CATETERI VENOSI CENTRALI TRATTATI CON ANTISETTICI O ANTITROMBOTICI: QUALI EVIDENZE

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FIRENZE

ANTIMICROBIAL and ANTITHROMBOTIC COATED CVCs

PERCHE'?

QUALI TIPI?

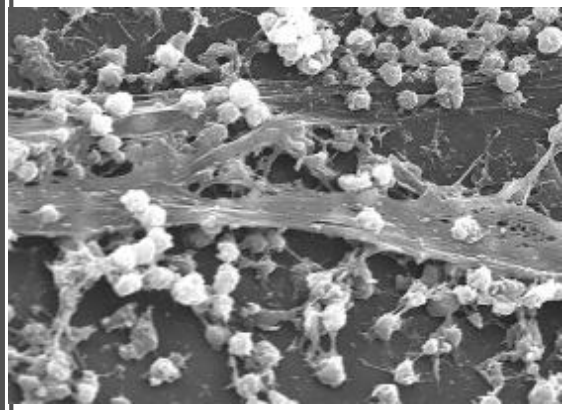
QUALI EVIDENZE?

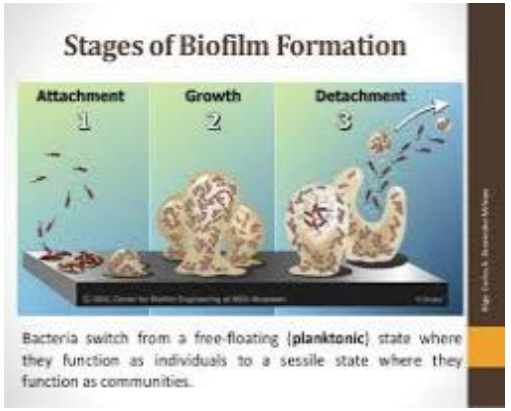
QUANDO USARLI?

QUALI USARE?

ANTIMICROBIAL COATED CVCs

PERCHE'?





FIBROBLASTIC SLEEVE AND BIOFILM

IL CATETERE IDEALE…

- Combat biofilm, thrombus formation and infection
- Biocompatible
- Prevent fibrin sheath formation
- Have a long-term effect
- Have a wide range of anti-microbial activity without producing resistance

ANTIMICROBIAL and ANTITHROMBOTIC COATED CVCs

QUALI TIPI?

CATETERI trattati con ANTITROMBOTICI

- HEPARIN

Material thrombogenicity in central venous catheterization. I. A comparison between uncoated and heparin-coated, long antebrachial, polyethylene catheters.

Bennegård K, Curelaru I, Gustavsson B, Linder LE, Zachrisson BF.

Acta Anaesthesiol Scand. 1982 Apr;26(2):112-20.

- CHLOREHEXIDINE

?

NO EVIDENCE

- ENDEXO (BIOFLOW™)

Outcomes in a nurse-led peripherally inserted central catheter program: a retrospective cohort study.

McDiarmid S, Scrivens N, Carrier M, Sabri E, Toye B, Huebsch L, Fergusson D.

CMAJ Open. 2017 Jun 30;5(3):E535-E539. doi: 10.9778/cmajo.20170010.

PMID: 28676535 **Free PMC Article**

Similar articles

CATETERI trattati con ANTIMICROBICI: QUALI TIPI

	Surface activity	Name (manufacturers or distributors)	Availability	
			UK	USA
Silver with platinum and carbon (iontophoretic)	External and internal	Vantex CVC kits (Edwards Life Sciences, Irvine, CA, USA)	Yes	Yes
Silver in a ceramic zeolite matrix (impregnated)	External and internal	Multicath Expert range (Vygon Ltd, Ecouen, France)	Yes	No
First-generation chlorhexidine and silver sulfadiazine	External	ARROWg+ard Blue (Arrow International, Inc, Reading, PA, USA)	Yes	Yes
Second-generation chlorhexidine and silver sulfadiazine	External (plus internal chlorhexidine coating)	ARROWg+ard Blue PLUS (Arrow International, Inc)	Yes	Yes
Benzalkonium chloride	External and internal	Hydrocath Assure (BD Ltd, Franklin Lakes, NJ, USA)	Yes	Yes
Benzalkonium chloride–heparin bonded	External and internal	AMC Thromboshield treatment (Edwards Life Sciences)	Yes	Yes
Minocycline and rifampicin	External and internal	Cook Spectrum (Cook Medical, Inc, Bloomington, IN, USA)	Yes	Yes
Miconazole and rifampicin	External and internal	Multistar (Vygon Ltd)	Yes	No

Table 1: Types of adult antimicrobial CVC commercially available in the UK and USA

ANTISEPTIC and ANTITHROMBOTIC COATED CVCs

QUALI EVIDENZE?

