3(17)	15(83)	18(100)	1	
CVC type					
Hickman	3(27)	8(73)	11(100)	1.27 (0.32 - 5.12)	0.73
Double-lumen	3(21)	11(79)	14(100)	1	
Chemotherapy conditioning regimen					
High intensity	3(25)	9(75)	12(100)	1.00 (0.21 - 4.71)	0.99
Medium intensity	1(20)	4(80)	5(100)	0.80 (0.10 - 6.7)	0.84
Low intensity	2(25)	6(75)	8(100)	1	
CHXGD removal					
Yes	3(60)	2(40)	5(100)	4.00 (1.13 - 14.17)	0.03
No	3(15)	17(85)	20(100)	1	
Type of HSCT					
Allogeneic	3(33)	6(67)	9(100)	1	
Autologous	3(19)	13(81)	16(100)	0.56 (0.14 - 2.23)	0.41

**p-value* refers to Fisher's exact test.

Discussion

CVC insertion is essential in HSCT, as it makes the procedure easier and safer. However, CVC insertion causes breakdown of skin integrity, creating a gateway to pathogenic microorganisms[28], therefore, it represents the main source of infection in patients undergoing HSCT.[29] Two types of catheters were used in this study: double-lumen catheter (56%, n=14) and Hickman catheter (44%, n=11). According to the literature, tunneled CVC inhibits microorganisms in the catheter path, reducing the CRBSI rates.[4] However, this study found no association between the type of CVC[9] and occurrence of CRBSI (RR=0.95; CI=0.27-3.40; p=0.94).

CRBSI with the highest growth of gram-negative bacteria was identified in 28% (n=7) of all patients. Infections caused by gram-negative bacteria are associated with greater severity and mortality,[30,31] but such results contrast with findings in the international literature that show higher growth of gram-positive bacteria.[9,12,17,32] Epidemiological studies[30,31] show that the presence of neutropenia and immunosuppression are associated factors for CRBSI caused by gram-negative bacteria.

Factors such as the type of HSCT, neutropenia at hospital admission, type of chemotherapy conditioning and time to bone marrow grafting, are associated with the development of infections;[8] however this study found no association with the risk of developing CRBSI. Allogeneic transplantation involves a higher risk of infectious complications, while patients undergoing autologous transplantation present a lower risk.[8] One of these factors is induced immunosuppression after allogeneic transplantation to avoid graft rejection. The intensity of the conditioning regimen that differs between transplant types influences the grafting time. The longer the time for bone marrow grafting, the longer the neutropenia time and, consequently, the higher the risk of infection.[8]

Neutropenia identified at hospital admission may be associated with pre-transplant factors such as prior immunosuppressive therapies and the disease itself.[8] In this study, febrile neutropenia presented a statistically significant association with CRBSI (p<0.01). Neutropenia may be a clinical manifestation of underlying disease due to the replacement of normal bone marrow cells with neoplastic cells.[28] Neutropenia is the major risk factor for the development of CVC-related infections and a frequent cause of death in this population.[8] The incidence of CRBSI can be reduced by adopting preventive measures and choosing proper dressing to cover the catheter exit site. CHXGD has been recommended for patients with high susceptibility to infection, including those with neutropenia.[16]

Despite the evidence of the effectiveness of chlorhexidine dressing in reducing the incidence of CRBSI in oncology hematology patients[9,17] or in intensive care patients,[7,12] this dressing should be evaluated in terms of indication and how long the catheter will be in place in cases of skin irritation at its application site because it is an adhesive dressing. Among the patients evaluated in this study, 24% (n=6) had skin irritation when using CHXGD, and the dressing was removed in 12% (n=3) of the patients due to skin irritation. No significant association (p=0.51) was found between the occurrence of skin irritation and the development of CRBSI in the patients.

The presence of blood (dirty dressing) was the main reason for unscheduled removal of the dressing (57.8%), a fact that highlights the importance of knowing the characteristics of patients, such as the time of bloody exudate from the catheter exit site and the interference of time between catheter insertion and the start of chemotherapy conditioning.[10,33] The literature indicates the period of seven days should be observed after invasive procedures like CVC insertion, before starting the chemotherapy cycles, which may attenuate the influence of chemotherapeutic agents on the healing process and bleeding at the catheter insertion site.[33]

CHXGDs were applied, on average, two days after catheter insertion, after evidence of absent active bleeding at the catheter exit site, as recommended in the literature.[4] However, in some cases,

the exit site presented subsequent bleeding, requiring dressing removal and temporary suspension of dressing use. This fact may be related to an early start of the chemotherapy cycle after catheter insertion and thrombocytopenia. Precautions should be adopted to minimize this issue, such as respecting the seven-day period after catheter insertion before starting the chemotherapy cycle, blood transfusions, or even the use of surgical glue at the catheter exit site to reduce bleeding.[16,34]

The second most frequent reason for change was dressing detachment (31.1%). This result may be related to conditions frequently observed in this population, such as febrile neutropenia, which can lead to excessive sweating during fever peaks, making dressings peel off more easily.[14,16] Dressing detachment is a risk factor for catheter-related infection.[14]

Study limitations were its small sample size and, due to the study design, the impossibility of establishing a cause-and-effect relationship between the chlorhexidine gel dressing and the occurrence of infection related to intravascular catheter. In addition, the results are applicable to a very specific population, that is, patients undergoing HSCT.

