Manuscript Number: EJCMI-D-10-00122R1

Title: REDUCTION IN CATHETER-RELATED BLOODSTREAM INFECTIONS IN CRITICALLY ILL PATIENTS THROUGH A MULTIPLE SYSTEM INTERVENTION.

Article Type: Brief Report

Keywords: prevention, ICU, CR-BSI

Corresponding Author: Mrs Raquel Peredo, M.D

Corresponding Author's Institution: Hospital De Sabadell

First Author: Raquel Peredo, M.D

Order of Authors: Raquel Peredo, M.D; Caroline Sabatier, M.D; Ana Villagrà, M.D; Josefa González; Concepción Hernández; Francisco Pérez; David Suárez; Jordi Vallés, M.D, PhD

Abstract: Objective: We aimed to determine the utility of a multiple system intervention to reduce catheter-related bloodstream infections (CR-BSI) in our intensive care unit (ICU).

Design: Prospective cohort study.

Intervention: We applied five measures: educational sessions about inserting and maintaining central venous catheters, skin cleaning, a checklist during catheter insertion, subclavian vein insertion whenever possible, and removing unnecessary catheters.

Methods: We determined the rate of CR-BSI per 1000 catheter-days during the intervention (March to December 2007) and compared it with the rate during the same period in 2006 in which we applied only conventional preventive measures. CR-BSI was defined as the recovery of the same organism (same species, same antibiotic susceptibility profile) from catheter tip and blood cultures.

Results: We registered 4289 patient-days and 3572 catheter-days in the control period and 4174 patient-days and 3296 catheter-days in the intervention period. Catheters were used in (81.5%) patients during the control period and in (80.6%) during the intervention period. During the control period, 24 CR-BSI were diagnosed (6.7/1000 catheter-days); during the intervention period, 8 CR-BSI were diagnosed (2.4/1000 catheter-days) (Relative Risk 0.36; 95% CI 0.16 to 0.80; p= 0.015).

Conclusions: A multiple system intervention applying evidence-based measures reduced CR-BSI in our ICU.

Figure 1. Incidence of CR-BSI (episodes per 1000 catheter-days).

Table 1. Location and mean catheter duration.			
	Control period	Intervention period	p-value
Location Catheter:			
Subclavian	19.3%	25.4%	p:NS
Jugular	47.1%	45.1%	p:NS
Basilic	20.2%	16.8%	p:NS
Femoral	13.4%	12.7%	p:NS
Mean Duration Catheter days.	7.5 ± 4.5	7.1 ± 4.1	p:NS

Answer to reviewers.

Reviewer #1:

Thanks for your comments.

We agree with you that the study was conducted in 2007 but in 2008 and 2009 the incidence of CR-BSI has remained in 3,4 and 1,4 respectively as we comment in the last paragraph of the results.

In the second paragraph of the discussion we emphasize that the most important difference between the control and intervention period is the incorporation of the checklist. Also in the fourth paragraph of the results we add which were the points corrected in the checklist during the procedure and the percentage.

Reviewer #2:

Thanks for yours comments.

We know that having an historical control is a limitation of the study and we would need a prospective multicenter study as we comment in the last paragraph of the discussion.

In Spain the incidence of CR-BSI is about 5 episodes per 1000 catheter-days, and is higher than in the rest of Europe. In our ICU during the control period the incidence of CR-BSI was about 6 episodes per 1000 catheter days. Starting from 6 episodes per 1000 catheters days, we reduced the incidence till 2,4, which is more than half. Even in 2009 the incidence remained 2,1 episodes per 1000 catheter days.

We apologize because there is a mistake in the number of catheter days. During the control period was 3572 catheter-days and during the intervention period was 3296 catheter-days. We reduce three hundred catheter-days between the control and intervention period. There is a tendency in reduce the number of catheter-days but there is no statistical significance.

We agree with you that we should reduce the number of catheter-days and increase the use of suclavian vein. Despite the duration of catheterization has been considered an important risk factor for infection guidelines don't suggest removing catheters routinely. (1,2)

We've add in the third paragraph of the discusion that we practically don't reduce the use of jugular vein and this is an important point to improve. Catheter-related infection is more common in the femoral site and in a lesser degree in jugular site compared with the subclavian vein (3,4,5,6).

As we designed the study we analyze prospectively the incidence of CR- BSI, and we count overall the number of catheter-days. We don't have separately the location and number of catheter-days. We don't have microbiological data and therefore this data can't be added in the results.

