

ANNEXES TO CHAPTER 6

**Clinical Question XXXI. Does catheter-related bacteraemia secondary to infection with *Staphylococcus aureus*, *Pseudomonas* sp. and *Candida* spp. force catheter withdrawal and therefore contraindicate antibiotic lock treatment to attempt to preserve the catheter?**

Although the removal of an infected catheter has long been accepted as the only way to eradicate infection of the blood stream, the shortage of vascular access sites for patients on haemodialysis has enlivened the debate about methods for treating bacteraemia which allow salvage of the catheter and preservation of the vascular access site (Vats 2012).

Maya (2008) notes that the majority of cases treated for bacteraemia of the catheter resolve without major complications, but that there is a high risk, up to 20%, of the infected catheters spreading bacteria to distant sites, including heart valves, bones, joints, epidural space, subcutaneous tissue or others.

A narrative review by Saxena (2005) reported that the rates for each infectious agent responsible for haemodialysis catheter-related bacteraemia ranged from 21.9% to 60% for *S. Aureus* and from 2.3% to 15.2% for *Pseudomonas aeruginosa*; no data were provided on *Candida*.

The Maya narrative review (2008) identified an RCT comparing *antibiotic lock* to placebo, both added to parenteral therapy, in the treatment of long-term catheter-related bacteraemia: The RCT included 46 patients, only one of whom had *S. Aureus* infection and none *Pseudomonas* or *Candida* species. Although those treated with *antibiotic lock* had better outcomes than those treated with placebo, the differences were not statistically significant in relation to treatment failure: bacteraemia not cured in 33% (7/21) of those in the antibiotic lock group compared to 57% (13/23) in the placebo group,  $p=0.10$ ; recurrent bacteraemia with the same strain in 3/31 *antibiotic lock* patients compared to 9/23 for placebo patients;  $p=0.06$ .

Infectious Diseases Society of America guidelines (Mermel 2009) state that haemodialysis catheters should be removed if bacteraemia is complicated by severe sepsis (haemodynamic instability), osteomyelitis, endocarditis, septic thrombophlebitis, or persistent positive blood cultures 72 hours after appropriate antibiotic therapy. In uncomplicated bacteraemia with coagulase-negative staphylococcus or Gram-negative microorganisms, they argue that an attempt may be made to treat, with 2 weeks of intravenous antibiotics and antibiotic lock, without changing the catheter. However, if the infecting organism is *Staphylococcus aureus*, *Pseudomonas aeruginosa* or *Fungi*, they do not recommend the *antibiotic lock*.

The Katneni narrative review (2007) on bacteraemia related to central venous catheters located observational studies included in other reviews, and argues that the evidence from these studies may be limited by lack of randomised control groups, selection bias, small numbers of patients and inadequate duration of follow-up.

No published studies have been found directly comparing the results of immediate catheter removal with leaving the catheter in place with antibiotic lock, in patients with catheter-related bacteraemia caused by *Staphylococcus aureus*, *Pseudomonas* species or *Candida* species.

## Spanish Clinical Guidelines on Vascular Access for Haemodialysis

<b>Bacteraemia caused by <i>Staphylococcus aureus</i> infection</b>	
<p>The Fitzgibbons narrative review (2011) notes that the incidence of catheter-related bacteraemia in patients receiving haemodialysis would be approximately 7.6 to 14.4 cases per 100 patient-years with catheter, with <i>Staphylococcus aureus</i> the pathogen responsible for 56% of cases.</p> <p>Data from three observational studies (Maya 2007; Fernández-Hidalgo 2006; Poole 2004) demonstrate that the combined use of systemic antibiotics and antibiotic solution in the catheter (<i>antibiotic lock</i>) for <i>Staphylococcus aureus</i> infections resulted in catheter preservation rates of 40% to 55%.</p> <p>Fitzgibbons (2011) considers that catheter removal is the best strategy for dealing with a <i>Staphylococcus aureus</i> bacteraemia in patients on haemodialysis via catheter.</p>	<b>Low quality</b>
<p>The Fernández-Hidalgo clinical series (2006) included 115 patients with long-term catheter-related bacteraemia, only 37 of whom had the catheter for haemodialysis.</p> <p>In 20 patients the bacteraemia was caused by <i>S. aureus</i> infection and the combined treatment with systemic therapy and <i>antibiotic lock</i> failed in nine cases (seven with catheter for haemodialysis and two for chemotherapy), with one of the patients dying from septic shock (treated for haemodialysis).</p>	<b>Low quality</b>
<p>In the Maya prospective clinical series (2007), with 113 patients with haemodialysis catheter-related <i>S. aureus</i> bacteraemia treated with <i>antibiotic lock</i>, the catheter was saved in 40.7% of the patients (46/113), and was removed in the remaining 67 patients: in 40 for persistent fever and in 27 for recurrent bacteraemia.</p> <p>In 9.7% of patients (11/113) serious complications of bacteraemia occurred. They concluded that routine therapy with <i>antibiotic lock</i> is not suitable in these patients.</p>	<b>Low quality</b>
<p>The Poole clinical series (2013) included ten cases of <i>S. aureus</i> bacteraemia, all systemic and treated by <i>antibiotic lock</i>. The treatment was only successful in four patients (40%).</p>	<b>Low quality</b>
<p>The Joshi clinical series (2013) included seven cases of <i>S. aureus</i> bacteraemia, all treated systemically and by <i>antibiotic lock</i>. In the two cases in which the germs were methicillin resistant and also in two of the five cases in which the germs were sensitive to methicillin, the treatment failed to eradicate the infection and the catheters had to be removed.</p> <p>One of the patients with methicillin-resistant <i>S. aureus</i> developed endocarditis due to metastatic infection and subsequently died.</p>	<b>Low quality</b>
<p>The Krishnasami clinical series (2002) included two cases of <i>S. aureus</i> bacteraemia treated systemically and by <i>antibiotic lock</i>. In one of the cases the germ was methicillin resistant and in the other not. Treatment failed to eradicate the infection in either case, requiring removal of the catheters.</p>	<b>Low quality</b>
<p>The Capdevila clinical series (1993) included two cases of antibiotic-sensitive <i>S. aureus</i> bacteraemia treated systemically and by <i>antibiotic lock</i>. In both cases the infection was brought under control and the catheters saved.</p>	<b>Low quality</b>

