Needleless connectors: the vascular access catheter's microbial gatekeeper

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Abstract

Needleless connectors (NCs) are essential devices which connect to the end of vascular catheters and enable catheter access for infusion and aspiration. There are various different designs which make it difficult for purchasers to identify the features which present the least risk and greatest safety. The NC is the microbial gatekeeper for vascular catheters; how it is disinfected pre access determines if, and how many, organisms enter and how quickly biofilm will form. This paper will consider these design variations and how differences in antiseptic testing methods have made it difficult to determine the best antiseptic practice pre access. One specific design characteristic is considered: the fluid pathway. The NC's fluid pathway creates a flow which can be either direct to produce a laminar flow or indirect which creates a turbulent flow. At present, the evidence does not support there being an advantage for a specific fluid pathway design in reducing infection risks.

Keywords

Intravenous devices, needleless connectors, biofilm

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Introduction

Although generally considered safe, intravenous (i.v.) access and drug administration remain potentially hazardous patient procedures with a vast array of possible errors and complications. One critical piece of equipment is the needleless connector (NC) which connects to the end of the catheter enabling safe i.v. access. NCs are themselves ill-defined devices; individual manufacturer's designs have varying technical specifications which makes optimal product selection difficult. This paper seeks to provide clarity with regard to the available evidence and opinions. It is the result of a rapid review of the available literature exploring the strengths and weaknesses of NCs related to the risks of catheter-related bloodstream infections (CRBSI). CRBSI will be the term used within this report unless a published paper specifically uses central line associated bloodstream infection (CLABSI).

This is the first of two papers. The second paper will be an Outbreak Column which will appraise NC outbreak reports from the mid-2000s and subsequent (perhaps unnecessary) recommendations against a particular type of NC. This first paper will consider NCs themselves, their design characteristics and the evidence for effective pre-access decontamination. First of all, the journey to now.

Developments in i.v. therapy

In the beginning there was nothing, which exploded. Pratchett

The first reported blood transfusion was in 1492; it resulted in a 400% mortality of a pope (the recipient) along with three 10-year-old boy donors (Rivera et al., 2005). However, it was in the 1950s when significant and reliable developments were introduced to meet the needs of advanced healthcare. Drug administration through established i.v. lines c.1970s was achieved with an administration set equipped with an integral injection bung, the frequent use of which led to leakage which enabled bacteria to enter and the infusate to flow out. As more drugs with irritant pH or chemical composition were administered, there was an increased phlebitis risk; one early report suggested that after 24 h most cannulated veins showed signs of phlebitis (Anon, 1971).

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Three-way stopcocks (taps) appear to have become part of the i.v. equipment armamentarium without significant announcement in the literature (possibly as they were adapted from existing drainage devices). Their use enabled almost limitless access to the catheter for drug administration separate from a continuous infusion—and without degradation of the administration system. Three-way stopcocks also permitted the aspiration of blood for laboratory tests. Healthcare workers (HCWs) often arrived to find its protective caps missing and thus the device left open to bacterial contamination. There was a further omnipresent design flaw, the female luer lockers were incapable of being disinfected. Concurrently, alongside frequent three-way stopcock usage, needles were used for many i.v. administrations.

Needlestick injuries were the inevitable result of needle design, usage and disposal; this left HCWs potentially exposed to the risk of blood-borne virus infection (Hu et al., 1991). It was mandated first in the US that the use of needles for i.v. access was to be avoided. This necessitated innovations in connections that excluded needles.

For all the ongoing advances in i.v. equipment design, the early identified vascular access complications remained, and the challenges from longer catheter usage and more irritant drugs necessitated ongoing developments and yet more advanced equipment specifications.

From the mid-2000s, healthcare quality improvement initiatives were introduced into the NHS's ways of working which led to procedural changes that utilised data to drive practice improvements. This has been done alongside what has been accepted as the most important 'bundled' practices to reduce the risk of CRBSI (Simpson et al., 2014). However, even with these improved procedure developments CRBSI remains a real and significant patient risk (García-Rodríguez et al., 2013). With increasing antimicrobial resistance, a future of untreatable infections is a realistic possibility (Balkan et al., 2014). Consequently, as long as i.v. therapy continues to be a critical component of modern healthcare it is vital for patients that HCWs have access to equipment which, when correctly used, will minimise all possible risks.