ANTIMICROBIAL CENTRAL VENOUS CATHETERS IN ADULTS: A SYSTEMATIC REVIEW AND METANALYSIS

Casey A. Lancet Infect Disease 2008

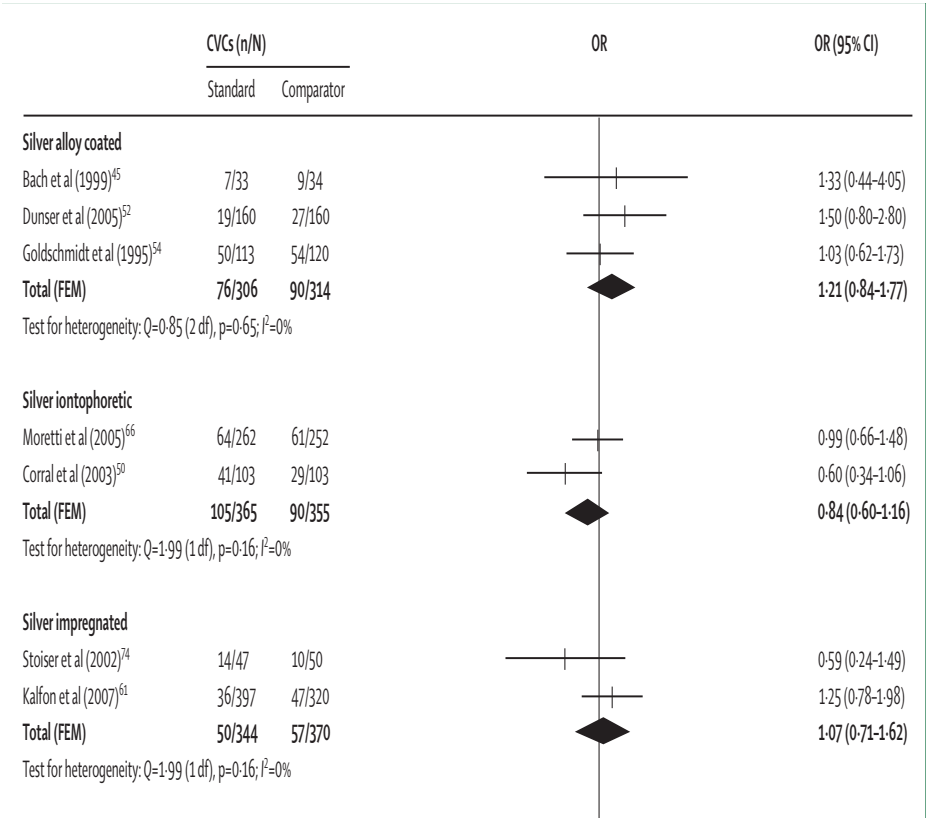
- 34 RCTs
- Silver, Chlorehexidine Silver- Sulfadiazine (CSS), Benzalkonium Chloride, Minocycline-Rifampicine, Rifampicine-Miconazole
- **ENDPOINTS**
  - **COLONISATION**
  - **CRBSI**

Risultati della metanalisi

I cateteri medicati rispetto agli standard **sono efficaci** nel ridurre la colonizzazione e, soprattutto, le CRBSI

Tuttavia, **non tutte le tipologie** di catetere sono egualmente efficaci…

CATETERI ALL'ARGENTO



FAVOURS ANTIMICROBIAL CVC

FAVOURS STANDARD CVC

I cateteri all'argento (impregnati, ricoperti o trattati con la iontoforesi) **NON SONO EFFICACI** nel ridurre la **colonizzazione** né le **CRBSI**

