



A prospective clinical trial to evaluate the microbial barrier of a needleless connector

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Summary Needleless connectors are being increasingly used for direct access to intravascular catheters. However, the potential for microbial contamination of these devices and subsequent infection risk is still widely debated. In this study the microbial contamination rate associated with three-way stopcock luers with standard caps attached was compared to those with Y-type extension set luers with Clearlink[®] needleless connectors attached. Fifty patients undergoing cardiothoracic surgery who required a central venous catheter (CVC) as part of their peri- and postoperative management were studied for microbial contamination of CVC luers following 72 hrs in situ. Each patient's CVC was randomly designated to have either the three-way stopcocks with caps (control patients) or Clearlink[®] Y-type extension sets (test patients). Prior to, and following each manipulation of the three-way stopcock luers or Clearlink[®] devices, a 70% (v/v) isopropyl alcohol swab was used for disinfection of the connections. The microbial contamination of 393 luers, 200 with standard caps and 193 with Clearlink[®] attached, was determined. The internal surfaces of 20 of 200 (10%) three-way stopcock luers with standard caps were contaminated with micro-organisms whereas only one of 193 (0.5%) luers with Clearlink[®] attached was contaminated ($P < 0.0001$). These results demonstrate that the use of the Clearlink[®] device with a dedicated disinfection regimen

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reduces the internal microbial contamination rate of CVC luers compared with standard caps. The use of such needle-free devices may therefore reduce the intraluminal risk of catheter-related bloodstream infection and thereby supplement current preventive guidelines.

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Introduction

In 1992, the Food and Drug Administration (FDA) issued a safety alert urging that needleless systems be used in place of hypodermic needles for accessing intravascular catheters.¹ The alert was raised following reports of hypodermic needles breaking off inside intravascular administration set ports and that the intravascular tubing–needle assemblies were associated with a higher risk of needlestick injuries than any other needle device. The use of needleless connectors potentially reduces the risk of intravenous catheter-related needlestick injuries and their use was therefore recommended.^{1,2}

At the time of this alert, there was thought to be no increased risk of bloodstream infection (BSI) associated with use of needleless devices.¹ However, there have subsequently been a number of reports of elevated BSI rates associated with their use. Some studies have demonstrated deviations from recommended use, extended time in situ, and other risk factors for the development of catheter-related bloodstream infection (CR-BSI), and this has raised the question of whether it was operational error rather than device failure that resulted in the increased number of infections.^{3–6} Conversely, other studies have demonstrated no increase or even decreases in BSI rates following the implementation of needleless connectors.^{7–9} The latter results support the contention that the devices not only give protection from needlestick injury but may also facilitate aseptic technique, by reducing manipulation time and avoidance of ports being left open. Improved technique could therefore potentially reduce internal contamination of luers and therefore the migration of micro-organisms down the intraluminal surfaces of the catheter to the tip. This is particularly relevant as hub colonization resulting from the high level of catheter manipulation is possibly the cause of many CR-BSIs.¹⁰

The Clearlink[®] needleless connector (Baxter Healthcare UK Ltd) is a single-piece bi-directional device with standard luer–lock connections. The

device incorporates an external silicone compression seal that opens a fluid pathway when a male luer is introduced. The seal automatically closes on withdrawal of the male luer, eliminating the need to remove and replace luer caps, which otherwise may leave the fluid pathway open to microbial contamination. In this study, the infection risk associated with Clearlink[®] was assessed by comparing the microbial contamination rate of three-way stopcock luers with standard caps to Y-type extension set luers with Clearlink[®] needleless connectors for 72 hrs in situ (Figure 1). A strict disinfection schedule was instituted for the standard luer caps and the needleless connector before use.