Although NCs were introduced to reduce needlestick injuries, initial reports showed an associated increased CRBSI risk (Do et al., 1999). NCs themselves should permit safe access to the catheter (without the use of needles) and:

- Minimise catheter occlusion risk.
- Allow for easy and effective decontamination between each use to prohibit microbial entry e.g via a flat surface which is flush with the housing.
- Withstand toxic drugs and antiseptics without device degradation.
- Minimise internal biofilm formation and microbial growth.
- With regard to usage, make it easy for the HCW to do the right thing and enable them to be sure what

the right thing to do is, e.g. a visible fluid pathway to ensure that flushing leaves the housing free of visible blood.

Today, continuous technical developments have resulted in a cornucopia of NC product options. The abundance of choice presents a difficulty in identifying whether there is a NC which is a patient-safety first among equals. Early (and later) reports of temporal associations of novel NC introduction and CRBSI have left purchasers wary. The purchasers' conundrum is to select a device which is compatible with all other currently used equipment that reduces infection risk—without decreasing catheter functionality or increasing procedure complexity—using only a limited literature. Undoubtedly, purchaser decision-making is influenced by financial budget constraints for which the bottom line will be misleading if some negative healthcare outcomes go unmeasured, misrepresented and/or excluded from the evaluation.

Objective and search

To conduct a critical rapid review of the literature exploring the strengths and weaknesses of NCs to CRBSI, a search was made of CINAHL, Medline, Clinicaltrials.gov, Cochrane, Professional Guidelines, Manufacturers' literature and MHRA Device Alerts using the terms: Needle free OR Needle-free OR Needlefree OR needleless AND connector OR device with Outbreak CLABSI OR CRBSI. Exclusions were: studies only on occlusion risks; catheter lock studies; non-English papers; haemodialysis only studies; and single case reports (single outbreak reports were included). After the removal of duplicates, for this project (including the Outbreak column) a total of 75 papers were read. Only eight were randomised controlled trials; in general these were generally small studies comparing usually two devices or antiseptic methods. Of the remaining literature, the majority of 39 were observational studies (uncontrolled before and after studies [including outbreak reports], case series or in vitro testing reports. There were five guidelines, eight reviews, seven opinion pieces, one meta-analysis and two surveys of practice/knowledge. Four alerts from the MHRA were included along with one independent testing report. Manufacturers' literature and videos were also read and observed.

Needleless connectors for i.v. access

A NC is a medical device accessed via a septum that connects to a catheter or the end of a catheter extension set by means of a luer lock/slip to enable intermittent catheter access for infusion or aspiration, while minimising the risk of occlusion, microbial and/or water ingress, or seepage

Figure 1. Variations in design and ways of working of 12 popular NCs.

from the catheter. This is a generic definition for a heterogeneous group of products that vary in design. NCs have several possible design characteristics which determines how they should operate and be operated.

All NCs are activated by pressure from the syringe luer. This pressure either enables the syringe luer to enter an already split septum direct, to open or depress the septum/plunger or allow a blunt cannula to pierce from below. The pink boxes in Figure 1 indicate the four different designs of mechanical valves, i.e. the moving mechanisms that create/open fluid pathways. The fluid pathways can be direct through a smooth or corrugated channel, flow around a depressed plunger, flow around a housing, or through eyelets, before entering a blunt cannula. Once access and flushing are complete, fluid displacement at the end of the catheter can be negative, positive or neutral. Positive fluid displacement forces a small amount of fluid into the catheter end to prevent occlusion from blood and conversely, negative displacement allows a small amount of blood to move back into the catheter. Neutral displacement indicates no movement of fluid back into the catheter after disconnection. However, independent testing of NCs marketed as neutral displacement has shown there is always at least a very small amount of displacement (ERCI, 2008). Thus, in reality, there is no true neutral displacement (ERCI 2008).

Of vital importance is the designated clamping-disconnection sequence, this allows the NCs to work as designed. NCs with a negative fluid displacement should be clamped before disconnection and positive fluid displacement NCs clamped after disconnection. Several manufacturers of 'neutral' displacement NCs state that their product does not require a clamping sequence for safe usage. Clamping per se is required to prevent air embolism.

There are further variations in NC design in terms of overall size and priming/residual volumes. What is obvious, however, is that NC development has come a long way since their introduction to prevent needlestick injury in the early 1990s. The variations in just 12 designs highlight the problem for purchases in selecting something which must be cost-effective and minimise all complications (Figure 1). Before considering the NC designs, it is necessary to consider how they can contribute to infection.