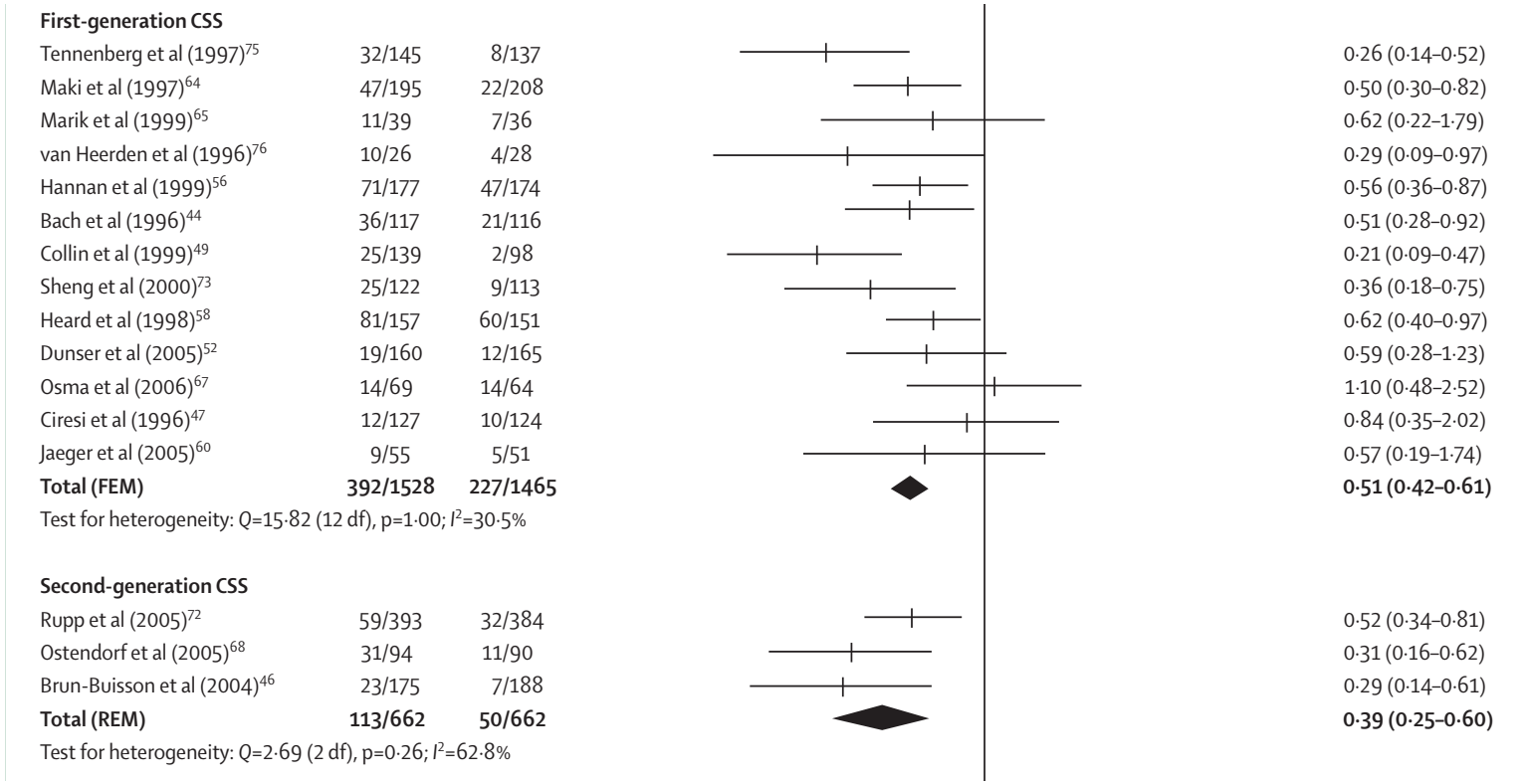
CATETERI AL BENZALCONIO CLORURO

- ✓Nessuna riduzione di colonizzazione o CRBSI
- ✓Attività antimicrobica limitata su C. albicans, E. coli, K. Pneumoniae
- ✓Nessuna attività su Pseudomonas aeruginosa
- ✓Concludendo: **nessuna efficacia**

CATETERI MICONAZOLO-RIFAMPICINA

- ✓I cateteri trattati con rifampicina e miconazolo si sono dimostrati capaci di **ridurre la colonizzazione da alcuni germi**
- ✓Attività limitata in vitro, su Candida albicans, E. coli, P. aeruginosa, Enterobacter spp
- ✓**Due soli studi pubblicati**
- ✓**Nessuna raccomandazione per l'uso clinico**

CATETERI CON CLOREXIDINA-SULFADIAZINA (CSS)



CATETERI CON CLOREXIDINA-SULFADIAZINA (CSS)

- I cateteri CSS di **prima e seconda generazione SONO EFFICACI** nella **riduzione della colonizzazione**
- I cateteri CSS di **prima generazione** sono efficaci nella **riduzione delle CRBSI**
- I cateteri CSS di **seconda generazione** sono efficaci nella riduzione delle **CRBSI**, ma **in maniera meno significativa**, probabilmente perché gli studi su di essi sono stati condotti in anni più recenti, in cui **l'incidenza di CRBSI era comunque diminuita** per l'implementazione di strategie di prevenzione

Limitazioni dei cateteri CSS

Sebbene assai infrequentemente, **reazioni di ipersensibilità** sono state riportate in UK e in Giappone, in caso di precedente esposizione a prodotti contenti clorexidina e probabilmente per predisposizione genetica

Case Report

Chlorhexidine impregnated central venous catheter inducing an anaphylatic shock in the Intensive Care Unit

A. Khoo * and P. Oziemski, FRACP

Intensive Care Unit, Epworth Hospital, 89 Bridge Road, Richmond, Victoria 3121, Australia

Chlorhexidine, a bisbiguanide, is widely used as an antiseptic agent in medical practice as it has the greatest residual antimicrobial activity.