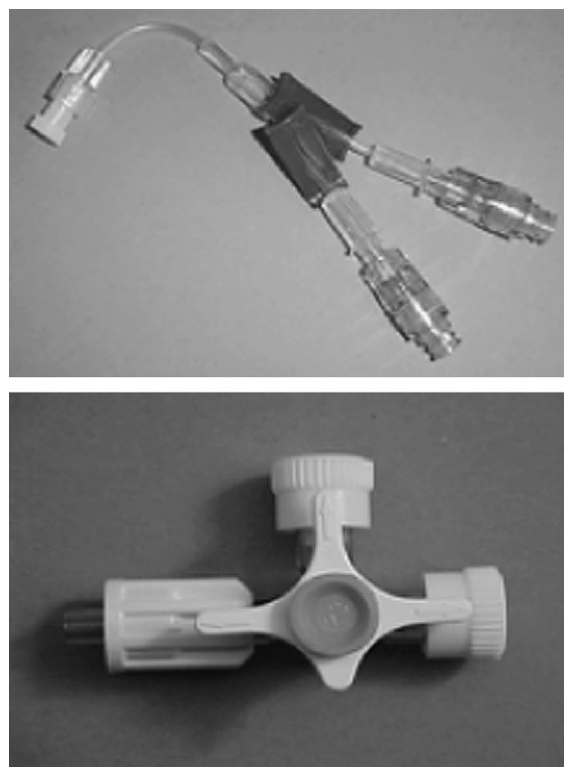


Figure 1 From top to bottom: Y-type luer extension set complete with Clearlink[®] needleless connectors and three-way stopcock with standard luer caps attached.

Methods

Patients

Approval was obtained from the South Birmingham Local Research Ethics Committee prior to study commencement. Any patient admitted for elective cardiothoracic surgery with postoperative admission to the Wellcome Building Critical Care Unit at the University Hospital Birmingham NHS Foundation Trust and able to provide informed, written consent was recruited into the clinical trial. Each patient required a central venous catheter (CVC) as part of his or her peri- and postoperative management.

Trial protocol

Recruited patients were randomly designated, using a computer-generated randomization table, either three-way stopcocks with caps attached (control patients) or Clearlink® Y-type extension sets (test patients) attached to their CVC. Prior to CVC insertion, the patients' skin was disinfected with 0.5% (w/v) chlorhexidine gluconate in 70% (v/v) isopropyl alcohol spray (Hydrex® derma spray, Adams Healthcare, Leeds, UK) and allowed to dry for 2 min. A quad-lumen CVC was then inserted into the right internal jugular vein of each patient using the Seldinger technique. Immediately post-CVC insertion, either four three-way stopcocks with caps attached or four Clearlink® Y-type extension sets were attached to each CVC. This provided a maximum of eight luers with either caps or Clearlink® attached for microbiological sampling from each patient.

Prior to, and following each manipulation of the three-way stopcock luers or Clearlink® devices, a 70% (v/v) isopropyl alcohol wipe (Sterets®, Seton Prebble Ltd, Merseyside, UK) was used to disinfect the connections. The wipes were applied firmly to the stopcock luer surfaces and rotated through 360° and the alcohol was allowed to dry for 2 min. The wipes were similarly applied to the external surfaces of the Clearlink® devices. Following every manipulation of the three-way stopcock luers, the caps were replaced with sterile caps. The number of manipulations of the luers was recorded during the study period.

After 72 hrs *in situ*, three-way stopcocks and Clearlink® Y-type extension sets were aseptically removed from the CVC. All specimens were placed in sterile containers and transported to the laboratory for microbiological culture. The duration

of time that the intravenous connections were *in situ* was recorded for each patient.

Laboratory investigations

Microbial contamination of the Clearlink® external silicone compression seal and its internal fluid pathway

Following removal from the CVC and without re-disinfecting the device, the surface of the external silicone compression seal of each Clearlink® device was sampled by pressing firmly onto the surface of a blood agar plate containing 7% defibrinated horse blood (Biomérieux, UK) 10 times. The external silicone compression seal was then disinfected by rotating a 70% (v/v) isopropyl alcohol wipe through 360° on the external silicone compression seal and allowed to dry for 2 min. One hundred microlitres of brain–heart infusion broth (Oxoid, Basingstoke, UK) was then flushed through each device three times using a 10 mL syringe. Eighty microlitres of this fluid was then inoculated onto the surface of a blood agar plate.