1. Bregenzer. T, Conen D, Sakmann.P, Widmer. AF. Is routine replacement of peripheral intravenous necessary?Arch Intern Med 1998; 158:151.
2. Cobb .DK, High. KP, Sawyer. RG, et al. A controlled trial of sheduled replacement of cental venous and pulmonary artery catheters. N Eng J Med 1992; 327:1062.
3. Merrer .J, Jonghe.BD, Golliot. F et al. Complications of femoral and subclavian venous catheterization in critically ill patients. A randomized controlled trial. JAMA 2001;286:700.

4. Lorente.L, Henry.C Martin.MM et al. Central venous catheter-related infection in a prospective and observational study of 2.595 catheters. Crit Care 2008;9:R631.
5. Richet.H, Hubert.B, Nitemberg G et al. Prospective multicenter study of vascular catheter-related complications and risk factors for positive central catheter cultures in intensive care unit patients. J Clin Microbiol 1990; 28:2520.
6. Mermel LA, McCormick RD, Springman SR, Maki DG. The pathogenesis and epidemiology of catheter- related infections with pulmonary artery Swan-Ganz catheters: A prospective study utilizing molecular subtyping. Am J Med 1991;91:197S.

REDUCTION IN CATHETER-RELATED BLOODSTREAM INFECTIONS IN CRITICALLY ILL PATIENTS THROUGH A MULTIPLE SYSTEM INTERVENTION.

R. Peredo, C. Sabatier, A. Villagr, J. Gonzlez, C. Hernndez, F. Prez, D. Surez*, J. Valls.

Critical Care Department, Hospital de Sabadell. CIBER Enfermedades Respiratorias.
* Epidemiology and Assessment Unit, Parc Taul Foundation, Autonomous University of Barcelona. Sabadell, Spain.

Acknowledgments, conflicts of interest:
All authors report no conflicts of interest relevant to this article except David Suarez that was supported by a research grant from both the Instituto de Salud Carlos III, Ministerio de Sanidad y Consumo, Spain and the Departament de Salut, Generalitat de Catalunya (FIS ECA07/041).

Correspondence: Raquel Peredo M.D.
Critical Care Department. Hospital de Sabadell.
rperedo@tauli.cat

Word Count: 1735

Abstract

Objective: We aimed to determine the utility of a multiple system intervention to reduce catheter-related bloodstream infections (CR-BSI) in our intensive care unit (ICU).

Design: Prospective cohort study.

Setting: Medical and surgical ICU in a university hospital.

Intervention: We applied five measures: educational sessions about inserting and maintaining central venous catheters, skin cleaning with chlorhexidine, a checklist during catheter insertion, subclavian vein insertion and avoiding femoral insertion whenever possible, and removing unnecessary catheters.

Methods: We determined the rate of CR-BSI per 1000 catheter-days during the intervention (March to December 2007) and compared it with the rate during the same period in 2006 in which we applied only conventional preventive measures. CR-BSI was defined as the recovery of the same organism (same species, same antibiotic susceptibility profile) from catheter tip and blood cultures.

Results: We registered 4289 patient-days and 3572 catheter-days in the control period and 4174 patient-days and 3296 catheter-days in the intervention period. No significant differences in the number of patients with central venous catheters during the two periods were observed: catheters were used in (81.5%) patients during the control period and in (80.6%) during the intervention period. During the control period, 24 CR-BSI were diagnosed (6.7/1000 catheter-days); during the intervention period, 8 CR-BSI were diagnosed (2.4/1000 catheter-days) (Relative Risk 0.36; 95% CI 0.16 to 0.80; $p=0.015$).

Nurses interrupted the procedure to correct at least one aspect when completing the checklist in (17.7%) insertions.

Conclusions: A multiple system intervention applying evidence-based measures
reduced CR-BSI in our ICU.

Introduction

Indwelling vascular catheters are often indispensable for the management of critically ill patients; however, they are also a leading source of bloodstream infections in these patients. More than 250,000 vascular catheter-related bloodstream infections (CR-BSI) occur annually in the USA [1,2,3], resulting in substantial morbidity, mortality and costs [4,5,6]. Despite the publication of clinical practice guidelines [1] on the management and prevention of intravascular catheter-related infection, CR-BSI are common. According to the National Nosocomial Infections Surveillance (NNIS) system of the Centers for Disease Control and Prevention (CDC), the median rate of all types of CR-BSI ranges from 1.8 to 5.2 episodes per 1000 catheter-days. In Spain, the mean rate of CR-BSI in the National Study of Nosocomial Infections Surveillance in the ICU (ENVIN-UCI) in 2006 was 5 episodes per 1000 catheter-days [7]. In our medical-surgical ICU in 2006, central venous catheters (CVC) were used in 83% of patients and the incidence of CR-BSI was 5.8 episodes per 1000 catheter-days.

