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# Should non-bacteraemic patients with a colonized catheter receive antimicrobial therapy?



V. De Egea<sup>a</sup>, M. Guembe<sup>a,\*</sup>, A. Rodríguez-Borlado<sup>a</sup>, M.J. Pérez-Granda<sup>b,c</sup>, C. Sánchez-Carrillo<sup>a</sup>, E. Bouza<sup>a,b,d</sup>

- <sup>a</sup> Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria del Hospital Gregorio Marañón, Madrid, Spain
- <sup>b</sup> Red Española de Investigación en Patología Infecciosa (REIPI), RD06/0008/1025, Spain
- <sup>c</sup> Cardiac Surgery Postoperative Care Unit, H. G. U. Gregorio Marañón, Madrid, Spain

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#### ABSTRACT

Objectives: The impact of antimicrobial therapy on the outcomes of patients with colonized catheters and no bacteraemia has not been assessed. This study assessed whether targeted antibiotic therapy is related to a poor outcome in patients with positive cultures of blood drawn through a non-tunnelled central venous catheter (CVC) and without concomitant bacteraemia.

Methods: This was a retrospective study involving adult patients with positive blood cultures drawn through a CVC and negative peripheral vein blood cultures. Patients were classified into two groups: those with clinical improvement and those with a poor outcome. These two groups were compared. The outcome was considered poor in the presence of one or more of the following: death, bacteraemia or other infection due to the same microorganism, and evidence of catheter-related bloodstream infection. Results: A total of 100 patients were included (31 with a poor outcome). The only independent predictors of a poor outcome were a McCabe and Jackson score of 1–2 and a median APACHE score of 5. No association was found between the use of targeted antimicrobial therapy and a poor outcome when its effect was adjusted for the rest of the variables.

*Conclusions:* This study showed that antimicrobial therapy was not associated with a poor outcome in non-bacteraemic patients with positive blood cultures drawn through a CVC.

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#### Introduction

Catheter-related bloodstream infection (CRBSI) is a major nosocomial disease occurring by extra- or intraluminal route, depending on the duration that the catheter is in place. Those catheters that are inserted for a short period of time (<7 days) are usually colonized extraluminally (skin), and those catheters that are inserted for a long period of time (>7 days) are usually colonized intraluminally (contamination of the hubs) (Mermel et al., 2009; Kumar et al., 2013; Ramritu et al., 2008). Therefore, the

E-mail addresses: Vivi\_de\_egea@hotmail.com (V. De Egea), mariaguembe@hotmail.com (M. Guembe), anabelborlado@yahoo.es (A. Rodríguez-Borlado), massus@hotmail.es (M.J. Pérez-Granda), cscarrillo@salud.madrid.org (C. Sánchez-Carrillo), ebouza@micorb.net (E. Bouza). diagnosis of catheter colonization can be made without catheter withdrawal using conservative diagnostic methods, such as the differential time to positivity, which has proven useful in various populations (Mermel et al., 2009; Guembe et al., 2010; Bouza et al., 2007; Chen et al., 2009; Freeman et al., 2013; Garcia et al., 2012; Park et al., 2014; Seifert et al., 2003). This approach requires blood cultures to be obtained simultaneously from all catheter lumens and from a peripheral vein, so that an episode of CRBSI is confirmed when the same microorganisms recovered from the lumen blood grow at least 2 h before those recovered from peripheral blood. However, sometimes only blood drawn through the catheter yields positive cultures, in which case the catheter is considered to be colonized.

The clinical significance of colonization of non-tunnelled central venous catheters (CVCs) in patients with no concomitant bacteraemia has not been properly assessed, and the decision of whether to start antimicrobial therapy in this situation is controversial (Guembe et al., 2014; Ruhe and Menon, 2006;

<sup>&</sup>lt;sup>d</sup> Universidad Complutense, Madrid, Spain

<sup>\*</sup> Corresponding author at: Servicio de Microbiología Clínica y Enfermedades Infecciosas, Hospital General Universitario Gregorio Marañón, C/ Dr. Esquerdo, 46, 28007 Madrid, Spain. Tel.: +34 91 586 84 53; Fax: +34 91 586 87 67.