Sampling for microbial contamination of the Clearlink® external silicone compression seal with disinfection of the device immediately prior to sampling

Following removal from the CVC and disinfection by rotating a 70% (v/v) isopropyl alcohol wipe through 360° on the external silicone compression seal with 2 min drying, the surface of some of the external silicone compression seals of Clearlink® devices was sampled. This was performed by pressing the seals firmly onto the surface of a blood agar plate containing 7% defibrinated horse blood (Biomérieux, UK). This was carried out at the end of the trial, using an additional 10 patients with 78 Clearlink® devices attached. This was to determine whether any potential microbial contamination on the Clearlink® external silicone compression seal present at the time of specimen receipt could be effectively removed from the devices by the standard disinfection procedure.

Sampling for microbial contamination of the three-way stopcock and Clearlink® Y-type extension set luers

The internal surfaces of the three-way stopcock and Clearlink® Y-type extension set luers were sampled by inserting a sterile nasopharyngeal swab (Bibby Sterilin, Aberbargoed, UK) moistened with 0.9% (w/v) saline and rotating it through 360° ten times. Each swab was then inoculated onto a 7% blood agar plate.

Microbiological culture conditions

All blood agar plates were incubated at 37 °C in air for 48 hrs and micro-organisms were identified using standard laboratory methods.

Statistical analysis

Microbial contamination rates of the various components of the intravenous connections were compared using Fisher's exact test. Comparisons of the number of manipulations made using each device was conveyed using a standard Student's *t*-test.

Results

Patients

Sixty patients in total were recruited into the study, 25 in the control group and 35 in the test groups (47 male, 13 female with a mean age of 60 years, range: 31–77). The additional 10 patients in the test group were recruited at the end of the study in order to determine whether any microbial contamination on the Clearlink® external silicone compression seal present at the time of specimen receipt could be effectively removed by an alcohol wipe. Patients studied during this trial underwent coronary artery bypass grafting (CABG) (83%), CABG and valve replacement (5%), valve replacement only (8%), repair of atrial septal defect (2%), and thoracotomy for drainage of pericardial effusion (2%). The internal surfaces of 393 luers, 200 with standard caps attached and 193 with Clearlink® attached recovered from 50 patients, were sampled following use. Seven (3.5%) Clearlink® devices were not received in the laboratory for analysis. This was due to non-compliance with study protocol regarding specimen collection and transportation, including devices transported to the laboratory in inappropriate containers. All devices not complying with the study protocol were therefore excluded from further investigation. Seventy-eight Clearlink® external silicone compression seals from the additional 10 patients were sampled for the presence of any micro-organisms after disinfection. None of the patients exhibited any clinical or microbiological symptoms of a catheter-related infection during and after the study period. On average, the Clearlink® device was activated significantly more times per patient than opening of the three-way stopcock luers (3.0 vs 2.3, ranges: 1–23 vs 0–16) ($P=0.004$). There was no significant difference between the

mean number of activations made to administer inotropic infusions to patients in the study or control group (4.5 vs 4.9, ranges: 3–6 vs 3–7) ($P=0.15$). Similarly, there was no significant difference between the mean number of activations made to administer antibiotics by the study or control group (2.8 vs 3.8, ranges: 1–7 vs 1–8) ($P=0.1$). During the study, all patients received antibiotics for prophylactic purposes only. However, the Clearlink® device on average was activated significantly more times per patient than the three-way stopcock luers for blood sampling (3 vs 0.8, ranges: 0–16 vs 0–4) ($P=0.02$), and this was the main reason for the difference in manipulation rate of the two devices.

There was no significant difference in the mean number of manipulations with Clearlink® for external silicone compression seal contamination (a) without re-disinfection before sampling, and (b) with disinfection immediately prior to sampling [3.0 (range: 1–23) vs 3.5 (range: 1–29)].

Laboratory investigations

Microbial contamination of the Clearlink® external silicone compression seal without re-disinfection prior to sampling

Forty out of 193 (21%) Clearlink® devices were contaminated with micro-organisms on the external silicone compression seal following a mean time of 72 hrs in situ and without re-disinfection prior to sampling (Table I). Of these, thirty-eight (95%) had cultures yielding coagulase-negative staphylococci (CoNS); the remaining two (5%) yielded *S. aureus*.