## Spanish Clinical Guidelines on Vascular Access for Haemodialysis

<b>Bacteraemia caused by <i>Pseudomonas</i> infection</b>	
<p>The Fernández-Hidalgo clinical series (2006) included 115 patients with long-term catheter-related bacteraemia, only 37 of whom had the catheter for haemodialysis.</p> <p>Five of the cases of bacteraemia were caused by <i>Pseudomonas</i> infection, but no data is provided on how many of these were patients on haemodialysis. Combined treatment with systemic therapy and <i>antibiotic lock</i> failed in one case, this case being a patient on haemodialysis.</p>	<b>Low quality</b>
<p>The Capdevila clinical series (1993) included five cases of antibiotic-sensitive <i>Pseudomonas aeruginosa</i> bacteraemia treated systemically and by <i>antibiotic lock</i>. In both cases the infection was brought under control and the catheters saved.</p>	<b>Low quality</b>
<p>The Joshi clinical series (2013) included two cases of <i>pseudomonas</i> bacteraemia, treated systemically and by <i>antibiotic lock</i>. Treatment failed to eradicate the infection in either case, requiring removal of the catheters.</p>	<b>Low quality</b>
<b>Bacteraemia caused by <i>Candida</i></b>	
<p>No published studies were found that provide outcomes of the <i>antibiotic lock</i> in cases of bacteraemia caused by <i>Candida</i> species.</p> <p><i>Candida</i> infection as initial causative pathogen of the bacteraemia appears to be considered as sufficient reason for removal of the catheter or as a criterion for exclusion in the study (Manierski 2006; Mermel 2009; Fernández-Hidalgo (2006).</p>	
<b>Summary of evidence</b>	
<p>Clinical series, which include a total of 154 cases of patients treated with antibiotic lock added to systemic therapy, show overall catheter preservation rates of around 40%, and rates of serious complications of around 9%, including two deaths. The authors of the largest clinical series and those of the Infectious Diseases Society of America guidelines recommend the removal of the catheter in such cases.</p>	<b>Low quality</b>
<p>Clinical series, which include in total 12 cases of patients treated with antibiotic lock added to systemic therapy, show overall catheter preservation rates of around 75%. The Infectious Diseases Society of America guidelines recommend catheter removal in such cases.</p>	<b>Low quality</b>
<p>No published studies were found that provide outcomes of the antibiotic lock in cases of bacteraemia caused by <i>Candida</i> species. The Infectious Diseases Society of America guidelines recommend catheter removal in such cases.</p>	<b>Low quality</b>

## Spanish Clinical Guidelines on Vascular Access for Haemodialysis

### Patients' values and preferences

*No relevant studies related to this aspect have been identified.*

### Use of resources and costs

*No relevant studies related to this aspect have been identified.*

### Recommendations [Proposal]

#### **Weak**

We recommend removal of the catheter in catheter-related bacteraemia caused by *Staphylococcus aureus*, *Pseudomonas* species or *Candida* species.

### References

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## Spanish Clinical Guidelines on Vascular Access for Haemodialysis

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**Table 1. STUDIES EXCLUDED**

<b>Study</b>	<b>Cause for exclusion</b>
Beathard 1999	Does not provide guidance regarding outcomes of <i>antibiotic locks</i> .
Marr 1997	Does not provide guidance regarding outcomes of <i>antibiotic locks</i> .
Mokrzycki 2002	Does not provide guidance regarding outcomes of <i>antibiotic locks</i> .

**GRADE TABLES**

**Date:** 2014-01-23

**Question:** Should Antibiotic lock be used for catheter-related bacteraemia secondary to infection by *Staphylococcus aureus*?

**Bibliography:** Fitzgibbons (2011), Fernández-Hidalgo (2006), Maya (2007), Poole (2013), Joshi (2013), Krishnasami (2002).

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic lock	Control	Relative (95% CI)	Absolute		
<b>Preservation of the catheter</b>												
6	observational studies <sup>1</sup>	serious <sup>1</sup>	very serious <sup>2</sup>	no indirectness	serious	serious <sup>3</sup>	none	-	-	-	-	CRITICAL

<sup>1</sup> case series.

<sup>2</sup> High variability of results: treatment success rates between 0% and 100% .

<sup>3</sup> Very small patient samples.

Date: 2014-01-23

Question: Should antibiotic lock be used for catheter-related bacteraemia secondary to infection by *Pseudomonas* species?

Bibliography: Capdevila (1993), Joshi (2013).

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic lock	Control	Relative (95% CI)	Absolute		
<b>Preservation of the catheter</b>												
2	observational studies <sup>1</sup>	serious <sup>1</sup>	very serious <sup>2</sup>	no indirectness	serious	serious <sup>3</sup>	none	5/7 (71.4%)	-	-	-	CRITICAL

<sup>1</sup> case series.

<sup>2</sup> High variability of results: treatment success rates between 0% and 100%..

<sup>3</sup> Very small patient samples.