Tissue adhesive for vascular access devices: who, what, where and when?

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ABSTRACT

Despite vascular access devices (VADs) being vital for patient care, device failure rates are unacceptably high with around 25% of central venous devices, and 30–40% of peripheral venous devices, developing complications that result in VAD failure. The use of tissue adhesive is a novel method of securing VADs and is gaining popularity, however the evidence base guiding its clinical use is still emerging. This article aims to review the types and properties of tissue adhesives, provide an overview of the existing evidence base, and discuss how tissue adhesives may be used in clinical practice.

Key words: Vascular access devices ■ Tissue adhesives ■ Cyanoacrylate glue ■ Dressing and securement methods ■ Infection control ■ Peripheral catheterisation ■ Central venous catheterisation

ARTICLE

Vascular access devices (VADs) are required by the majority of hospitalised patients and many patients in the community so that intravenous treatment may be delivered (Zingg and Pittet, 2009). The term VAD refers to both short peripheral and longer centrally inserted devices as well as those inserted into veins and arteries. Despite their importance and prevalence, failure rates for VADs are unacceptably high with around 25% of central venous devices, and 30–40% of peripheral intravenous devices developing complications that impair function or cause removal (McGee and Gould, 2003; Bolton, 2010; Rickard et al, 2010; Chopra et al, 2013). Reasons for VAD failure are multifactorial and include occlusion, accidental dislodgement, breakage, extravasation, phlebitis, thrombosis, and local or systemic infection (Ullman et al, 2015a). The implications of VAD failure are missed or delayed treatment for the patient, pain, and increased costs to the health care system. Additionally, re-siting failed VADs can be distressing and increases risk to the patient (Helm et al, 2015).

A wide range of dressing and securement options are available to clinicians and these are important in preventing VAD failure (Ullman et al, 2015b). They provide a barrier to microbial contamination by fully covering the wound, facilitating moisture vapour transmission, preventing or containing ooze, and providing antimicrobial impregnation (Gabriel, 2010; Campbell and Bowden, 2011). Dressings and securements should also reduce VAD movement, both within the vessel by preventing micro-motion and pistoning, and outside the vessel by maintaining the VAD safely within the vein. These dressings and securements should facilitate insertion site assessment, minimise skin irritation, and be comfortable, affordable and easy to use (Ullman et al, 2015b). Tissue adhesives could potentially fulfil these requirements due to their purported ability to ‘seal’ the insertion site to prevent ooze and entry of microorganisms; bacteriostatic properties; and high tensile strength. Most likely due to these properties, the clinical usage of tissue adhesive to secure VADs appears to be increasing.

Medical-grade cyanoacrylate glues (tissue adhesives) were originally developed in 1949 with the first reported usage for wound closure 10 years later (Cooever, 1959). The first tissue adhesives were damaging to tissue and it was not until the 1970s that a more refined formula (N-butyly-2-cyanoacrylate (NBCA)) was made, which had negligible tissue toxicity, in addition to high bonding strength (Bruns and Worthington, 2000). On contact with the skin as a liquid, tissue adhesive polymerises within 60 seconds to become hard, and form a strong bond (Chow et al, 2010). Subsequent to the development of NBCA, a stronger and more flexible tissue adhesive was formulated, 2-octyl-cyanoacrylate (OCA), which is also said to last longer owing to its slower degradation (Chow et al, 2010).

More recently, another tissue adhesive preparation that combines both NBCA and OCA has been released commercially. Tissue adhesives are used as an alternative to sutures to close skin...
lacerations (Singer et al, 2011); for vascular embolisation (Rosen and Contractor, 2004); for bleeding gastric varices (Linhares et al, 2008), as an internal agent to stem bleeding or as a fixative during various surgeries (Kukleta et al, 2012; Tammaro et al, 2014); and to secure epidural catheters (Wilkinson and Fitz-Henry, 2008). Table 1 summarises a selection of commercially available tissue adhesives.

The use of tissue adhesive to dress VAD insertion sites and secure the catheter is a relatively new concept and, as such, the evidence-base which guides practice is small. There are no specific instructions from manufacturers on how to apply tissue adhesive to VADs as its use in this area, while covered by approval for use on internal and external tissue, is currently ‘off-label’. This means it cannot be marketed for this particular purpose. For wound closure, manufacturers recommend applying a thin layer of product at the intended site and some also recommend applying a second thin layer if necessary. The exothermic reaction of polymerisation produces heat, however the newer generations of tissue adhesive (OCA and NBCA + OCA) are said to polymerise at a lower temperature than older generations, thereby generating less heat. Patients will feel a warm sensation after tissue adhesive has been applied, but this is not typically considered to be painful. However, manufacturers advise that if large amounts of liquid tissue adhesive are allowed to collect and remain ‘pooled’ then the patient may feel heat and pain or discomfort. Thus if only small amounts are used for VADs, patient comfort should be maintained.

