What is new for the prevention of catheter-related bloodstream infections?

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Abstract: After the publication in 2011 of latest guidelines of the Centers for Disease Control and Prevention (CDC) for the prevention of catheter-related bloodstream infections (CRBSI) some interesting findings have been published in that field. There has been published that skin disinfection with chlorhexidine alcohol reduced the risk of CRBSI compared to skin disinfection with povidone iodine alcohol, that the implementation of quality improvement interventions reduced the incidence of CRBSI, that the use of chlorhexidine impregnated dressing compared to standard dressings reduced the risk of CRBSI and catheter related cost in an health economic model, and that the use of antimicrobial/antiseptic impregnated catheters reduced the incidence of CRBSI and catheter related cost in clinical studies.

Keywords: Central venous catheter (CVC); bacteremia; prevention; skin disinfection; impregnated catheter; impregnated dressing

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Different measures have been proposed for the prevention of catheter-related bloodstream infections (CRBSI) and have been revised by different scientific societies and the Centers for Disease Control and Prevention (CDC) (1). After the publication of those guidelines in 2011 some interesting articles have been published and could be considered in the prevention of CRBSI.

In this sense, one interesting article has been recently published in September of 2015 by Mimoz *et al.* studying the skin antisepsis (2). In this study were randomized 5,159 catheters to 4 groups of skin disinfection, 2% chlorhexidine and 70% isopropyl alcohol with scrubbing of the skin with detergent before antiseptic application (4% chlorhexidine), 2% chlorhexidine and 70% isopropyl alcohol without scrubbing of the skin with detergent before antiseptic application, 5% povidone iodine and 69% ethanol with detergent before antiseptic application (5% povidone iodine), or 5% povidone iodine and 69% ethanol without detergent before antiseptic application. The authors found that skin disinfection with chlorhexidine alcohol showed a lower risk of CRBSI that skin disinfection with povidone iodine alcohol, with or without scrubbing of the skin with detergent before antiseptic application. Previously, in a study published by Maki *et al.* in 1991 was found that the use of 2% aqueous chlorhexidine decreased the risk of catheter related infection compared to 10% povidone iodine or 70% alcohol (3). In other study by Mimoz *et al.* published in 1996 was found that the use of 0.25% chlorhexidine gluconate plus 0.025% benzalkonium chloride plus 4% benzylic alcohol for skin disinfection compared to 10% povidone iodine reduced the incidence of catheter colonization and catheter related sepsis (4). In a meta-analysis published in 2002 by Chaiyakunapruk *et al.* was found a lower risk of CRBSI with the skin disinfection with chlorhexidine gluconate compared to povidone iodine (5). In a study by Parienti *et al.* published in 2004 was found that the use of 5% povidone iodine in 70% ethanol compared with 10% aqueous povidone iodine for skin disinfection reduced the incidence of catheter colonization (6). In two studies, one published in 2007 and other in 2012, was found that the use of 0.25% chlorhexidine gluconate plus 0.025% benzalkonium chloride plus 4% benzylic alcohol for skin

disinfection compared to 5% povidone iodine in 70% ethanol reduced significantly the risk of catheter colonization and non-significantly the risk of CRBSI (7,8). Thus, the new key points of the study by Mimoz *et al.* (2) compared with those two previous studies (7,8) were that skin disinfection with chlorhexidine alcohol showed a significantly lower incidence of CRBSI that skin disinfection with povidone iodine alcohol, and that in the chlorhexidine alcohol group were used only two compounds. However, that study by Mimoz *et al.* also has some limitations (2), such as the concentrations of antiseptic agents, and the type and concentrations of alcohol components were different in the different catheter groups. In the guidelines published in 2011 was recommended the use of >0.5% chlorhexidine preparation with alcohol for skin antisepsis (1). That recommendation (with category IA) was based in the findings of the two oldest studies previously commented (3,4). Thus, we think that there is enough evidence to recommend the use of >0.5% chlorhexidine preparation with alcohol for skin antisepsis.