Sampling for microbial contamination of the Clearlink® internal fluid pathway

Following disinfection and flushing with brain–heart infusion broth, none of the Clearlink® devices was internally contaminated with micro-organisms during the study period (Table I).

Microbial contamination of the Clearlink® external silicone compression seal with disinfection of the device immediately prior to sampling

Only three of the 78 (3.8%) Clearlink® devices had micro-organisms on the external silicone compression seal following a mean time of 72 hrs in situ and disinfection with 70% (v/v) isopropyl alcohol swabs immediately prior to sampling. There was a significant reduction in the number of contaminated silicone compression seals after disinfection compared with non-disinfected devices (3.8 vs 21%, $P=0.0004$). Each of the three positive silicone

Table I Rates of microbial contamination after 72 h of: the external and internal surfaces of the Clearlink® device, Y-type luer extension set with Clearlink® attached and three-way stopcock luer with standard caps attached

	Clearlink® Y-type luer extension set	Three-way stopcock luer with caps
No. of patients	25	25
No. of Clearlink®/ luers	193	200
Luers contaminated, % (N)	0.5 (1)	10 (20)
Patients with one or more luer contaminated with micro-organisms, % (N)	4 (1)	36 (9)
Clearlink® contaminated with micro-organisms on the external silicone compression seal without disinfection prior to sampling, % (N)	21 (40)	NA
Clearlink® contaminated with micro-organisms on the external silicone compression seal with disinfection prior to sampling, % (N)	3.8 (3/78)	NA
Clearlink® contaminated with micro-organisms in the internal fluid pathway following disinfection, % (N)	0 (0)	NA

NA = not applicable.

compression seal cultures contained only one cfu; two grew *Pseudomonas* spp. and one grew CoNS.

Microbial contamination of the internal pathway of luer devices with either standard caps or Clearlink® connectors attached

The fluid pathway from one of 193 (0.5%) Y-type extension set luer devices with Clearlink® attached was contaminated with micro-organisms compared to 20 out of 200 (10%) three-way stopcock luer devices with standard caps attached ($P < 0.0001$). However, the contaminated three-way stopcock luers were not identified in a limited number of control patients. Indeed, nine out of 25 (36%) patients had one or more luers contaminated

with micro-organisms in the control group compared to one out of 25 (4%) patients in the Clearlink® group ($P = 0.01$) (Table I). Of the nine control patients with contaminated luers, six had just one contaminated with micro-organisms and the three remaining patients had two, five and six luers contaminated, respectively. The positive culture obtained from the Clearlink® group yielded *Streptococcus sanguis*. Of the 20 positive three-way stopcock cultures, six (30%) yielded CoNS, six (30%) *Bacillus* spp. and 12 (40%) Gram-negative bacilli (eight *Serratia* spp. and four *Klebsiella* spp.).

The number of activations made through the intravenous connections and the percentage of luers, which were contaminated with micro-organisms are listed in Table II. Of the intravenous connections activated once, there were significantly more luers contaminated in the three-way stopcock group than the Clearlink® group ($P = 0.03$). This trend was also observed for intravenous connections activated two, three and four times respectively ($P = 0.07$, 0.07 and 1.0 , respectively).

Discussion

Patients who undergo major surgical procedures such as cardiothoracic surgery require central venous access for haemodynamic monitoring and the administration of drugs, antibiotics, fluids and blood products. However, the major iatrogenic complication of CVC use is the development of CR-BSI. This is one of the most common nosocomial infections in intensive care units (ICU). Indeed, in a recent surveillance report of bacteraemia acquired in English hospitals between 1997 and 2002, 41% of bacteraemias were associated with CVC in patients undergoing cardiothoracic surgery.¹¹

Many strategies have been proposed to prevent catheter-related infection. These target risk factors are associated with the CVC insertion process, CVC care and the design of the intravascular catheter itself.¹² One such preventive measure investigated is the use of needleless connectors. In addition to reducing the rate of needlestick injuries, needleless connectors may reduce the rate of CR-BSI.⁹ However, studies investigating this hypothesis have produced conflicting results.^{3–6}

