

A fall in bloodstream infections followed a change to 2% chlorhexidine in 70% isopropanol for catheter connection antisepsis: A pediatric single center before/after study on a hemopoietic stem cell transplant ward

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Background: Some catheter-related bloodstream infections originate from catheter connectors; therefore, improved antisepsis of these might be expected to reduce the incidence of such infections.

Methods: In this observational before/after study at a pediatric tertiary referral hospital, inpatients up to 16 years old undergoing hemopoietic stem cell transplants were studied. Catheter connection antisepsis was changed from 70% isopropanol alone to 2% chlorhexidine in 70% isopropanol. Numbers of catheter-related bloodstream infections before and after the change were monitored as were the numbers of catheter days experienced by patients.

Results: The infection rate before the change was 12 per 1000 catheter-days, and, following the change, this fell to 3 per 1000 catheter-days ($P = .004$). Similar falls followed the introduction of chlorhexidine to other wards.

Conclusion: The introduction of chlorhexidine was followed by a profound, sustained fall in catheter-related infections. The results support the 2007 United Kingdom guidelines recommending 2% chlorhexidine in 70% isopropanol as a disinfectant of needleless connectors and hubs of central venous catheters.

Key Words: Catheter; chlorhexidine; connector.

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Catheter-related bloodstream infections (CRBSI) are common, preventable, hospital-acquired infections.¹ They lead to illness and even deaths of patients, longer patient stays, disruption of services, and greater costs,² and much effort has been devoted to reducing their incidence.³ The catheter hub has long⁴ been regarded as a source of infection. The introduction of needleless connectors has been associated with rises in CRBSIs.^{5,6} Disinfection of connectors has been recommended^{7,8} for many years. Chlorhexidine in isopropanol is

recommended for catheter connector antisepsis in the 2007 United Kingdom guidelines⁹ and was found to be more effective than isopropanol alone for the antisepsis of needleless connectors in clinical use.¹⁰ That study did not provide evidence that this led to less CRBSI,¹⁰ and we know of no studies that do so. In this observational, single center study, we investigated whether catheter connector antisepsis with 2% chlorhexidine in 70% isopropanol prevents more CRBSI than does antisepsis with 70% isopropanol alone.

METHODS

The study was carried out during a period of routine surveillance of CRBSI in Great Ormond Street Hospital (GOSH) during which the hemopoietic stem cell transplant (HSCT) ward (10 beds) changed from using swabs containing 70% isopropanol (Iso-sachets from Griffiths and Nielsen Ltd, Billingshurst, UK) to those containing 2% chlorhexidine in 70% isopropanol (Clinell wipes from Gama Healthcare, London, UK). Four other wards (for hematology, oncology, infectious disease, and

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immunology patients) changed over at the same time, but the main study was of the HSCT ward because, on the other wards, the change coincided with intensive handwashing audits that might be a confounding factor. The study was surveillance of a routine change in line with national guidelines and, therefore, did not require ethical permission. Most of the catheters used were long-term and included mostly tunnelled central venous catheters (CVCs) (90% of catheters on the HSCT ward). The usual insertion site was the upper front chest wall, the lines being tunnelled to the internal (sometimes the external) jugular vein. Most were double lumen, a frequently used one being a size 7 French silicone catheter (Bard, Murray Hill, NJ). There were also central catheters that were peripherally inserted into the cephalic or basilic vein and a few totally implanted central venous ports, eg, Bard large and low profile. None of the catheters were coated. Most of the catheters were inserted by the GOSH interventional radiology department, and catheter care in the HSCT and 4 other wards was overseen by a dedicated intravenous team following United Kingdom recommended guidelines.⁹ The swabs were used for disinfecting the hubs of the CVCs, but most of the disinfection was carried out on needle-free valve ports (SmartSite; supplied by Cardinal Health, Dublin, OH). The method recommended for cleaning the connectors was to swab for 30 seconds then leave to dry completely. The rate of BSI in each ward before the change was compared with that after changing. Blood samples for culture were obtained according to written hospital guidelines and cultures performed using the Biomerieux BactAlert system (Biomerieux, Marcy L'Etoile, France).

All positive blood cultures taken more than 48 hours after admission from patients with features of sepsis were assessed as to whether they represented a new episode of CRBSI. The definition of CRBSI we used, described in the next paragraph, was aimed at finding patients who were bacteremic and unwell as a result of having a CVC in place. We modified the Centers for Disease Control and Prevention (CDC) surveillance⁸ definition of CRBSI, adapting it to the patients at GOSH and shortening it to ease its implementation.