Central venous catheters coated extraluminally with chlorhexidine have been made to reduce extraluminal contamination. By using both the chlorhexidine–alchohol skin preparation and antimicrobial-coated catheters during vascular cannulation, it can reduce catheter related bloodstream significantly [1]. The reduction in infection rate is especially vital in critically ill patients who require long-term vascular access.

Adverse reactions to chlorhexidine are rare and uncommon, and have been under-recognised as a cause of anaphylaxis. There are several reports of allergic reactions following exposure to chlorhexidine. We report of a case of anaphylaxis shock requiring cardiopulmonary resuscitation during the placement of a chlorhexidine impregnated central venous catheters.

(Heart, Lung and Circulation 2010;xxx:1–2)

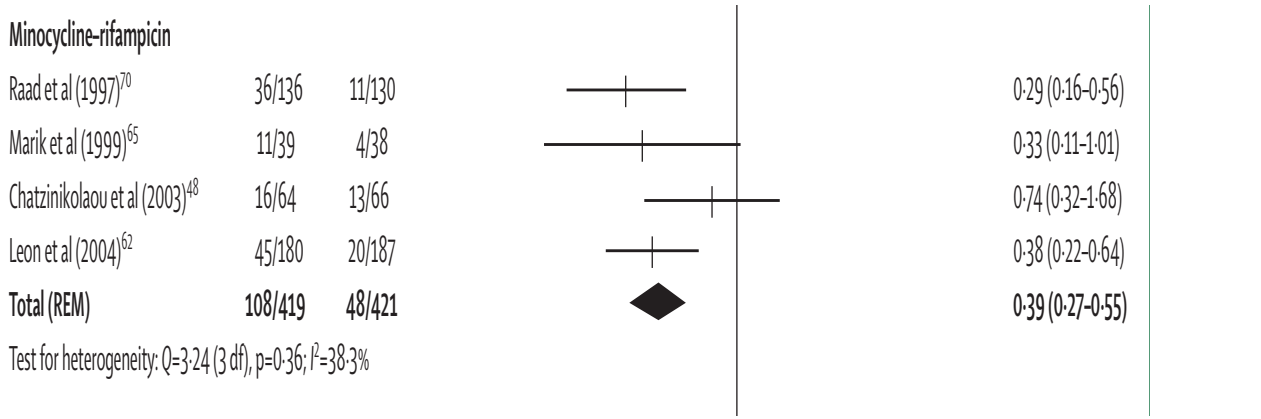
Keywords. Chlorhexidine; Anaphylaxis; Intensive care unit

Limitazioni dei cateteri CSS

- **Resistenze in vitro** a Acinetobacter baumanii, Stenotrophomoas maltophilia, Enterobacter cloacae
- **Resistenze in vivo**, però, **mai segnalate**

Raad, 1996; Marik, 1999; Maki, 1997; Veenstra, 1999; Bassetti, 2001; Rupp, 2005

CATETERI con MINOCICLINA-RIFAMPICINA (MR)



CATETERI con MINOCICLINA-RIFAMPICINA (MR)

- ✓I cateteri MR **SONO EFFICACI** nella riduzione della colonizzazione e delle CRBSI
- ✓**Superiorità** in **un trial** di confronto **rispetto a CSS di prima generazione** (necessità, però,di un nuovo trial di confronto con i CSS di seconda generazione!)