Recently, Pronovost et al [8] implemented an evidence-based intervention in 108 ICUs to reduce CR-BSI, designating a team leader for each hospital instructed in the different interventions and responsible for disseminating this information among their colleagues. The evidence-based intervention consisted of five evidence-based procedures recommended by the CDC: hand washing, using full-barrier precautions during the insertion of CVCs, cleaning the skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters. A checklist was used to ensure adherence to infection-control practices. Three months after implementing the intervention, their median rate of CR-BSI had decreased from 2.7/1000 catheter-days at baseline to 0/1000 catheter-days ($p < 0.002$), and their mean rate had decreased from

1 7.7/1000 catheter-days at baseline to 1.4/1000 catheter-days ($p<0.002$); this
2 improvement was maintained throughout the 18-month study period.
3

4 We aimed to evaluate the effect of the evidenced-based intervention proposed by
5 Pronovost et al in our medical-surgical ICU.
6
7
8
9

Methods

We conducted a prospective cohort study of adult patients admitted to our 16-bed medical-surgical ICU in a 500-bed teaching hospital from March 2007 to December 2007. Our hospital does not attend burn, transplantation, or heart-surgery patients.

We applied a multiple system intervention to nonemergency CVC insertion aimed at lowering CR-BSI based on the recommendations of Pronovost et al [8]. The intervention consisted of five elements: 1) Educational sessions about how to insert and maintain CVCs. [9,10] 2) Cleaning the skin with alcoholic chlorhexidine 0.5%. [11,12] 3) Using a checklist during catheter insertion to ensure adherence to infection-control practices. 4) Using the subclavian vein as the preferred insertion site and avoiding the femoral vein if possible And 5) Daily evaluation to determine whether catheters were unnecessary and could be removed [13, 14, 15, 16, 17, 18]. The study protocol was approved by the hospital's institutional review board and informed consent was not required.

Before implementing any of the components of the study intervention, nurses and physicians were instructed at meetings from January 2007 to February 2007. The educational sessions were mainly focused on recommended procedures to control infection, such as hand washing and using full-barrier precautions during the insertion of CVCs. In addition, staff were introduced to the checklist intended to ensure adherence to infection-control practices and instructed to interrupt the procedure whenever these practices were not being followed.

The procedure for CVC maintenance was the same in all the patients in both the control and intervention periods: guidelines for managing CVCs were posted in each box. The main measures included in these guidelines were the use of sterile gloves for

1 inspecting and cleaning the skin at the catheter insertion site, replacement of
2 administration sets every 72 h, and replacement of administration sets used to
3 administer blood products and parenteral nutrition or propofol every 24h. The attending
4 physician decided on a daily basis whether to remove the catheter in function of whether
5 the catheter was considered unnecessary or catheter-related infection was suspected.
6
7
8
9

10
11 A definitive diagnosis of CR-BSI required that the same microorganism be found
12 in at least one percutaneous blood culture and in a culture of the catheter tip [19]. The
13 catheter was considered positive when a semiquantitative (roll-plate) culture of a 5cm
14 catheter tip yielded > 15 colony-forming units (cfu) of a microorganism.
15
16
17
18
19

20 Routine replacement of CVCs to prevent CR-BSI was not permitted [20, 21] , and
21 antibiotic or antiseptic impregnated catheters were not used during the study period.
22 Moreover, no other infection-reducing practices were implemented during the study.
23
24
25
26

27 We determined the rate of CR-BSI during the application of the evidence-based
28 intervention from March to December of 2007, and we compared it with the rate of CR-
29 BSI obtained in the same period (from March to December) of 2006 in which we
30 applied conventional preventive measures during CVC insertion, such as using full-
31 barrier precautions during insertion and cleaning the skin with chlorhexidine
32
33
34
35
36
37
38
39
40

41 Demographic data, patient-days, catheter-days, catheter insertion site, APACHE
42 II, mean catheter duration, and number of CR-BSI were collected prospectively during
43 the intervention period (from March to December 2007) and were compared with the
44 data collected in the same period (from March to December) in 2006.
45
46
47
48
49

50 Statistical analysis

51 Descriptive statistics included frequencies and percentages for categorical
52 variables and means and standard deviations for continuous variables. Associations
53 between categorical variables were assessed with the chi-square test or the Fisher's
54
55
56
57
58
59
60
61
62
63
64
65

exact test. Student's t-test was used to compare groups on continuous variables.
Relative risk ratios were used to compare rates of CR-BSI. All statistical tests were 2-
tailed and significance was set at 0.05. Statistical analysis was carried out using SPSS
software, version 11.5.