The NC is the catheter's microbial gatekeeper

There are three routes by which micro-organisms can enter to contaminate vascular catheters: extra-luminal, intraluminal and via haematogenous spread (Mermel, 2011; Segura et al., 1993). Both intra- and extra-luminal routes are considered

important (Mermel, 2011). Infection from haematogenous spread is considered of least importance as most people are not concurrently infected. The NC is the microbial gatekeeper between blood which should be free of pathogens and the external, unsterile and highly contaminated outside. NCs aim to prevent micro-organisms on the septum surface gaining intraluminal entry during any NC actuation. Biofilm begins to form on vascular catheters almost instantly after catheterisation with the development of a conditioning layer; plasma proteins adhere to the catheter surface, platelets and neutrophils then attach (Donlan, 2001; Donlan, 2002; Ryder, 2006). Free-floating bacteria then adhere. As the biofilm matures, bits slough off. The detached biofilm containing bacteria (and or their toxins) enter the bloodstream and the patient presents with symptoms. As blood is sampled through the catheter the same process begins on the catheter's (and NC's) lumen as occurs on the catheter surface within the vein.

The ubiquity of biofilm formation was illustrated in a single-centre study of blood culture samples from 91 patients. The study compared positive blood culture results from samples taken with unchanged NCs, changed NCs and peripheral cultures (Mathew et al., 2009). Samples taken when the NCs were unchanged yielded a false positive rate of 53% (19/36) (Mathew et al., 2009). As the external surface of a NC will always be contaminated, disinfection of the NC surface is of primary importance. A key question therefore is how to disinfect the septum surface.

Antiseptics and needleless connectors

There are several problems in trying to interpret the antiseptic studies that have been undertaken over the past 20 years. First, the in vitro studies vary by test organism (species and amount), and second the in vivo studies are rarely if ever randomised controlled trials. As an example, Menyhay and Maki (2006) undertook in vitro studies of three different NCs comparing after immersion in 10^8 colony forming units of *E. faecalis* residual contamination; this amount of organism was described by others as 'supranormal' (Yévenes & Serra-Prat, 2008).

There are two different types of NC disinfection: a disinfectant wipe or cap. The wipe involves 'active' disinfection, i.e. the wipe is actively manoeuvred covering all areas of the NC enabling the disinfectant to remove and kill surface bacteria. Conversely, the disinfectant cap acts passively by leaving the NC in continuous disinfectant contact. The disinfectant caps are essentially trying to negate the weakest link in the successful use of NCs: the HCW. HCWs should all be aware of how to decontaminate but some often omit to effectively disinfect pre access. Several studies of observed compliance with disinfection pre access have found practice sub-optimal. Disappointingly, one researcher found NC disinfection to be poor (<50%) even after specific education (Drew, 2013).

In general, there seems to be confusion in some papers regarding the capabilities of antiseptics with erroneous statements about 'sterilising'. Antiseptics are incapable of sterilising. Importantly, however, alcohols are known to harden plastics and crack rubber over time (WHO, 2014). The question researchers have been asking of in vitro experiments using disinfectant caps is this: is a longer antiseptic application time (via a disinfectant cap) associated with a higher microbial kill? The answer to this is surely known. The question that is yet to be asked is: given the negative consequences of prolonged alcohol application, are there any unintended consequences of a continuously applied alcohol-based antiseptic to NCs?

Other non-randomised studies include one by Sweet et al. (2013) who monitored CLABSI following the introduction of disinfectant caps. They found a reduction in CLABSI from 2.3 reduced to 0.3 CLABSI per 1000 catheter days. This was a twinned intervention with a change to a neutral displacement NC Microclave® (compared to controls: RR = 0.14; 95% CI, 0.02–1.07; $P = 0.3$); the researchers state that a separate analysis showed independent benefit from the port protection (Sweet et al., 2012). Another prospective non-randomised, single-centre, before-and-after study showed an apparent statistically significant 50% CLABSI reduction with the addition of this new disinfectant cap (Stango et al., 2014). A closer look at the data, however, shows an apparent reduction in CLABSI in the 9 months before the introduction of the cap in both critical and non-critical care units.

