

Antimicrobial-impregnated catheters for the prevention of catheter-related bloodstream infections

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Abstract

Central venous catheters are commonly used in critically ill patients. Such catheterization may entail mechanical and infectious complications. The interest in catheter-related infection lies in the morbidity, mortality and costs that it involved. Numerous contributions have been made in the prevention of catheter-related infection and the current review focuses on the possible

current role of antimicrobial impregnated catheters to reduce catheter-related bloodstream infections (CRBSI). There is evidence that the use of chlorhexidine-silver sulfadiazine (CHSS), rifampicin-minocycline, or rifampicin-miconazol impregnated catheters reduce the incidence of CRBSI and costs. In addition, there are some clinical circumstances associated with higher risk of CRBSI, such as the venous catheter access and the presence of tracheostomy. Current guidelines for the prevention of CRBSI recommended the use of a CHSS or rifampicin-minocycline impregnated catheter in patients whose catheter is expected to remain in place > 5 d and if the CRBSI rate has not decreased after implementation of a comprehensive strategy to reduce it.

Key words: Catheter; Venous; Prevention; Impregnated; Bloodstream

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Core tip: The catheter-related bloodstream infections (CRBSI) are associated with an increase of mortality and costs. Thus it is necessary to adopt preventive measures to reduce it. In my opinion of view, the use of antimicrobial impregnated catheters could be considered in some clinical circumstances associated with higher risk of CRBSI, such as vascular accesses with higher risk of CRBSI (such as internal jugular venous site with tracheostomy or femoral venous site) or patients with higher risk of CRBSI (such as immunocompromised patients or patients with disorders of skin integrity).

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INTRODUCTION

Some central venous catheter (CVC) could be needed by different reasons, such as administration of fluids, parenteral nutrition, blood products, medications and/or monitor the hemodynamic status. Critically ill patients frequently needed some CVC, and the 78% of them had inserted some CVC^[1]. The catheterization of CVC may have different complications, such as infection, thrombosis and haemorrhage^[2]. Catheter-related infection lead to an increase of mortality, morbidity, and costs^[3-10].

Numerous contributions have been made to analyse the efficacy of different measures to prevent catheter-related infection^[11]. In addition, there have been found that the implementation of different bundles have reduced the incidence of catheter-related bloodstream infections (CRBSI)^[12-15]. This review focuses on the possible current role of antimicrobial impregnated catheters to reduce CRBSI.

BUNDLES TO REDUCE CRBSI

The first published experience reducing CRBSI with the implementation of a bundle was that by Pronovost *et al*^[12], and afterwards other experiences reported lower CRBSI incidence with the implementation of bundles with this proposal^[13-15].

The Keystone Intensive Care Unit (ICU) project by Pronovost *et al*^[12] was carried out in the Michigan state in 103 ICUs between March 2004 and September 2005. In this project was found that 3 mo after intervention implementation was reduced the median incidence of CRBSI from 2.7 (mean of 7.7) infections per 1000 d of catheter to 0 (mean of 2.3) ($P \leq 0.002$) and that during the follow-up of 18 mo was maintained at 0 (mean of 1.4). The prevention measures were avoid the femoral site if possible, the use of full-barrier precautions for CVC insertion, hand washing, chlorhexidine to clean the skin, and remove unnecessary CVC. In addition, an intervention to ventilator-associated pneumonia prevention, the use of a daily goals sheet to improve the communication between clinician within the ICU, and a program to improve the safety culture were implemented.

Afterwards to Michigan experience was carried out the Spanish experience, which was developed in 192 ICUs between April 2008 and June 2010^[13]. The bundle to reduce CRBSI proposed by BZ project included the subclavian venous access as the site of choice (while in Keystone project was recommended to avoid the femoral venous site) and added a measure on the catheter maintenance (such isopropyl alcohol 70° to clean injection ports system and reduce the handling of hubs). In this project was found, that after 18 mo of intervention implementation, a significant decrease ($P < 0.001$) on the overall median CRBSI rate from 3.07 to 1.12 infections per 1000 catheter-days.

There are other experiences showing the beneficial

effect of the implementation of bundles to reduce CRBSI incidence. In a project in 29 pediatric ICUs across the United States, carried out between October 2006 to September 2007, the implementation of a bundle reduce CRBSI incidence from 5.4 vs 3.1 per 1000 catheter-days ($P < 0.001$)^[14]. In other project in 12 ICUs across the United States, the CRBSI incidence decreased from 11.2 to 8.9 infections per 1000 catheter-days (RR = 0.79; 95%CI: 0.67-0.93) after the implementation of a bundle^[15].