Limiti dei cateteri MR

- ✓Attività limitata in vitro su **Pseudomonas aeruginosa**
- ✓Attivi su Gram positivi e Gram negativi ma **non sui miceti**
- ✓Significativo aumento della **colonizzazione da Candida**
- ✓**Resistenze in vitro** di cocchi Gram positivi
- ✓In alcuni studi, aumento delle **resistenze in vivo** degli Stafilococchi coagulasi negativi

Wright, 2001; Tambe, 2001; Sampath, 2001; Chatzinikolau, 2003; Leon, 2004;

ANTIMICROBIAL CENTRAL VENOUS CATHETERS IN ADULTS: A SYSTEMATIC REVIEW AND METANALYSIS

Casey A. Lancet Infect Disease 2008

Pur con i limiti indicati, i cateteri medicati tipo **MR** e **CSS** **sono provatamente efficaci nella riduzione** della colonizzazione e delle CRBSI

Cochrane Library

Cochrane Database of Systematic Reviews

Antimicrobial-impregnated central venous catheters for prevention of catheter-related bloodstream infection in newborn infants (Review)

Balain M, Oddie SJ, McGuire W

2015

CVO con argento

ABSTRACT

Background

Central venous catheter-related bloodstream infection is an important cause of mortality and morbidity in newborn infants cared for in neonatal units. Potential strategies to prevent these infections include the use of central venous catheters impregnated with antimicrobial agents.

Objectives

To determine the effect of antimicrobial-impregnated central venous catheters in preventing catheter-related bloodstream infection in newborn infants.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 8), MEDLINE (1966 to September 2015), EMBASE (1980 to September 2015), CINAHL (1982 to September 2015), conference proceedings and previous reviews.

Selection criteria

Randomised or quasi-randomised controlled trials comparing central venous catheters impregnated or coated with any antibiotic or antiseptic versus central venous catheters without antibiotic or antiseptic coating or impregnation in newborn infants.

Data collection and analysis

We extracted data using the standard methods of the Cochrane Neonatal Group, with independent evaluation of risk of bias and data extraction by two review authors.

Main results

We found only one small trial (N = 98). This trial found that silver zeolite-impregnated umbilical venous catheters reduced the incidence of bloodstream infection in very preterm infants (risk ratio 0.11, 95% confidence interval 0.01 to 0.87; risk difference -0.17, 95% CI -0.30 to -0.04; number needed to treat for benefit 6, 95% CI 3 to 25].

Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults (Review)

Cochrane Library

Cochrane Database of Systematic Reviews

Lai NM et al. 2015

- 57 studies with 16,784 catheters
- Different Types of Catheters (Impregnated vs non impregnated)
- **PRIMARY ENDPOINTS**
  - **COLONISATION**
  - **CRBSI**
  - **SEPSIS AND MORTALITY**

Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults (Review)

Cochrane Library

Cochrane Database of Systematic Reviews

Lai NM et al. 2015

- Impregnated catheter **(MR and CCS) DID REDUCE** the rate of **CRBSI** and **colonization**
- Significant benefits **only** in studies conducted for patients **ICUs**
- No effects on sepsis and mortality

*"should be great caution in recommending the use of antimicrobial-impregnated CVCs **across all settings** without incorporating the current uncertainties on their overall benefits."*

Impregnated central venous catheters for prevention of bloodstream infection in children (the CATCH trial): a randomised controlled trial

2016

*Ruth E Gilbert, Quen Mok, Kerry Dwan, Katie Harron, Tracy Moitt, Mike Millar, Padmanabhan Ramnarayan, Shane M Tibby, Dyfrig Hughes, Carrol Gamble, for the CATCH trial investigators**

- 1485 **children in ICU**
- **Minocicline/rifampicine** reduced the **risk of bloodstream infection by 57%** compared with standard central venous catheters
- No effects on mortality

PLOS ONE

RESEARCH ARTICLE

Generalisability and Cost-Impact of Antibiotic-Impregnated Central Venous Catheters for Reducing Risk of Bloodstream Infection in Paediatric Intensive Care Units in England

Katie Harron[1]*, Quen Mok[2], Dyfrig Hughes[3], Berit Muller-Pebody[4], Roger Parslow[5], Padmanabhan Ramnarayan[6], Ruth Gilbert[1]

- The additional cost of antibiotic-impregnated CVCs= **£36** for each child
- Total additional costs of **£317,916** (8831 CVCs required in PICUs in 2012)
- BSI rates >1.2 per 1000 CVC-days (2012)
- Management of BSI in PICUs = **£2.5 million** annually

Clinical Infectious Diseases

SUPPLEMENT ARTICLE

IDSA
Infectious Diseases Society of America

Comparative Efficacy of Antimicrobial Central Venous Catheters in Reducing Catheter-Related Bloodstream Infections in Adults: Abridged Cochrane Systematic Review and Network Meta-Analysis

2017

Huey Yi Chong,[1] Nai Ming Lai,[1,2] Anucha Apisarnthanarak,[3] and Nathorn Chaiyakunapruk[1,4,5,6]