One further important study of disinfectant caps was undertaken by Merrill et al. (2014). They found using an interrupted time series analysis that the use of a 70% alcohol disinfectant cap was associated with a 40% decrease in CLABSI (incidence rate ratios 0.477; $P = 0.004$) (Merrill et al., 2014). These researchers importantly note the ability to audit disinfectant usage with the cap (Merrill et al., 2014). This is important because what the disinfectant cap seems to be offering is this: (1) increased compliance with disinfection pre-access; (2) easy compliance monitoring; and (3) preventing exposure of the NC in-between usage. Compatibility studies and NC manufacturers' approval are required pre usage.

Moureau and Dawson (2010) asserted that '...each solution appears to be effective if used with the appropriate method and contact time'. Indeed, a systematic review of disinfection was undertaken and led by Moureau (Moureau and Flynn, 2015). They comment that the optimal contact time 'has not been identified' (Moureau and Flynn, 2015). They do state that disinfectant ports are recommended in combination with manufacturers' instructions (Moureau and Flynn, 2015). This presumably is the manufacturers of both the NCs as well as the disinfectant caps.

Perhaps the best study on NC disinfection was done by Rupp et al. (2012), who studied both in vivo hub contamination and in vitro laboratory contamination of Interlink® NCs. They found that unless heavy contamination was

present, a 5-s scrub with an alcohol impregnated hub was an effective means of decontamination—in clinical results only one of 71 NCs yielded microbial growth compared to baseline $P < 0.005$; in vitro at 10^3 and 10^5 inoculum, all in vitro NCs yielded no growth when scrubbed for 5-s or longer, $P < 0.001$ (Rupp et al., 2012). They further suggest that unless ‘heavy contamination’ is suspected, 5-s decontamination with the tested device is sufficient (Rupp et al., 2012). The question remains how ‘heavy contamination’ can be suspected in vivo as microbes are invisible to the naked eye. As HCWs cannot determine the microbial contamination level of any NC pre-disinfection, it seems logical to treat NCs as though they were heavily contaminated. The efficacy of the process being dependent on the existing (but unknown) NC contamination, the duration and vigorous application of disinfectant to the NC, and the disinfectant being allowed to dry—these data do not present a case for reducing current Epic3 (IVAD30) (Loveday et al., 2014) recommended a disinfectant time of 15 s—rather they again indicate the need for further research to identify optimal times covering all possible contamination levels.

The variant findings in the above studies might be the result of the differences between in vivo and in vitro testing methodologies, unrealistic NC contamination in some in vitro studies being a major contributor to conflicting results. An agreed and standardised test methodology would make for more reliable recommendations and be of value to manufacturers, purchasers and NC users. The researchers were trying to answer the same question: does this disinfectant, used in this way, negate likely microbial NC surface contamination? The variation in their methodologies has left an urgent need for further and uniform studies.

What can be stated is that antiseptic application pre NC access is critical—the antiseptic should be alcohol-based and come into contact with the entire access area. The application should be accompanied by vigorous rubbing as discussed above. Furthermore, reliance on HCW compliance with disinfection regimens is likely to be significantly less than 100%. Disinfection caps may be more reliable but must be NC compatible.

NB the use of silver as a component part of the NC has not been considered in this paper.

The fluid pathway: laminar and turbulent flows

A straight, uninterrupted fluid pathway will deliver the infusate in a laminar or smooth layered flow with the different layers having different speeds of flow. The administration of drugs and infusions through a smooth catheter is via a laminar flow which has extremely slow velocity close to the lumen surface, regardless of the velocity at the centre of the flow. Slow flow at this barrier facilitates biofilm formation (Donlan, 2002). Conversely, to prevent occlusion (and surface conditioning), catheters are flushed with saline or

Figure 2. Turbulent and laminar flows.

heparin using a push–pause flushing technique that creates a turbulent flow to minimise surface adherence (Figure 2). This method is recommended by the Royal College of Nursing (RCN, 2010). Hadaway (2006) accepts there is widespread clinical practice for the push–pause technique, but makes no recommendation for its use due a lack of evidence. This is a case of absence of evidence for the benefit, rather than evidence of absence of effect. NCs can be of a design which creates in the housing either a turbulent or laminar flow with its inherent slow surface flow rates. Biofilm can occur regardless of the flow pattern. Which of these flow patterns is the best design for least or slowest biofilm formation in NC (and catheters) is yet to be established.

