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## [Intervention Review]

# Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis

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# ABSTRACT

#### Background

Patients undergoing haemodialysis (HD) through a central venous catheter (CVC) are exposed to several risks, being a catheter-related infection (CRI) and a CVC lumen thrombosis among the most serious. Standard of care regarding CVCs includes their sealing with heparin lock solutions to prevent catheter lumen thrombosis. Other lock solutions to prevent CRI, such as antimicrobial lock solutions, have proven useful with antibiotics solutions, but not as yet for non-antibiotic antimicrobial solutions. Furthermore, it is uncertain if these solutions have a negative effect on thrombosis incidence.

#### Objectives

To assess the efficacy and safety of antimicrobial (antibiotic, non-antibiotic, or both) catheter lock solutions for preventing CRI in participants undergoing HD with a CVC.

## Search methods

We searched the Cochrane Kidney and Transplant Specialised Register up to 18 December 2017 through contact with the Information Specialist using search terms relevant to this review. Studies in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register (ICTRP) Search Portal, and ClinicalTrials.gov.

#### **Selection criteria**

We included all randomised or quasi-randomised control trials (RCTs) comparing antimicrobial (antibiotic and non-antibiotic) lock solutions to standard lock solutions, in participants using a CVC for HD, without language restriction.

## Data collection and analysis

Two authors independently assessed studies for eligibility, and two additional authors assessed for risk of bias and extracted data. We expressed results as rate ratios (RR) per 1000 catheter-days or 1000 dialysis sessions with 95% confidence intervals (CI). Statistical analyses were performed using the random-effects model.

## **Main results**

Thirty-nine studies, enrolling 4216 participants, were included in this review, however only 30 studies, involving 3392 participants, contained enough data to be meta-analysed. Risk of bias was low or unclear for most domains in the majority of the included studies.

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Studies compared antimicrobial lock solutions (antibiotic and non-antibiotic) to standard sealing solutions (usually heparin) of the CVC for HD. Fifteen studies used antibiotic lock solutions, 21 used non-antibiotic antimicrobial lock solutions, and 4 used both (antibiotic and non-antibiotic) lock solutions. Studies reported the incidence of CRI, catheter thrombosis, or both.

Antimicrobial lock solutions probably reduces CRI per 1000 catheter-days (27 studies: RR 0.38, 95% CI 0.27 to 0.53; I<sup>2</sup> = 54%; low certainty evidence), however antimicrobial lock solutions probably makes little or no difference to the risk of thrombosis per 1000 catheter days (14 studies: RR 0.79, 95% CI 0.52 to 1.22; I<sup>2</sup> = 83%; very low certainty evidence). Subgroup analysis of antibiotic and the combination of both lock solutions showed that both probably reduced CRI per 1000 catheter-days (13 studies: RR 0.30, 95% CI 0.22 to 0.42; I<sup>2</sup> = 47%) and risk of thrombosis per 1000 catheter-days (4 studies: RR 0.26, 95% CI: 0.14 to 0.49; I<sup>2</sup> = 0%), respectively. Non-antibiotic antimicrobial lock solutions probably reduced CRI per 1000 catheter-days for tunnelled CVC (9 studies: RR 0.60, 95% CI 0.40 to 0.91) but probably made little or no difference with non-tunnelled CVC (4 studies: RR 0.39, 95% CI 0.48 to 1.81). Subgroup analyses showed that antibiotic (5 studies: RR 0.76, 95% CI 0.42 to 1.38), non-antibiotic (8 studies: RR 0.85, 95% CI 0.44 to 1.66), and the combination of both lock solutions (3 studies: RR 0.63, 95% CI 0.22 to 1.81) made little or no difference to thrombosis per 1000 catheter-days compared to control lock solutions.

# Authors' conclusions

Antibiotic antimicrobial and combined (antibiotic-non antibiotic) lock solutions decreased the incidence of CRI compared to control lock solutions, whereas non-antibiotic lock solutions reduce CRI only for tunnelled CVC. The effect on thrombosis incidence is uncertain for all antimicrobial lock solutions. Our confidence in the evidence is low and very low; therefore, better-designed studies are needed to confirm the efficacy and safety of antimicrobial lock solutions.

# PLAIN LANGUAGE SUMMARY

## Antimicrobial lock solutions for preventing infections in patients using a catheter for haemodialysis

## What is the issue?

Most of the people presenting end-stage kidney disease use haemodialysis (HD) to replace kidney function. Frequently, a central venous catheter (CVC) is needed to begin HD. In between HD sessions, the CVC needs a sealing solution to avoid catheter thrombosis (an obstruction due to clots), and this is frequently heparin.

In addition to catheter thrombosis, another frequent complication is catheter-related infection (CRI). CRI originates in the catheter and then spreads to the blood or other organs.

Heparin prevents clot formation but does not prevent infections. Therefore, instead of heparin, the use of sealing solutions that can reduce CRIs has been proposed. These antimicrobial lock solutions could be divided into antibiotic (e.g. vancomycin) and non-antibiotic (e.g. citrate) solutions. Antimicrobial lock solutions should fill the catheter lumen and then be locked in the catheter during in-between HD sessions with or without heparin.

# What did we do?

We did a systematic review to assess the question whether antimicrobial (antibiotic or non-antibiotic) lock solutions were better than heparin to prevent CRIs in patients undergoing HD through a CVC and thrombosis compared to heparin. We searched the literature up until 18 December 2017 and identified 39 studies enrolling 4216 patients that met our inclusion criteria.

#### What did we find?

We included 39 studies, including 3,945 participants undergoing HD through a CVC. The studies compared CVC sealing solutions with heparin to antimicrobial lock solutions. Fifteen studies used only antibiotic lock solutions, 21 used non-antibiotic lock solutions, and 4 used both (antibiotic and non-antibiotic) lock solutions. Studies measured the incidence of CRIs and catheter thrombosis, or both. Overall quality of the studies was low for CRIs and very low for thrombosis. There was no information on funding sources for most of the studies.

In general antimicrobial lock solutions are likely superior to standard solutions in preventing CRIs among patients undergoing HD through a CVC, but non-antibiotic solutions did not prove to reduce CRI. They are no worse than heparin at preventing thrombosis. Other adverse effects were not reported in most studies. Our confidence in these results is low due to the quality of the studies.

#### Conclusion

Some antimicrobial (antibiotic and the combination of antibiotic-non antibiotic) lock solutions decrease the incidence of CRIs compared to heparin. Their effect on CVC permeability remains unclear. The quality of the studies is low and very low, respectively; therefore, more studies are needed to confirm the benefits and harms of antimicrobial lock solutions.