Patients with a positive blood culture were considered to have a GOSH-acquired CRBSI if the following were the case: The blood culture was taken while a CVC was in place from a GOSH inpatient more than 48 hours after admission. The patient was not known to have a clinical condition (other than the presence of the CVC) likely to have caused a bacteremia. The bacterial strain grown was not similar to one grown from a blood culture taken before admission to GOSH. The patient developed at least 1 of the following signs within 24 hours of the culture being taken: fever $>38^{\circ}\text{C}$, hypothermia $<36^{\circ}\text{C}$, chills, rigors, systolic

blood pressure 20 mm Hg below that expected; and a second blood or CVC tip cultured positive for a similar strain to that cultured from the blood, OR there was resolution of signs of infection after appropriate antibiotics or removal of the CVC. In patients with CRBSI who had a further blood culture positive, this was only counted as a new episode if the above criteria were met and a new bacterial strain was isolated from a new blood culture.

Catheter-days were recorded by ward staff using the hospital computer system. If 1 patient had a catheter in place for 1 day, this was scored as 1 catheter-day. Missing data were estimated by 2 rules: (1) If no entries for a patient were made for a period that was flanked by periods for which identical numerical returns had been made, then the nonentered period was scored the same as those flanking it. (2) The computer calculated for the current calendar month the proportion of patients on the ward that would be expected to score 1 catheter day. This proportion was then multiplied by the number of nonentered patient-days (after rule 1 had been applied). For each ward, the numbers of CRBSIs and the numbers of catheter-days were recorded for the year before and after February 12, 2007, which was the date chlorhexidine was started on the HSCT ward and the 4 other wards.

After the study, chlorhexidine was introduced between late February and April 2007 for cleaning catheter hubs on 12 other wards, including 2 intensive care units and medical wards including renal medicine. The alcohol swabs were changed to 2% chlorhexidine in 70% isopropanol with little change in packaging, and ward staff were not aware of the change, which was thus blind. We recorded catheter-related bacteremias before and after this change.

Significance was assessed by fitting a Poisson model, taking account of the nonindependent structure of the data, and compared 2 sets of 12 equivalent consecutive 30-day periods before and after the introduction of chlorhexidine.

RESULTS

The subjects were all tertiary referral inpatients. For the purposes of estimating their demography, subjects are defined as patients who at some time during the period of observation were scored by the ward as having a CVC. Some of the patients were included in both years, and there was a total of 112 patients involved on the HSCT ward and 895 patients involved on the other 4 wards over the 2 years. On the HSCT ward in the 1-year period before the change, there were 59 patients, of which 59% were male; in the year after the change, there were 63 patients, of which 62% were male. The mean ages of the HSCT subjects before (4.8 years) and

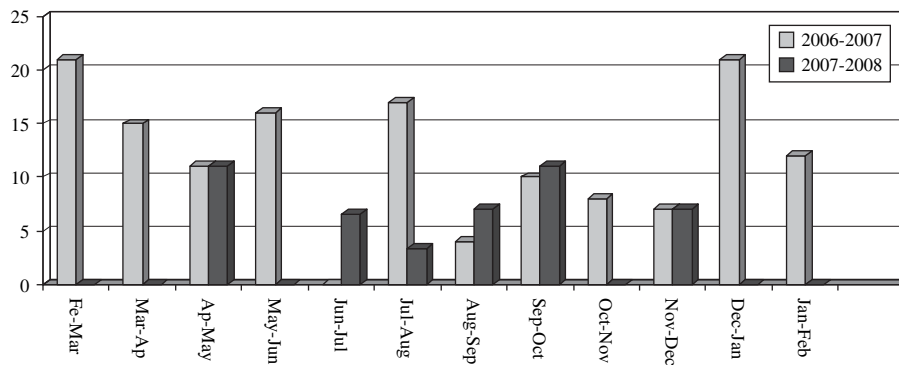


Fig 1. CRBSI per 1000 catheter-days for the HSCT ward during 24 consecutive 30 day periods before (2006/2007) and after (2007/2008) the introduction of chlorhexidine. Please note that many of the 2007-2008 scores are 0.