- 60 STUDIES
- 17,255 Catheters
- 14 types of impregnation

❖ ***Minocycline-Rifampicin—impregnated CVC*** *appears to be the* ***most effective*** *in preventing CRBSI*

❖ Its **overall benefits in reducing clinical sepsis and mortality** remain **uncertain**

AJIC
American Journal of Infection Control

Major Article

Are antimicrobial peripherally inserted central catheters associated with reduction in central line-associated bloodstream infection? A systematic review and meta-analysis

Rachel D. Kramer BS [a,*], Mary A.M. Rogers PhD [b,c], Marisa Conte MLIS [d], Jason Mann MSA [b], Sanjay Saint MD, MPH [b,c], Vineet Chopra MD, MSc [b,c]

2016

PICC

- Compared with non-coated PICCs, **antimicrobial PICCs** were associated with a **significant reduction in CRBSI** ([RR], 0.29; 95% CI, 0.10-0.78)
- **Twenty- six patients** (95% CI, 21-75) **need to be treated** with antimicrobial PICCs **to prevent 1 CRBSI**
- Studies of adults **at greater baseline risk of CRBSI** experienced **greater reduction** in CRBSI (RR, 0.20; P = .003)

PERCHE’ NON SONO COSì DIFFUSI NELLA PRATICA CLINICA?

COSA DICONO LE LINEE GUIDA?

2011

Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Cateteri e Cuffie Trattati con Antimicrobici/Antisettici

Utilizzare un CVC trattato con clorexidina/sulfadiazina argento o con minociclina/rifampicina nei pazienti in cui si prevede di lasciare il catetere oltre 5 giorni se, dopo l'implementazione di un progetto strategico per ridurre l'incidenza di CLABSI, questa non si riduce. La strategia di cui sopra dovrebbe comprendere almeno i seguenti tre componenti: la formazione del personale che impianta e gestisce il catetere, l'adozione di massime precauzioni di barriera durante l'impianto e l'utilizzo di preparazioni di clorexidina > 0.5% in alcool per l'antisepsi cutanea [106–113].

Categoria IA

Journal of Hospital Infection 86S1 (2014) S1-S70

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England

2013

H.P. Loveday[a*], J.A. Wilson[a], R.J. Pratt[a], M. Golsorkhi[a], A. Tingle[a], A. Bak[a], J. Browne[a], J. Prieto[b], M. Wilcox[c]

[a] Richard Wells Research Centre, College of Nursing, Midwifery and Healthcare, University of West London (London).
[b] Faculty of Health Sciences, University of Southampton (Southampton).
[c] Microbiology and Infection Control, Leeds Teaching Hospitals and University of Leeds (Leeds).

CVAD 10 Consider the use of an antimicrobial impregnated central venous access device for adult patients who require short-term (1 to 3 weeks) central venous catheterisation and who are at high risk for catheter-related bloodstream infection (CR-BSI) if rates of CR-BSI remain high despite implementing a comprehensive strategy to reduce rates of CR-BSI.

Class A

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY JULY 2014, VOL. 35, NO. 7

2014

SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Central Line–Associated Bloodstream Infections in Acute Care Hospitals: 2014 Update

Jonas Marschall, MD;[1,2,a] Leonard A. Mermel, DO, ScM;[3,a] Mohamad Fakih, MD, MPH;[4] Lynn Hadaway, MEd, RN, BC, CRNI;[5] Alexander Kallen, MD, MPH;[6] Naomi P. O'Grady, MD;[7] Ann Marie Pettis, RN, BSN, CIC;[8] Mark E. Rupp, MD;[9] Thomas Sandora, MD, MPH;[10] Lisa L. Maragakis, MD, MPH;[11] Deborah S. Yokoe, MD, MPH[12]