EVIDENCE ON ANTIMICROBIAL-IMPREGNATED CATHETERS

CVC impregnated in antimicrobial agents, such as cefazolin, vancomycin, chlorhexidine-silver sulfadiazine (CHSS), rifampicin-minocycline, or rifampicin-miconazol, has been proposed for the prevention of CRBSI^[16].

First generation of CVC impregnated in CHSS (external surface impregnation) compared with non impregnated catheters have reduced CRBSI risk in a meta-analysis (OR = 0.56; 95%CI: 0.37-0.84; $P = 0.005$)^[17]. Afterwards CHSS impregnated catheters of second generation (impregnated in the external and internal surfaces) reduced the CRBSI incidence compared to standard catheters, according the findings of a meta-analysis^[18] including 3 randomised controlled trials (RCTs) and 1176 patients^[19-21].

In addition, other meta-analysis was found a reduction of CRBSI with the use of CVC impregnated on antimicrobial agents compared with non-coated catheters^[22]. In this meta-analysis were included 3452 CVCs from 8 RCTs, 7 RCTs using rifampicin-minocycline impregnated catheters and one using rifampicin-miconazole impregnated catheters.

A multicenter RCT showed that CVC impregnated in rifampicin-minocycline had a lower risk of CRBSI compared to first generation CHSS impregnated^[23]. However, there is not reported a comparison in the incidence of CRBSI between rifampicin-minocycline and CHSS impregnated catheters of second generation.

Antimicrobial impregnated catheters have reduced the CRBSI risk and costs associated with CVC in several cost-effectiveness analyses^[18,24,25]. The cost related to the increase of hospital stay was included in all those cost-effectiveness studies^[18,24,25]. The cost associated to CRBSI was approximately \$10000^[18,24,25]; however, this cost in some studies was as high as \$40000^[5] and \$71000^[7] due to hospital stay increase. To simply the cost-effectiveness analyses, our team carried out several studies to compare the costs associated with CVC using antimicrobial impregnated catheters or standard catheters (including only the cost related to the diagnosis of CRBSI, the antimicrobials used for the treatment of CRBSI, and avoiding the cost due to increased hospital stay)^[26-31].

Initially, we carried out performed one study to analyze the efficacy of rifampicin-miconazole (RM)

impregnated catheters to decrease the CRBSI risk^[26]. There were included 73 RM in femoral site, 111 standard catheters in femoral site, 114 RM in jugular site and 127 standard catheters in jugular site. We found RM impregnated catheters showed a lower risk of CRBSI than standard catheters femoral venous access and in jugular venous access. Afterwards, we found that the use of RM impregnated catheters compared to standard catheters was associated with lower costs related to CVC in the jugular venous access with tracheostomy^[27], and in the femoral venous access^[28].

Afterwards, we studied the cost-effectiveness analyses of second generation of CVC impregnated in CHSS in different venous accesses^[29-31]. We included 64 CHSS during 569 d and 190 standard catheters during 1626 d in femoral venous site; and there was found a lower CRBSI incidence and lower cost related to CVC in patients with CVC impregnated in CHSS than in patients with standard catheters^[29]. In the jugular venous access analysis were included 245 CHSS impregnated catheters during 1685 d of catheter and 391 standard catheters during 1586 d of catheter; and there was found that patients with CVC impregnated in CHSS in comparison with patients with standard catheter showed a lower CRBSI incidence and a lower cost related to CVC^[30]. In the analysis of subclavian venous including 353 patients with CHSS impregnated catheters during 2743 d and 518 with standard catheters during 3297 d, we found a lower incidence of CRBSI and lower CVC related cost per day of catheter in those patients with CHSS impregnated catheters than in those with standard catheters^[31].

RECOMMENDATION OF GUIDELINES ABOUT THE USE OF ANTIMICROBIAL-IMPREGNATED CATHETERS

The 2011 published guidelines for CRBSI prevention recommended CVC impregnated in CHSS or rifampicin-minocycline impregnated catheter in patients whose catheter is expected to remain in place during more than 5 d and the incidence of CRBSI has not been reduced after the implementation of a comprehensive strategy^[11].

I would like to make some comments about some issues of those recommendations. First, the recommendation about the use of CVC impregnated on rifampicin-minocycline was based on two RCTs showing that the use of CVC impregnated on rifampicin-minocycline reduced the risk of CRBSI^[32,33]. However, the guidelines do not mentioned the meta-analysis by Falagas *et al*^[22], which included also other four RCTs, and showing that CVC impregnated on rifampicin-minocycline reduced CRBSI rate. Besides, in those guidelines was not mentioned the published observational study reporting the reduction of CRBSI incidence with CVC impregnated on RM^[26]. Second, there was recommended by those guidelines the use of CHSS impregnated based on 3

RCTs showing second generation of CVC impregnated in CHSS decreased catheter tip colonisation rate^[19-21]. However, there was not specified which generation (first, second or both) of CHSS impregnated catheter was recommended. In addition, in those RCTs were not found significant differences in CRBSI rate with second generation of CVC impregnated in CHSS. Besides, in those guidelines was not mentioned the meta-analysis published by Hockenhull *et al*^[18], which included those 3 RCTs and reported a lower risk of CRBSI using second generation of CVC impregnated in CHSS.