For application of tissue adhesive to VADs, reports in the literature (which will be discussed later) suggest that one to two drops at both the insertion site and under the hub/stabilisation wings is sufficient for sealing the insertion site and contributing to the stability of the VAD. Given that tissue adhesive can take up to 10 days to completely degrade and that VADs may need to be removed prior to this time, tissue adhesive removal agents may be required. Products recommended by manufacturers for this use include petroleum jelly/paraffin and acetone. However acetone has been shown to weaken the polyurethane from which most VADs are made therefore must not be used to remove tissue adhesive from VADs (Simonova et al, 2012). In the same study, Remove adhesive remover wipes (Smith & Nephew, North Ryde, NSW, Australia) were found to be compatible with polyurethane (Simonova et al, 2012) and have been used successfully to dissolve tissue adhesive in a number of subsequent trials (Edwards et al, 2014; Marsh et al, 2015a; Kickard et al, 2016). Uni-solve wipes (Smith & Nephew, North Ryde, NSW, Australia) have also been used to remove tissue adhesive from peripheral intravenous catheters (PIVCs) (Bugden et al, 2016) (Table 2). The authors of this study provided a link to videos that show both application and removal of tissue adhesive from a PIVC (https://youtu.be/DEW8mNLzw8A and https://youtu.be/_L5YzL3Xc).

Preliminary in vitro testing of the properties of tissue adhesive was conducted to determine the chemical compatibility with VAD materials, tensile strength, and bacterial inhibition abilities. This has informed its clinical use and future research directions. In this in vitro study testing PIVCs inserted into porcine skin, the investigators (Simonova et al, 2012) found that both NBCA and OCA did not weaken the PIVC materials tested in the study (Insite Autoguard (BD, Franklin Lakes, NJ, USA), made of BD Vialon) after 1 hour’s exposure. In the same study, the tensile strength of a number of different dressing and securement options was tested: simple polyurethane dressing, bordered polyurethane dressing, sutureless securement device, NBCA (Histoacryl) and OCA (Dermabond). Securement of the PIVC with Histoacryl created a bond that was double the strength of Dermabond and was four times stronger than a simple polyurethane dressing.

The same in vitro study (Simonova et al, 2012) also tested the ability of tissue adhesive to inhibit microbial growth by seeding agar plates with Staphylococcus aureus and Staphylococcus epidermidis around PIVCs covered with either a simple polyurethane dressing, Dermabond or Histoacryl. The agar plates with the PIVC and either simple polyurethane dressing or tissue adhesive were then incubated for 72 hours. After this time, there was no bacterial growth evident under the tissue adhesive itself nor any growth along the associated PIVC tract. By comparison, the simple polyurethane dressing showed bacterial growth beneath the dressing, along the PIVC tract and at the PIVC insertion point (Figure 1).

In another study investigating the antimicrobial effects of tissue adhesive used to secure epidural catheters (Wilkinson et al, 2008), NBCA (Histoacryl) was dropped onto agar plates

Figure 1. Microbiological test results. Positive control with S. aureus on pH selective agar (a). PIVC secured with tissue adhesive and inoculated with S. aureus around the adhesives. No growth evident under tissue adhesive or along PIVC tract at 72 hours (b). PIVC secured with bordered polyurethane dressing and inoculated with S. aureus around the dressing edge. Bacterial growth evident under dressing, along the PIVC tract and at the insertion point at 72 hours (c). Source: Simonova et al, 2012. Reproduced from Anaesthesia and Intensive Care with the kind permission of the Australian Society of Anaesthetists.
Table 1. A selection of tissue adhesives used for skin closure or with vascular access devices*

<table>
<thead>
<tr>
<th>Brand name (manufacturer)</th>
<th>Chemical constitution</th>
<th>Presentation (ml)</th>
<th>Storage (Celsius)</th>
<th>Time to degradation (days)</th>
<th>Properties</th>
</tr>
</thead>
</table>
| Histoacryl/Histoacryl Blue (B.Braun, Melsungen, Germany) | NBCA                  | 0.5               | < 22             | 7–10                      | High tensile strength  
Microbial barrier  
Quick setting time |
| Histoacryl Flexible (B.Braun, Melsungen, Germany)    | NBCA + softener       | 0.5               | < 25             | 7–10                      | High tensile strength  
More flexible than NBCA  
Less heat production on application  
Microbial barrier |
| Dermabond (Ethicon, Somerville, NJ, USA)            | OCA                   | 0.36, 0.7         | < 30             | 5–10                      | Higher tensile strength than NBCA  
More flexible than NBCA  
Microbial barrier |
| Surgiseal/SecurePortIV (Adhezion Biomedical, Wyomissing, PA, USA) | OCA                   | 0.35, 0.5 (Surgiseal) 0.15 (SecurePortIV) | < 30 | 5–10 | Higher tensile strength than NBCA  
More flexible than NBCA  
High moisture vapour transmission rate  
Microbial barrier |
| Glubran Tiss2 (GEM, Viareggio, Italy)              | NBCA + OCA            | 0.25, 0.35, 0.5   | 0–4              | 5–8                       | Improved flexibility  
High tensile strength  
Breathable  
Less heat production on application  
Microbial barrier |
| Indermil flexifuse (Connexicon, Dublin, Ireland)  | NBCA + OCA            | 0.75              | 4–30             | 5–8                       | Flexibility  
High tensile strength  
Minimal heat produced  
Microbial barrier |