In a review article it was reported that ‘turbulent flow actually enhances bacterial adhesion and that a steady flush minimizes adhesion’ (Chernecky and Macklin, 2014). This statement is attributed to Donlan (2002). However, I can find no such statement in Donlan (2002) or evidence elsewhere to support the view that turbulent flows create more, or less biofilm, than laminar flows. This lack of evidence confirms studies are needed which measure both occlusion and infection risks concurrently.

Jarvis (2010) (among other NC characteristics) suggests that the fluid pathway should be ‘direct, i.e. straight which facilitates adequate flushing and reduces the internal surface for biofilm development’. Although he also acknowledges that this characteristic lacks supporting evidence. However, in later work with other colleagues he showed that in six of seven identified studies involving 111,255 catheter days a significantly lower CLABSI rate of 0.5 per 1000 days (cumulative) was achieved with a NC which creates a flow around the depressed septum (Tabak et al., 2014). Royer (2010) reports an achieved zero CLABSI with the same NC design—albeit combined with a comprehensive quality approach. Before selecting a NC, it is perhaps more important to confirm that low CLABSI rates are achievable with it, rather than seeking the presence of characteristics which have yet to be tested.

Manufacturers have taken the Jarvis (2010) design recommendations and identified within their own NC (and their literature) where these features are present—even if for the author of this paper the said design features are sometimes difficult to find. For example, one manufacturer describes a straight fluid pathway when, at the lumen edges (where flow is slowest), the flow takes an obvious wave pattern through a corrugated channel. Other literature describes a straight fluid pathway when the flow is through

eyelets in a housing. Manufacturers are undoubtedly trying to frame their products positively (and if you look closely frame their competitors' products negatively) with regard to the Jarvis (2010) characteristics which have become accepted despite a lack of evidence to support them.

For a busy purchaser, being guided by opinion leaders, i.e. using Jarvis (2010) as a checklist, may be all the time and analysis available. It is imperative that purchasers can distinguish between opinions, evidence and be able to identify whether the manufacturers' identification of Jarvis' 2010 characteristics are actually present. Having specialists, e.g. infection control nurses and i.v. team leaders, well informed is of paramount importance.

Complexity

From a human factors perspective, i.e. is it easy for the HCW to do the right thing and to be sure what the right thing to do is, the answer is simply 'No'. That HCWs are confused with what device is being used, and how to use it, was ably illustrated in a study on nurses' knowledge (Hadaway, 2011). The researcher identified from 554 survey responses that 25% of HCWs did not know the type of NC being used and 53% did not know the correct clamping sequence for it (Hadaway, 2011).

In any given hospital, the NCs used must be compatible with all syringe luers that could be used. At least one NC is incompatible with glass-filled syringes such as those used in emergencies. Although an alternative device compatible with glass syringes is now available from that manufacturer. However, an emergency situation is a dangerous time to discover product incompatibility.

Conclusions

This rapid review considered published evidence, guidance and opinion on NCs to conclude that in this rapidly evolving arena there are few certainties apart from this: bacteria will gain access and flourish on the internal surface of NCs and eventually result in infection.

NCs are essential devices that are de facto the microbial gatekeepers to vascular catheters. Therefore, access via an NC must only ever be through an effectively disinfected septum. The evidence suggests this should be an alcohol-based antiseptic vigorously applied (or passive disinfection via a compatible disinfectant cap). Although a shorter duration has been effective in one study, in general there is insufficient evidence to reduce down from the accepted Epic3 disinfectant times of 15-s. The disinfectant must be allowed to dry pre access.

Once micro-organisms gain entry, biofilm develops and will eventually result in infection. The optimal fluid pathway design that achieves least biofilm formation is at present unknown.

The many NC design variations make it difficult for the HCWs to do the right thing.

For all the research that has been done, more is needed to generate evidence for optimal safe NC practice. What is clearly lacking with regard to NCs is standardised testing of: antiseptic application methods, microbial ingress and biofilm formation under simulated and in vivo conditions. This will enable those purchasing and using NCs to have confidence in the products being used.

Limitation: this work did not consider novel silver NCs nor the time between NC changes. The optimal time between NCs changes to reduce infection risks is difficult to elucidate from the literature as there are other key variables that cannot be determined, specifically, the number of times the NC is accessed between changes, the drugs (in terms of bacterial growth medium), the amount and type of microbial contamination and the duration of any infusates. These factors have been considered separately (Curran, 2011).

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