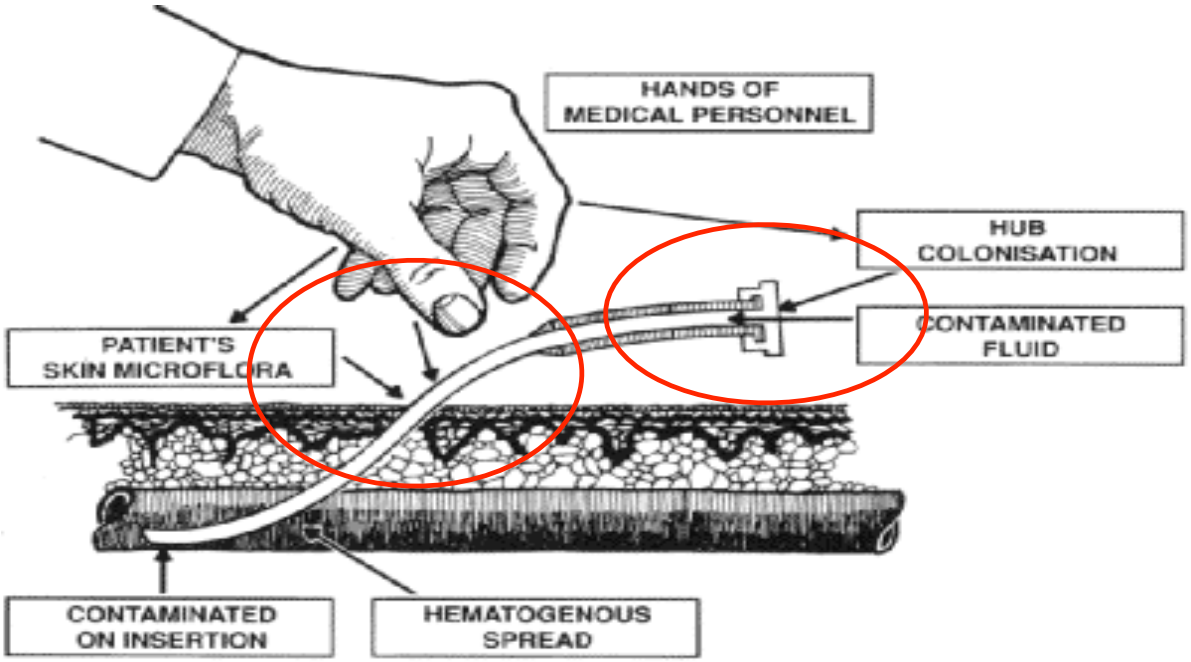
1. Use antiseptic- or antimicrobial-impregnated CVCs in adult patients (quality of evidence: I).[29,30,146-152]
   a. The risk of CLABSI is reduced with some currently marketed antiseptic-impregnated (eg, chlorhexidine–silver sulfadiazine) catheters and antimicrobial-impregnated (eg, minocycline-rifampin) catheters. Use such catheters in the following instances.
      i. Hospital units or patient populations have a CLABSI rate above institutional goals despite compliance with basic CLABSI prevention practices. Some evidence suggests that use of antimicrobial CVCs may have no additional benefit in patient care units that have already established a low incidence of catheter infections.[153]
      ii. Patients have limited venous access and a history of recurrent CLABSI.
      iii. Patients are at heightened risk of severe sequelae from a CLABSI (eg, patients with recently implanted intravascular devices, such as a prosthetic heart valve or aortic graft).
   b. Monitor patients for untoward effects, such as anaphylaxis.[154]

Prevenzione efficace della contaminazione intraluminale:

- Igiene delle mani
- Cambio periodico delle linee infusionali
- Scelta appropriata del needle-free connector
- Disinfezione di tutti gli hub, attiva o ancor meglio passiva (port protectors)
- Appropriata policy di flush/lock con fisiologica
- Profilassi con lock antisettico (taurolidina, citrato, EDTA) (?)
- Filtri in linea (?)

Cateteri medicati

PATOGENESI



Maki, 2001

ANTIMICROBIAL COATED CVCs

QUANDO USARLI?

QUANDO USARLI

1. Pazienti adulti
2. Previsione di cateterizzazione > 5 giorni (CDC) o > 7 giorni (EPIC)
3. Solo se, dopo aver aderito alle strategie di prevenzione infettiva, il tasso di CRBSI non si riduca
4. Costo-efficacia dimostrata solo per CRBSI > 3.3 giorni/1000 gg
5. Pazienti ad alto rischio (ICU… USTIONATI… NEUTROPENICI…)

ANTIMICROBIAL COATED CVCs

QUALI USARE?

QUALI USARE

- Più efficaci i cateteri ricoperti (interno e esterno; II generazione) di **clorexidina e sulfadiazina d'argento** e i cateteri trattati con antibiotici (**minociclina e rifampicina**)
- Non vi sono dati forti a sostegno dell'uno o dell'altro tipo
- Ma…

QUALI USARE

- **Gli studi sui cateteri CSS sono molto più numerosi** rispetto a quelli trattati con minociclina e rifampicina
- La **superiorità dei cateteri MR** si basa su **uno studio** di confronto con cateteri **CSS di I generazione**; sarebbe necessario un RCT che confronti cateteri MR vs. cateteri CSS di II generazione
- Clorexidina e sulfadiazina sono agenti **battericidi**; minociclina e rifampicina hanno un effetto **batteriostatico**