Two other interesting articles has been the meta-analysis by Blot *et al.* (9) and the Spanish experience (10) reporting that the implementation of quality improvement interventions reduced the incidence of CRBSI. In 2014 was published a meta-analysis by Blot *et al.*, which included 41 articles published between 1995 and 2012, reporting a reduction on CRBSI incidence with the implementation of quality improvement intervention for CRBSI prevention (9). In addition, Palomar *et al.* published in 2013 the Spanish Experience in 192 ICUs, and this Bacteremia Zero project decreased the overall median rate of CRBSI from 3.07 to 1.12 infections per 1,000 days of catheter (10). Those quality improvement interventions for CRBSI prevention were different in the different projects and included items as education, training, feedback, clinical reminders, bundle (hand hygiene, chlorhexidine skin antisepsis, maximal sterile barrier precautions, optimal catheter site selection, daily review of line necessity), checklist, empowerment to stop procedure, surveillance, leader designation, prepackaging of central venous catheter (CVC) materials, infrastructure changes, organizational changes. In the guidelines published in 2011 was recommended the use of hospital or collaborative improvement initiatives with the combination of different preventive measures (1). That recommendation (with category IB) was based in different experiences that reported a decrease in the CTBSI incidence after the implementation of those initiatives compared to before practice (11-14). Pronovost *et al.* reported in 2006 a reduction in the median incidence of CRBSI from 2.7 (mean of 7.7) infections per 1,000 days of catheter to 0 (mean, 2.3) after the implementation of the intervention in 103 intensive care units (ICUs) in the Michigan state (13). Thus, we think that there is enough evidence to recommend the implementation of quality improvement interventions; in this sense, we are implementing the Spanish Bacteremia Zero project.

Another two interesting articles have been a RCT by Timsit *et al.* (15) and the meta-analysis published by Safdar (16) reporting a reduction in CRBSI incidence with the use of chlorhexidine impregnated dressing. In the RCT published in 2012 by Timsit *et al.*, which included 4,163 CVC and arterial catheters from critically ill patients, was reported a significant lower incidence of CRBSI with the use of chlorhexidine impregnated dressing compared to standard dressings (15). In a meta-analysis published by Safdar *et al.* in 2014, including 9 RCTs and 11,247 catheters, was found that the use of impregnated dressing reduced the risk of CRBSI (16). In addition, a cost-effectiveness analysis recently published in June of 2015 by Maunoury *et al.* found that antimicrobial chlorhexidine gluconate dressing is more cost-effective that non-antimicrobial transparent dressings using a health economic model (17). In the guidelines published in 2011 was recommended the use of chlorhexidine impregnated dressing if the CRBSI rate has not decreased after implementation of a strategy based in basic preventive measures (which include education, the use of a >0.5% chlorhexidine preparation with alcohol for skin antisepsis, and the use of maximal sterile barrier precautions) (1). That recommendation (with category IB) was based in a meta-analysis (18) and two RCTs (19,20). In the meta-analysis published by Ho *et al.* (18) in 2006, including 5 RCTs and 2,396 catheters (CVC and arterial catheters), was found a significant reduction in catheter colonization and a trend to lower incidence of CRBSI with the use of chlorhexidine impregnated dressing compared to standard dressings (18). In the RCT published in 2009 by Timsit *et al.*, which included 3,778 CVC and arterial catheters from critically ill patients, was reported a significant lower incidence of CRBSI with the use of chlorhexidine impregnated dressing (19). In the RCT published in 2009 by Ruschulte *et al.*, which included CVC and arterial catheters from 631 cancer patients, was reported that the use of chlorhexidine impregnated dressing reduced significantly the incidence of CRBSI (20). Thus, we think that the use of chlorhexidine impregnated dressing could reduce the incidence CRBSI and catheter related costs.