Results

We registered 4289 patient-days and 3572 catheter-days during the control period and 4174 patient-days and 3296 catheter-days during the intervention period (p:NS). Mean age was 62 ± 17 years in the control period and 62 ± 16 years in the intervention period (p:NS), and the mean APACHE II score was 14 ± 8 in both periods (p:NS).

We found no significant differences between the two groups in catheter insertion site, although the subclavian vein was used in 25.4% during the intervention period and in 19.4% during control period (p:NS). Mean catheter duration was 7.1 ± 4.1 days during the intervention period compared with 7.5 ± 4.5 during the control period (Table 1) (p>0.05).

During the control period, 24 CR-BSI occurred in 3296 catheter-days and during the intervention period 8 CR-BSI occurred in 3572 catheter-days. Thus, the rate of CR-BSI was 6.7 episodes per 1000 catheter-days during the control period and 2.4 episodes per 1000 catheter-days during the intervention period (Relative Risk 0.36; 95% CI 0.16 to 0.80; p= 0.015) (Figure 1). Four months during the intervention period were free of episodes of CR-BSI; in comparison, only one month was free of CR-BSI during the control period. No differences were found in the number of patients with CVCs during the two periods: catheters were used in (81.5%) patients during the control period and in (80.6%) during the intervention period (p:NS).

In 38 of 214 catheters used during the intervention period (17.7%), nurses interrupted the procedure to correct at least one aspect mentioned in the checklist during the insertion of catheter. The following aspects were corrected: failure to use a large sterile drape n=12 (31%); failure to use a mask for all personnel entering the box n=11 (29%); failure to maintain a sterile field n= 8 (21%); failure to use of hat, mask, and sterile

gown n=5 (13%); failure to use sterile gloves n=1 (3%); and inadequate cleaning of the
insertion site n=1 (3%).

We have applied the evidenced-based intervention for the prevention of CR-BSI
in our ICU since December 2007 and the benefits of this intervention have persisted.
During 2008, the rate of CR-BSI was 3.4 episodes per 1000 catheter-days and during
the first 6 months of 2009 it was 1.7 episodes per 1000 catheter-days, representing an
overall rate of 2.7 episodes per 1000 catheter-days during 18 months' follow-up.

Discussion

We aimed to determine whether following the recommendations of Pronovost et al [8] would reduce the incidence of CR-BSI in our medical-surgical ICU. Our results confirm that applying an inexpensive multiple evidence-based system intervention can significantly reduce the incidence of CR-BSI. No expensive technology or additional staff were required for the intervention, and we emphasize that these measures can easily be applied in most ICUs. Furthermore, CR-BSI rates remained lower 18 months after the intervention was initiated.

We also evaluated the relative impact of the individual components of this multifaceted intervention. Among the five recommendations used, the most significant change between the study and control periods resulted from the implementation of a checklist to ensure adherence to infection-control practices during CVC insertion. In 17.7% of cases, nurses interrupted the procedure to correct at least one point mentioned in the checklist during CVC insertion; failure to maintain a sterile field, failure to use a mask for all personnel entering the box, and failure to use a large sterile drape were the most frequently corrected aspects. On the other hand, we also observed a trend toward greater use of the subclavian vein, a trend toward shorter duration of catheter use during the intervention period and a small tendency to reduce the use of jugular vein, and this is an important point to improve. In addition, educational sessions led by a team of ICU nurses about how to insert and maintain CVCs were repeated twice a year after the implementation of the preventive measures as a complementary measure.

This study has several limitations. First, it was conducted in a single hospital with particular clinical and microbiological characteristics. It would be necessary to conduct

1 a multicenter study to generalize our findings. However, whereas our incidence before
2 the implementation of prevention measures was similar to the mean rate of CR-BSI
3 reported in the National Study of Nosocomial Infections Surveillance in the ICU in
4 Spain (ENVIN-UCI) in 2007 and 2008 (4.6 and 4.9 episodes per 1000 catheter-days,
5 respectively), it has been much lower since the implementation of these measures.
6
7 Second, the design of the study did not allow randomization of patients to the
8 intervention and control groups; instead, we compared the CR-BSI rate during the
9 intervention period with that of a baseline period. However, patients and CVC use in
10 both periods were similar, no additional infection-reducing practices were implemented
11 during the study period compared with the baseline period, and the same months of the
12 year were compared to avoid possible effects from a seasonal trend. These factors
13 support a strong association between the implementation of the intervention and the
14 lower rates of CR-BSI in our ICU.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