QUALI USARE

- **Clorexidina e sulfadiazina** hanno una comprovata **attività sui miceti**, a differenza di minociclina e rifampicina
- **In vivo**, al momento, **non sono segnalate resistenze** né con una tipologia né con l'altra di catetere; in vitro, i dati sono lievemente più favorevoli a CSS
- **Costo-efficacia** più comprovata per i cateteri CSS

CONCLUSIONI

- ✓CATETERI ANTITROMBOTICI: NESSUNA EVIDENZA
- ✓CATETERI ANTIMICROBICI: EVIDENZE A SOSTEGNO DI CSS E MR
- ✓I CATETERI MEDICATI SONO INDICATI IN POPOLAZIONI LIMITATE DI PAZIENTI AD ALTO RISCHIO (ICU..USTIONATI..NEUTROPENICI..) E SOLO DOPO AVER APPLICATO TUTTE LE STRATEGIE PREVENTIVE
- ✓MONITORAGGIO PER RESISTENZE E REAZIONI DI IPERSENSIBILITA’

GRAZIE

FULVIO PINELLI

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Chaftari *et al. BMC Infectious Diseases* 2014, **14**:518
http://www.biomedcentral.com/1471-2334/14/518

BMC
Infectious Diseases

RESEARCH ARTICLE Open Access

The use of minocycline-rifampin coated central venous catheters for exchange of catheters in the setting of staphylococcus *aureus* central line associated bloodstream infections

2014

Anne-Marie Chaftari*, Aline El Zakhem, Mohamed A Jamal, Ying Jiang, Ray Hachem and Issam Raad

CATETERI MEDICATI: QUALI TIPI

TWO TYPES

1. ANTIMICROBIC/ANTISEPTIC COATINGS
   - chlorhexidine and silver sulfadiazine
   - rifampicine and minocycline
   - silver
2. ANTITHROMBOTIC COATINGS
   - heparin (+/- benzalkonium chloride)

The primary and secondary endpoints in most of these studies are **catheter colonization rate and bacteremia**. Fibrin sheath and thrombus formation and how they influence the appearance of infections are **not assessed**.

Abstract

Background: Central venous catheters (CVC) removal and reinsertion of a new CVC in the setting of central line associated bloodstream infections (CLABSI) is not always possible in septic patients. The purpose of this study was to evaluate the outcome of patients with *Staphylococcus aureus*-CLABSI (SA-CLABSI) who had their CVCs exchanged over guidewire for minocycline/rifampin-coated (M/R)-CVC within seven days of bacteremia.

Methods: Each case was matched with two control patients who had SA-CLABSI and had their CVC removed within seven days and two control patients who had their CVC retained beyond seven days. In addition, an in vitro model was developed for exchange of catheters.

Results: We identified 40 patients with SA-CLABSI. Eight patients had their CVC exchanged over guidewire with M/R-CVC and were compared to 16 patients who had their CVC removed and 16 other patients who had their CVC retained. Patients who had their CVC exchanged over guidewire had a similar clinical response and relapse rates compared to patients whose CVC was removed or retained. However the rate of overall mortality was higher in patients who retained their CVC compared to those whose CVC was exchanged or removed ($p = 0.034$). The in vitro catheter exchange model showed that catheter exchange over guidewire using M/R-CVC completely prevented biofilm colonization compared to exchange using uncoated CVC ($p < 0.0001$).

Conclusions: In the setting of SA-CLABSI, exchanging the CVC over guidewire with M/R-CVC could be an alternative to removing the CVC and reinserting another CVC at a different site and may be associated with a lower rate of overall mortality. Further large prospective randomized clinical trials are warranted.

Keywords: Central venous catheters, Staphylococcus aureus, Central line associated bloodstream infections

Quindi: cateteri CSS

Ma quale indicazione?

Soltanto per prevenire colonizzazione e CRBSI ?

LIMITATIONS

- DURATA (CSS 3-7d; M/R 4 wk)
- RESISTENZE
- ANAFILASSI

EVIDENZE DALLA LETTERATURA

- Casey A. Lancet Infect Disease 2008
- Balain M. Cochrane 2015
- Lai NM. Cochrane 2016
- Gilbert RE. Catch Trial. The Lancet 2016
- Huey Yi Chong. Clin Infectious Disease 2017
- Kramer R. American J Infection Control 2017

COLONIZZAZIONE BATTERICA

INFEZIONE CATETERE CORRELATA (CRBSI)

MALFUNZIONAMENTO DEL CATETERE (OCCLUSIONE)

TROMBOSI

FIBROBLASTIC SLEEVE AND BIOFILM