Contributions of this study to clinical practice include knowledge about a new technology to cover the central venous catheter exit site and its daily application management. Then, it describes the nursing care that is essential for safe maintenance of this dressing to avoid adverse events such as catheter-related infections and skin irritation caused by dressing adhesion in a specific and fragile population such as patients undergoing HSCT. Future studies should analyze neutropenia not only at hospital admission, but at other specific moments of the hospitalization period, as it is the main risk factor for bleeding at venous catheter insertion in oncology patients.

Conclusion

This study confirms the findings in the literature that recommend chlorhexidine gel dressing in patients with neutropenia, who are more susceptible to infectious complications, as it is an effective measure to reduce the occurrence of catheter-related infections. Transplant centers should develop protocols for indication, maintenance and replacement of this dressing, in order to optimize its use, considering it is an effective measure to reduce the occurrence of CRBSI. The adoption of practices that ensure CHXGD in place as long as it is necessary and minimize the risk of skin irritation is essential to ensure safe patient care and contribute to improve quality of life during the treatment. This study found no association between the presence of skin irritation and the occurrence of CRBSI.

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Collaborations

Castanho LEC, Santos BN, Margatho AS, Braga FTMM, Reis PED, Oliveira MC and Silveira RCCP contributed to project design, data analysis and interpretation, relevant critical review of intellectual content and approval of the final version to be published.

References

1. Li HW, Sykes M. Emerging concepts in haematopoietic cell transplantation. Nat Rev Immunol. 2012;12(6):403-16.

2. Rodrigues HF, Garbin LM, Castranho LC, Simoes BP, Curcioli AC, Silveira RC. [Hickman catheters in hematopoietic stem cell transplantation: surgical implantation, removal and nursing care]. Rev Enferm UERJ. 2015;23(3):304-9. Portuguese.

3. Centers for Diseases Control and Prevention (CDC). Bloodstream infection event (central line-associated bloodstream infection and non-central line associated bloodstream infection). CDC; 2018. Available from: https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf

4. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control. 2011; 39(4 Suppl 1):1-34.

5. Castanho LC, Silveira RC, Braga FT, Canini SR, Reis PE, Voltarelli JC. [Rationale for Hickman catheter removal in patients undergoing hematopoietic stem cell transplantation] Acta Paul Enferm. 2011;24:244-8. Portuguese.

6. Yilmaz MC, Aksoylar S, Erdogan D, Demirag B. Complications of central venous catheters in children undergoing hematopoietic stem cell transplantation in Turkey. J Pediatr Oncol Nurs. 2012;29(4):199-205.

7. Ullman AJ, Cooke ML, Mitchell M, Lin F, New K, Long DA, et al. Dressings and securement devices for central venous catheters (CVC). Cochrane Database Syst Rev. 2015; (9):CD010367.

8. Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek J, et al. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. Biol Blood Marrow Transplant. 2009;44(8):453-5.

9. Biehl LM, Huth A, Panse J, Krämer C, Hentrich M, Engelhardt M, et al. A Randomized trial on chlorhexidine dressings for the prevention of catheter-related bloodstream infections in neutropenic patients. Ann Oncol. 2016;27(10):1916-22.

10. Benhamou E, Fessard E, Com-Nougue C, Beaussier PS, Nitenberg G, Tancrede C, et al. Less frequent catheter dressing changes decrease local cutaneous toxicity of high-dose chemotherapy in children, without increasing the rate of catheter-related infections: results of a randomised trial. Bone Marrow Transplant. 2002;29(8):653-8.

11. Marschall J, Mermel LA, Fakih M, Hadaway L, Kallen A, O'Grady NP, et al. Strategies to prevent central line–associated bloodstream infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014;35(7):753-71.

12. Safdar N, O'Horo JC, Ghufran A, Bearden A, Didier ME, Chateau D, et al. Chlorhexidine-impregnated dressing for prevention of catheter-related bloodstream infection: a meta-analysis*. Crit Care Med. 2014;42(7):1703-13.

13. Karpanen TJ, Casey AL, Whitehouse T, Nightingale P, Das I, Elliott TSJ. Clinical evaluation of a chlorhexidine intravascular catheter gel dressing on short-term central venous catheters. Am J Infect Control. 2016;44(1):54-60.