31 In summary, our study confirms that the implementation of a simple and
32 inexpensive evidence-based intervention is useful in the sustained reduction of CRBSI
33 in a medical-surgical ICU.
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

References

1. O'Grady N, Patchen Dellinger A, Gerberding J et al. Guidelines for the prevention of intravascular catheter-related infections. CID 2002; 35 :1281-1307.
2. Mermel LA. Prevention of intravascular catheter-related infections. Ann Intern Med 2000; 132:391-402.
3. Warren DK., Cosgrove SE., Diekema DJ. et al. A multicenter intervention to prevent catheter-associated bloodstream infections. Infect Control Hosp Epidemiol 2006; 27:662-669.
4. Renaud B., Brun-Buisson C. et al. Outcomes of primary and catheter-related bacteremia. Am J Respir Crit Care Med 2001; 163:1584-1590.
5. Blot SI., Depuydt P., Annemans L. et al. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. Clin Infect Dis 2005; 41:1591-1598.
6. Warren DK., Quadir WW., Hollenbeak CS. et al. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. Crit Care Med 2006; 34:2084-2089.
7. Alvarez-Lerma J, Palomar M, Olaechea P et al. National Study of Control of Nosocomial Infection in Intensive Care Units. Evolutive report of the years 2003-2005. (Article in Spanish). Med Intensiva 2007; 31:6-17.
8. Pronovost P, Needham D, Berenholtz S et al. An intervention to decrease catheter-related bloodstream infections in the ICU. NEJM 2006; 355: 2725-2732.
9. Warren DK, Zack JE, Mayfield JL et al. The effect of an education program in the incidence of central venous catheter-associated bloodstream infection in a medical ICU. Chest 2004; 126:1612-8.

10. Cohran J., Larson E., Roach H et al. Effect of intravascular surveillance and education program on rates of nosocomial bloodstream infections. *Heart Lung* 1996; 25:161-164.
11. Langgartner J, Linded HJ, Lehn N et al. Combined skin disinfection with chlorhexidine/propanol and aqueous povidone-iodine reduces bacterial colonisation of central venous catheters. *Intensive Care Med* 2004; 30:1081-1088.
12. Valles J, Fernández I, Alcaraz D et al. Prospective Randomized Trial of 3 Antiseptic Solutions for Prevention of Catheter Colonization in an Intensive Care Unit for Adult Patients. *Infect Control Hosp Epidemiol* 2008; 29:847– 853
13. Garnacho J, Aldabó-Pallas T, Palomar M. et al. Risk factors and prognosis of catheter-related bloodstream infection in critically ill patients: a multicenter study. *Intensive Care Med* 2008; 34:2185-2193.
14. Escresca AM. National Multicenter study: risk factors for bacteriemia associated with central venous catheter in Intensive Care Unit. *Intensive Care Med* 2007; 33:S102.
15. Lorente L, Henry C, Martin MM et al. Central venous catheter-related infection in a prospective and observational study of 2,595 catheters. *Crit Care* 2005; 9:631-635.
16. Merrer J, Jonghe BD, Golliot F et al. Complications of femoral and subclavian venous catheterization in critically ill patients. A randomized controlled trial. *JAMA* 2001;286:700.
17. Richet H, Hubert B, Nitemberg G et al. Prospective multicenter study of vascular catheter-related complications and risk factors for positive central catheter cultures in intensive care unit patients. *J Clin Microbiol* 1990; 28:2520.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

18. Mermel LA, McCormick RD, Springman SR, Maki DG. The pathogenesis and epidemiology of catheter- related infections with pulmonary artery Swan-Ganz catheters: A prospective study utilizing molecular subtyping. *Am J Med* 1991;91:197S.

19. Raad I, Hannah H, Maki D et al. Intravascular catheter-related infections: advances in diagnosis, prevention and management. *Lancet Infec Dis* 2007; 7:645-657.

20. Bregenzer T, Conen D, Sakmann P, Widmer AF. Is routine replacement of peripheral intravenous necessary? *Arch Intern Med* 1998; 158:151.

21. Cobb DK, High KP, Sawyer RG, et al. A controlled trial of sheduled replacement of cental venous and pulmonary artery catheters. *N Eng J Med* 1992; 327:1062.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65