Table 1. Catheter-related bloodstream infections, catheter-days, and catheter-related bloodstream infections per 1000 catheter-days recorded during the year immediately before chlorhexidine was introduced for catheter connector antisepsis and during the 9 months after its introduction

Ward	CRBSI before Chlor	CRBSI after Chlor	CD before Chlor	CD after Chlor	CRBSI per 1000 CDs before Chlor	CRBSI per 1000 CDs after Chlor
HSCT	35	10	3000	3350	12	3
4 Wards	102	30	9777	10,925	10	3

NOTE. The "4 wards" were for hematology, oncology, infectious diseases, and immunology patients.

CRBSI, Catheter-related bloodstream infections; CD, catheter-days; Chlor, chlorhexidine; HSCT, hemopoietic stem cell transplant.

after (4.5 years) were similar. On the other 4 wards in the 1-year period before the change, there were 494 patients, of which 63% were male; in the 1 year after the change, there were 508 patients, of which 56% were male. The mean ages of the subjects on the 4 wards before (4.7 years) and after (4.9 years) were similar. Twenty percent of the catheter-day data for the HSCT ward and 28% of that for the other 4 wards was estimated by rules rather than entered by ward staff. In the 4 wards, the proportion (2/3) of CRBSIs from which the usual cause, coagulase-negative staphylococcus, was isolated was the same before and after the change to chlorhexidine. Other isolates included *Enterococcus* spp, *Streptococcus* spp, *Staphylococcus aureus*, *Enterobacteriaceae*, *Pseudomonas* spp, and *Candida* spp.

For 10 of 12 consecutive 30-day periods after the introduction of chlorhexidine, the HSCT ward experienced less ($P = .004$) catheter-related bacteremias than in the equivalent 30-day period before its introduction (Fig 1). There was a fall (Table 1) from 12 infections per 1000 catheter-days in the year before chlorhexidine to 3 per 1000 CRBSIs in the year after its introduction. Similar results were seen for the other 4 wards on which chlorhexidine was introduced in February 2007 (Fig 2): There was a fall from 10 CRBSIs per 1000 catheter-days in the year before chlorhexidine to 3 per 1000 CRBSIs in the year after its introduction ($P < .001$). Seventy-two patients had episodes of

CRBSI on the 4 wards before and 26 after the introduction of chlorhexidine. During the study, on the 4 wards, 33 patients had >1 episode of CRBSI. Positive blood cultures fell following chlorhexidine introduction. On the HSCT ward, there were 175 in 2005, 131 in 2006, 66 in 2007, and 55 in 2008.

In the 12 wards in which chlorhexidine was introduced blindly, there was a marked fall in catheter infections after the time the chlorhexidine was introduced (Fig 3). We do not have a precise change date, so we are unable to analyze before/after data in this area. No adverse effects of the swabs on the plastic of the ports were reported.

DISCUSSION

In this observational study, the fall in CRBSIs after the introduction of 2% chlorhexidine is striking, and its blind introduction to other wards was followed by similar falls. Whereas previous studies have indicated how effective 2% chlorhexidine solutions can be,¹¹ we know of no previous evidence that their use on catheter connectors prevents CRBSIs. Chlorhexidine solutions, unlike isopropanol alone, leave a residue that might continue to kill bacteria contaminating the connector, long after the disinfectant was applied.

This is an observational before/after study, so other confounding factors may have been responsible at least

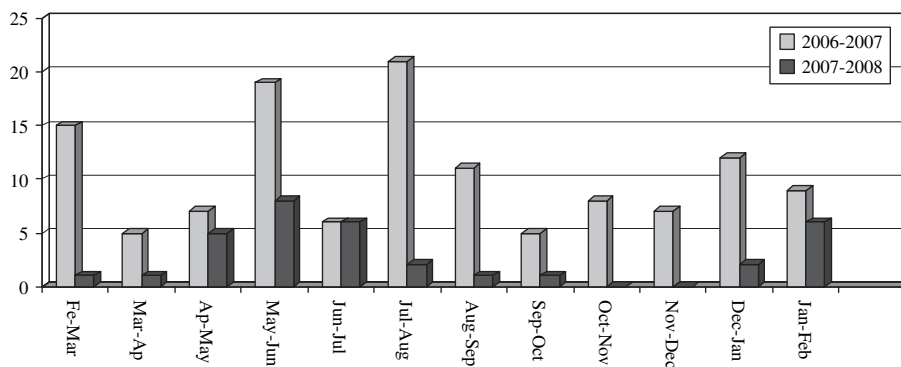


Fig 2. CRBSI per 1000 catheter-days on 4 wards together during 24 consecutive 30-day periods before (2006/2007) and after (2007/2008) the introduction of chlorhexidine.