In this study, 21% of the Clearlink® external surfaces of the silicone compression seals were contaminated with micro-organisms after 72 hrs of clinical use. In a previous study, we demonstrated that 69.2% of external silicone compression seals of a different type of needleless connector were contaminated after 72 hrs in situ.¹³ In both studies the external silicone compression seals were

Table II The number of activations made via the three-way stopcock luers or Clearlink® needleless connectors and the percentage of luers contaminated with micro-organisms

No. of activations ^a	Three-way stopcock luer			Clearlink® needleless connector			P-value
	Total no. of luers studied	No. of luers contaminated	% luers contaminated	Total no. of luers studied	No. of luers contaminated	% luers contaminated	
0	26	0	0	8	0	0	ND
1	52	11	21.2	22	0	0	0.03
2	56	4	7.1	90	1	1.1	0.07
3	27	3	11.1	37	0	0	0.07
4	11	1	9.1	9	0	0	1.0
5	5	0	0	7	0	0	ND
6	5	0	0	4	0	0	ND
7	10	0	0	6	0	0	ND

ND = not done.

^a A further 16 activation categories were included in the overall luer contamination rate calculations but not outlined here due to insufficient numbers for statistical analysis.

disinfected with 70% (v/v) isopropyl alcohol. In the current study, however, disinfectant wipes were utilized rather than spray as in the previous study. This suggests that a disinfection regime involving physical forces in addition to the action of the disinfectant may be more effective. Similarly, during the current study, the internal contamination rate of three-way tap luers with standard caps attached following 72 hrs (10%) was also significantly lower than in previous reports.^{13–15} In these previous studies, unlike the current study disinfectants were utilized in spray form. These results advocate the use of a disinfectant wipe rather than a spray. This was supported by the significantly lower (3.8%) surface contamination rate of the 78 external silicone compression seals sampled following removal and disinfection with 70% (v/v) isopropyl alcohol wipes. Each of the positive cultures obtained from the Clearlink® external silicone compression seals following disinfection contained only 1 cfu, which is unlikely to be clinically significant.

None of the internal fluid pathways of the Clearlink® devices were contaminated with micro-organisms. Similarly the rate of luer contamination was significantly lower with the Clearlink® devices attached as compared with standard caps. This overall reduction in microbial contamination may have been due to the ease with which the flat surface of the Clearlink® silicone compression seal could be disinfected before use as compared with a standard luer and cap. This would have in turn reduced the risk of micro-organisms being transferred into the internal fluid pathway on activation. These results were also obtained despite the Clearlink® devices being manipulated significantly more times than the three-way taps with standard caps attached. In order to determine whether the

reduction in luer contamination rate was due to the Clearlink® device itself or the more frequent activation and therefore disinfection of the device, luer contamination rates were compared in groups according to number of activations. This confirmed that there were fewer contaminated luers in the Clearlink® group than in the three-way stopcock group, suggesting that the reduced contamination rate was due to the Clearlink® device itself. There was no significant difference between the level of inotropic or antimicrobial support that the patients required in each group. Indeed, all patients were undergoing elective cardiothoracic surgery that follows a set postoperative protocol on the ITU with a defined policy on intravenous drug use and administration. However, the frequency of blood sampling from the CVC was significantly higher in the Clearlink® group. The difference in number of manipulations was therefore primarily due to post-operative monitoring of electrolytes and blood indices including white blood cell and haemoglobin counts. The reason for the increased level of post-operative monitoring in the Clearlink® group most likely reflected the patient's underlying clinical condition.

The results of this clinical trial suggest that if appropriate aseptic precautions are taken, the contamination of CVC luer connections may be reduced with the introduction of needleless connectors into clinical practice in place of standard caps. Disinfection should include a wiping action rather than just a spray and should always precede needleless connector activation. This approach may further reduce the risk of CR-BSI in conjunction with other preventive strategies and requires further clinical evaluation to confirm.

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