In respect to another measure for the prevention of CRBSI, such the use of antimicrobial/antiseptic impregnated

catheters, our team has published the efficacy and efficiency of rifampicin-miconazole impregnated catheters and chlorhexidine-silver sulfadiazine (CHSS) impregnated catheters in different clinical circumstances (21-27). Different antimicrobial agents have been used for the impregnation, such as CHSS, rifampicin-minocycline, and rifampicin-miconazole. Veenstra *et al*. published in 1999 a meta-analysis, which included 11 RCTs and 2,603 catheters, reporting that catheters impregnated with CHSS on the external surface (first generation) reduced the risk of CRBSI compared with non-impregnated catheters (28). Later, a meta-analysis published in 2008 by Hockenhull *et al*., including 3 RCTs and 1,176 patients, reported that catheters impregnated in CHSS on external and internal surfaces (second generation) reduced the CRBSI incidence compared to standard catheters (29). In addition, in a meta-analysis by Falagas *et al*. published in 2007, including 3,452 CVCs from 8 RCTs (using rifampicin-minocycline impregnated catheters in 7 RCTs and rifampicin-miconazole impregnated catheters in 1 RCT), was found a reduction of CRBSI with the use of antimicrobial impregnated catheters compared with non-coated catheters (30). Besides, the use of antimicrobial impregnated catheters has been found to reduce the catheter related cost in some cost-effectiveness analyses (29,31,32). However, in all those cost-effectiveness analyses was included the cost associated with the increase of hospital stay. To simply the cost-effectiveness analyses, our team has carried out several studies to compare the immediate catheter related cost (including only the cost of CVC, diagnosis of CRBSI and antimicrobials for the treatment of CRBSI, and avoiding the cost due to increased hospital stay) using antimicrobial or antiseptic impregnated catheters or standard catheters (22-26). Initially, we found that the use of rifampicin miconazole impregnated catheters could reduce CRBSI incidence and catheter related cost in the jugular venous access with tracheostomy and in the femoral venous access (22,23). Afterwards, we found that the use of second generation of CHSS catheters could reduce CRBSI incidence and catheter related cost in femoral venous access, jugular venous access and subclavian access (24-26). In the guidelines published in 2011 was recommended the use of antimicrobial/antiseptic impregnated catheters (CHSS or rifampicin-minocycline impregnated catheters) if the CRBSI rate has not decreased after implementation of a strategy based in basic preventive measures (which include education, the use of a >0.5% chlorhexidine preparation with alcohol for skin antisepsis, and the use of maximal sterile barrier precautions) (1). This recommendation (with category IA) was based in 3 RCTs showed a reduction on the incidence of catheter tip colonisation with the use of second-generation CHSS-impregnated catheters (33-35) and two RCTs showing that rifampicin-minocycline impregnated catheters reduced the risk of CRBSI (36,37). We think that the use of antimicrobial/antiseptic impregnated catheters could reduce the incidence of CRBSI and catheter related costs.

Conclusions

After the publication in 2011 of latest CDC guidelines for the prevention of CRBSI some interesting findings have been published in that field. There has been published that skin disinfection with chlorhexidine alcohol reduced the risk of CRBSI compared to skin disinfection with povidone iodine alcohol, that the implementation of quality improvement interventions reduced the incidence of CRBSI, that the use of chlorhexidine impregnated dressing compared to standard dressings reduced the risk of CRBSI and catheter related cost in an health economic model, and that the use of antimicrobial/antiseptic impregnated catheters reduced the incidence of CRBSI and catheter related cost in clinical studies.

In our opinion, there is enough scientific evidence to recommend the use of a preparation with >0.5% chlorhexidine alcohol for skin disinfection and the implementation of quality improvement interventions. In addition, the use of chlorhexidine impregnated dressing or antimicrobial/antiseptic impregnated catheters could help in the reduction of CRBSI incidence and catheter related costs.

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Footnote

Conflicts of Interest: L Lorente has been a speaker invited by Teleflex.

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