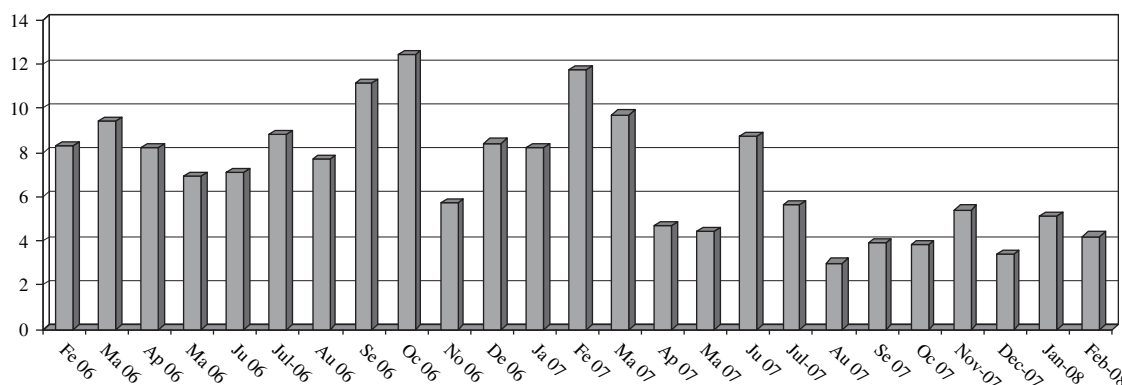


Fig 3. CRBSI per 1000 catheter-days in wards that were blind to a change to chlorhexidine antiseptics that occurred between late February 2007 and April 2007.

in part for the fall. The rate of CRBSIs at the start of the study was high, but children tend to contaminate lines, and most were immunocompromised. It was not mandatory in our definition of CRBSI to include a positive line tip culture because some of our patients with long-term catheters were successfully treated for infection without catheter removal, so they still had their catheters in at the end of the study. Some of the bacteremias recorded as CRBSIs may not have been catheter related. More emphasis had been given locally, nationally, and internationally to catheter-related bacteremias at the time of this study, but this was the case before the change to chlorhexidine. During the time of the study, there was an update on guidance on reducing catheter-related infections from the United Kingdom Department of Health, but this was published 3 months after the change to chlorhexidine when the fall in infections had already happened. There were no changes to the hospital's practice guidelines on catheter care during the study. Repeated handwashing audits were carried out on 4 wards at a similar time to the introduction of chlorhexidine and, therefore, might have in part been responsible for the fall on these wards, but a very similar

fall was seen on the HSCT ward where the introduction of chlorhexidine did not coincide with handwashing audits. When chlorhexidine was introduced to the wards studied, reinforcement was given to the standard connector cleaning procedure. Whereas this was not universally followed after the change, adherence to this procedure probably improved, and this might have accounted, at least in part, for the fall. However, in areas of the hospital in which chlorhexidine was introduced blindly, there was a substantial fall in CRBSIs without any reinforcement of technique, suggesting that it was the change to chlorhexidine rather than any associated changes in technique that led to most of the fall in infections. The sustained fall in the number of blood cultures positive both in study areas (see results) and then in all areas after chlorhexidine introduction (data not shown) supports the view that this profound change is real and not the result of inconsistencies of judgement because blood culture bottles are read automatically by machine.

Chlorhexidine 2% in 70% isopropanol is recommended in the United Kingdom⁹ for the disinfection of the injection port, unless this is against the manufacturer's recommendations, in which case aqueous

chlorhexidine or aqueous povidone iodine is recommended. Whereas the manufacturer recommends 70% isopropanol alone for the cleaning of SmartSite ports, the use of chlorhexidine with the ports is not contraindicated. In practice, no adverse effects on the ports were reported.

Our data suggest that, in our setting, the main route of infection was via needleless connectors and catheter hubs, which concurs with the finding¹² that colonization of long-term catheters is predominately in the lumen. Further work on preventing colonization of these sites is needed, including the use of antiseptics and other measures.¹³⁻¹⁶

CONCLUSION

Changing catheter connector antisepsis from isopropanol alone to 2% chlorhexidine in 70% isopropanol may lead to a substantial fall in CRBSI.

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