Ekkelenkamp et al., 2008; Perez-Parra et al., 2009; Mrozek et al., 2011; Park et al., 2010; Perez-Parra et al., 2011; Munoz et al., 2012; Peacock et al., 1998; Leenders et al., 2011; van Eck van der Sluijs et al., 2012; Hetem et al., 2011). This issue remains unresolved in current clinical guidelines (Mermel et al., 2009; Mermel et al., 2001).

The objective of this study was to assess whether targeted antibiotic therapy is a protector factor or a risk factor for having a poor outcome in patients with colonized CVCs and without concomitant bacteraemia.

#### Methods

#### Setting

The study hospital is a 1550-bed general teaching institution, with approximately 50 000 admissions per year. The hospital provides all of the services of a general teaching hospital.

#### Design

This was an observational retrospective cohort study that included all adult patients admitted to the institution between January 2010 and December 2012 with positive cultures of blood drawn through a non-tunnelled CVC and a negative peripheral blood culture. Patients could not have had bacteraemia during the previous month. Children under 16 years old and patients with oncological and haematological conditions were excluded. Patients were identified and analyzed by reviewing the microbiology databases and medical records (Figure 1).

For the patient follow-up, clinical data from the patient records and hospital databases were reviewed at least until discharge, as well as survivors for up to 1 year.

Patients were classified into two groups according to the clinical outcome: good outcome or poor outcome. The outcome was considered poor in the presence of one or more of the following variables during the year after culture: death, bacteraemia or any other infection due to the same microorganism isolated in blood from a catheter, or evidence of CRBSI. The two groups were compared in order to analyze risk factors for a poor outcome, including the influence of targeted antimicrobial therapy for catheter colonization as the most important variable.

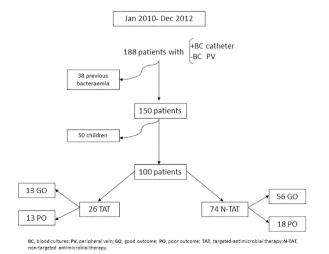


Figure 1. Flow chart of patient inclusion.

#### Clinical data collection

Patient characteristics were recorded using a pre-established protocol and included age, sex, intensive care unit (ICU) admission, neutropenia, surgical procedure, recent parenteral nutrition, endocarditis, defined daily doses (DDDs), antibiotic treatment, other infections, underlying diseases, comorbidity factors, severity of illness scores such as APACHE II, and the maximum severity reached before the catheter was shown to be colonized. Microbiological data from blood cultures and data on antimicrobial therapy and end-points (mortality, bacteraemia, and CRBSI) were also recorded.

#### Laboratory procedures

Blood cultures were processed following routine methods using a semi-automated culture detector (Bactec 9240, Bactec Plus Aerobic/F; Becton Dickinson Microbiology Systems, Maryland, DE, USA). The microorganisms recovered were fully identified using standard microbiological methods.

#### **Definitions**

Targeted antimicrobial therapy after catheter colonization was considered adequate when an oral or parenteral antimicrobial agent was active in vitro against the microorganism causing catheter colonization.

#### Statistical analysis

Normally distributed continuous variables were compared using the *t*-test; non-normally distributed variables were compared using the Mann–Whitney test, median test, or Kruskal–Wallis test. Categorical variables were evaluated using the Chisquare test or two-tailed Fisher's exact test.

Values for continuous variables were expressed as the mean and standard deviation (SD), or median and interquartile range (IQR); values for categorical variables were expressed as percentages, with a 95% confidence interval (95% CI) when applicable. A two-tailed test was used to determine statistical significance, which was set at p < 0.05.

Multivariate analysis was used to identify independent prognostic factors including those variables that showed a statistically significant difference between the two groups on univariate analysis. This analysis was performed using binary logistic regression and incorporated variables found to be significant (p-value of <0.1) on univariate testing. The statistical analysis was performed using PASW Statistics for Windows version 18.0 (SPSS Inc., Chicago, IL, USA).

#### **Ethics**

The local ethics committee of the Hospital General Universitario Gregorio Marañón approved the study. The study was exempted from the need for participant written or verbal informed consent given its retrospective nature.

#### Results

A total 100 patients were identified during the study period. Their median age was 61.5 years (IQR 50.6–73.3 years). Clinical and demographic data are summarized in Table 1.

According to the study definition, 69 patients had a good outcome and 31 a poor outcome. Overall, 26 patients received targeted antibiotic treatment after CVC colonization, 18.8% in the good outcome group and 41.9% in the poor outcome group

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