14. Timsit JF, Bouadma L, Ruckly S, Schwebel C, Garrouste-Orgeas M, Bronchard R, et al. Dressing disruption is a major risk factor for catheter-related infections. Crit Care Med. 2012;40(6):1707-14.

15. Pfaff B, Heithaus T, Emanuelsen M. Use of a 1-peace chlorhexidine gluconate transparent dressing on critically ill patients. Crit Care Nurse. 2012;32(4):35-40.

16. Jeanes A, Bitmead J. Reducing bloodstream infection with a chlorhexidine gel IV dressing. Br J Nurs. 2015;24(19):S14-9.

17. Chambers ST, Sanders J, Patton WN, Ganly P, Birch M, Crump JA, et al. Reduction of exit-site infections of tunnelled intravascular catheters among neutropenic patients by sustained-release chlorhexidine dressings: results from a prospective randomized controlled trial. J Hosp Infect. 2005;61(1):53-61.

18. Santos BN, Oliveira MC, Braga FT, Margatho AS, Esparrachiari LC, Silveira RC. Local cutaneous effects associated with chlorhexidine-impregnated gel dressing in hematopoietic stem cell transplantation patients. Open J Nurs. 2018;8(2):115-29.

19. Bashir MH, Olson LK, Walters SA. Suppression of regrowth of normal skin flora under chlorhexidine gluconate dressings applied to chlorhexidine gluconate-prepped skin. Am J Infect Control. 2012; 40(4):344-8.

20. Kawamura H, Takahashi N, Takahashi M, Taketomi A. Differences in microorganism growth on various dressings used to cover injection sites: inspection of the risk of catheter-related bloodstream infections caused by Gram-negative bacilli. Surg Today. 2014;44(12):2339-44.

21. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;49(1):1-45.

22. Wilkinson DS, Fregert S, Magnusson B, Bandmann HJ, Calnan CD, Cronin E, et al. Terminology of contact dermatitis. Acta Derm Venereol. 1970;50(4):287-92.

23. Schoemans HM, Lee SJ, Ferrara JL, Wolff D, Levine JE, Schultz KR, et al. EBMT–NIH–CIBMTR Task Force position statement on standardized terminology & guidance for graft-versus-host disease assessment. Bone Marrow Transplant. 2018;53(11):1401-15.

24. Bacigalupo A, Ballen K, Rizzo D, Giralt S, Lazarus H, Ho V, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant. 2009;15(12):1628-33.

25. Popat U, Mehta RS, Rezvani K, Fox P, Kondo K, Marin D, et al. Enforced fucosylation of cord blood hematopoietic cells accelerates neutrophil and platelet engraftment after transplantation. Blood. 2015;125(19):2885-92.

26. Centers for Disease Control and Prevention; Infectious Disease Society of America; American Society of Blood and Marrow Transplantation. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipientes. MMWR Recomm Rep. 2000 Oct;49(RR-10):1-125, CE1-7. Erratum in: MMWR Recomm Rep. 2004;53(19):396.

27. U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute. Common terminology criteria for adverse events (CTCAE) Version 5.0. 2017:3. Avaliable from: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf

28. Khayr W, Haddad RY, Noor SA. Infections in hematological malignancies. Dis Mon. 2012;58(4):239-49.

29. Gudiol C, Garcia-Vidal C, Arnan M, Sánchez-Ortega I, Patiño B, Duarte R, et al. Etiology, clinical features and outcomes of pre-engraftment and post-engraftment bloodstream infection in hematopoietic SCT recipients. Bone Marrow Transplant. 2014;49(6):824-30.

30. Braun E, Hussein K, Geffen Y, Rabino G, Bar-Lavie Y, Paul M. Predominance of Gram-negative bacilli among patients with catheter-related bloodstream infections. Clin Microbiol Infect 2014;20(10):O627-9.

31. Hajjej Z, Nasri M, Sellami W, Gharsallah H, Labben I, Ferjani M. Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit. J Infect Chemother. 2014;20(3):163-8.

32. Ruschulte H, Franke M, Gastmeier P, Zenz S, Mahr KH, Buchholz S, et al. Prevention of central venous catheter related infections with chlorhexidine gluconate impregnated wound dressings: a randomized controlled trial. Ann Hematol. 2009;88(3):267-72.

33. Payne WG, Naidu DK, Wheeler CK, Barkoe D, Mentis M, Salas RE, et al. Wound healing in patients with cancer. Eplasty. 2008;8:9.

34. Pittiruti M, Scoppettuolo G, Emoli A, Musarò A, Biasucci D. Cyanoacrylate glue and central venous access device insertion [abstract]. JAVA. 2016; 21(4):249.