FACTORS ASSOCIATED WITH HIGHER RISK OF CRBSI

I believe that antimicrobial impregnated catheters could be used in some clinical circumstances associated with high CRBSI incidence. About this issue, I will focus in the CRBSI risk according to the venous catheter access and the presence of tracheostomy.

Risk of CRBSI according the CVC access

In a systematic, which included 2 RCTs and 8 observational studies, was concluded that there is no significant difference in the CRBSI incidence between subclavian and femoral venous accesses, and between internal jugular and femoral venous accesses^[34]. To establish those conclusions, the authors excluded two studies from the analysis (one of our team^[35], and other from the team of Nagashima *et al*^[36]), and the criteria that motivate the exclusion of those 2 studies are no clear^[37]. The authors remove these 2 studies due to heterogeneity of the analysis; however, the heterogeneity analysis showed $I^2 = 35\%$ and $P = 0.14$ (and in methods section the authors statement that $I^2 < 49\%$ suggested low heterogeneity and that $P \leq 0.10$ was considered as significant heterogeneity), the same direction on the effect was found in the results of seven of studies included in the review (with a tendency to higher CRBSI risk in femoral venous access than in internal jugular venous access), and the two studies deleted showed the same effect. When these two studies were included, then femoral venous access exhibit a higher risk of CRBSI than internal jugular sites^[34].

In a study published by our team including 2595 CVC (including 917 subclavian, 1390 internal jugular and 288 femoral venous accesses) was reported a higher risk of CRBSI in femoral than in jugular and subclavian accesses, and in jugular than in subclavian access^[35].

In addition, in a study of our team was found a higher CRBSI risk in the central access than in the posterior access of internal jugular vein^[38]. We believed that those findings could be probably due to lower risk of contamination in the posterior access group by oropharyngeal secretion. Critically ill patient undergoing to mechanical ventilation are in a semirecumbent

position to decrease esophageal reflux risk and aspiration risk, according the recommendation by the guidelines of the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America for the prevention of ventilator associated pneumonia^[39]. Thus, in that position the oropharyngeal secretions due to gravity could reach easily the internal jugular vein by the central than by the posterior access.

Afterwards, we found a higher CRBSI risk in femoral venous site than in internal jugular vein by central access^[40]. In addition, we did not find significant differences in CRBSI risk between subclavian venous site and internal jugular vein by posterior access^[41].

Risk of CRBSI according the existence of tracheostomy
Tracheostomy has been found as risk factor of CRBSI^[42,43]. In a study published by the team of Garnacho-Montero *et al*^[42], including 1211 subclavian or jugular venous catheters, the presence of tracheostomy was found to be associated with CRBSI; however, the authors did not report the comparison between the both venous accesses with the presence of tracheostomy^[42]. In another study by our team, which included 89 subclavian venous catheters with tracheostomy, 788 subclavian venous catheters without tracheostomy, 52 central internal jugular venous catheters with tracheostomy and 463 central internal jugular venous catheters without tracheostomy, was found that tracheostomy was associated with higher CRBSI risk. In addition, we found a higher incidence of CRBSI in patients with the presence of tracheostomy in the jugular venous access than in subclavian venous site^[43].

Afterwards, we found that internal jugular venous site by central access and tracheostomy had a higher CRBSI risk than femoral venous site^[44]. In addition, we found a lower CRBSI risk in the subclavian venous site with tracheostomy than in femoral venous site^[45]. Besides, we found a higher CRBSI risk in internal jugular venous site by posterior access with tracheostomy than without tracheostomy^[46].

The guidelines for CRBSI prevention recommend avoid the femoral venous access, and recommended the subclavian venous access rather than jugular or femoral venous accesses to reduce CRBSI risk for non-tunneled CVC placement^[11]. However, there any recommendation about the different internal jugular venous sites and the venous access with tracheostomy.

CONCLUSION

In my opinion, antimicrobial impregnated catheters could be used in some clinical circumstances associated with higher risk of CRBSI, such as vascular sited with high CRBSI risk (femoral venous access or internal jugular venous access with tracheostomy) or patients with high CRBSI risk (patients with disorders of skin integrity or immunocompromised patients).

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