*Information in this table is obtained from manufacturers’ website and/or product information brochures; NBCA, N-butyl-2-cyanoacrylate; OCA, 2-octyl-cyanoacrylate.

Inoculated with meticillin-sensitive Staphylococcus aureus, meticillin-resistant Staphylococcus aureus (MRSA), Enterococcus faecalis, Escherichia coli, Streptococcus pneumoniae, Pseudomonas aeruginosa, a coagulase-negative staphylococcus or Candida albicans. After 72 hours’ incubation, Histoacryl showed an inhibitory effect on all Gram-positive organisms, but no effect on Gram-negative organisms or Candida albicans. However, two recent studies have found OCA (SurgiSeal and FloraSeal) to be effective in inhibiting growth of Gram-negative organisms (Prince et al, 2017). The inhibition of Gram-positive and negative organisms by tissue adhesive is clinically important as these organisms are a significant source of catheter-related bloodstream infections.

Anecdotally, the use of tissue adhesive on VADs is increasing and manufacturers are currently pursuing new indications for tissue adhesive use specific to VADs. This review aims to summarise the existing evidence base to inform nurses’ clinical practice.

Use of tissue adhesive for peripheral intravenous and peripheral arterial catheters

The insertion of a PIVC is one of the most common medical procedures and up to 80% of hospitalised patients will require one during their stay (Zingg and Pittet, 2009). There have been four pilot randomised controlled trials (RCTs) investigating the use of tissue adhesive to secure peripherally terminating short-dwell VADs in the adult population (Table 3), which have generally supported its use (Edwards et al, 2014; Marsh et al, 2015a; Reynolds et al, 2015; Bugden et al, 2016). In a pilot trial (n=85), Marsh et al (2015a) tested the utility of tissue adhesive (combined with a simple polyurethane dressing) for securement of PIVCs in a medical surgical population where PIVCs had an average dwell time of 2.6 days. This trial found that PIVC failure was lowest in the tissue adhesive group however, four skin reactions were noted in this group (one skin tear, two rashes and one blister), all resolving without further intervention. Three of these skin reactions were directly associated with incorrect/incomplete removal of tissue adhesive prior to removal of the PIVC. This demonstrates that if tissue adhesive is introduced into clinical practice then extensive education would be required to ensure that nursing staff use the correct removal techniques to avoid damaging the patients’ skin. The authors also concluded that tissue adhesive may not be suitable for all skin types.

A second pilot RCT for PIVCs compared tissue adhesive covered with a bordered polyurethane dressing against the dressing alone in the emergency department (Bugden et al, 2016). One drop of tissue adhesive was applied to the insertion site with another drop under the hub and drying time was noted to be less than 30 seconds, after which a bordered polyurethane dressing was applied. Tissue adhesive was found to be a useful securement option with an absolute reduction of 10% in PIVC failure and 7% with tissue adhesive use. There were no adverse skin reactions noted during the study, however, there were
occasional comments made by study participants that there was a pulling sensation on PIVC removal, likely to be due to inadequate removal of tissue adhesive or the presence of dense hair at the insertion site.

Peripheral arterial catheters (PACs)—commonly inserted into the radial artery—are widely used in the management of patients in the operating theatre and intensive care unit (ICU) for continuous blood pressure monitoring and blood sampling purposes. Two pilot RCTs conducted in the operating theatre and/or ICU tested the use of tissue adhesive to secure peripheral arterial catheters and prevent failure (Edwards et al, 2014; Reynolds et al, 2015). In 2012, the first pilot RCT (Edwards et al, 2014) included 195 elective cardiac surgical and general ICU patients and all PACs were inserted by medical staff who also applied the study products. Peripheral arterial catheters failure was highest in the simple polyurethane dressing group (10/47, 21%) and lowest with the bordered polyurethane dressing and simple polyurethane dressing combination (2/43, 5%). PACs secured with tissue adhesive had a failure rate of 11% (6/56). The study authors concluded that tissue adhesive appeared to be a safe and feasible dressing product that would benefit from further investigation. There were three adverse skin events related to study products during the trial—two in tissue adhesive (skin tear and redness) and one in the sutureless securement device group (skin tear)—all of which were minor in nature and did not require any treatment to resolve. Staff satisfaction on application and removal was high in all groups however the application and removal of tissue adhesive took slightly longer than standard care (simple polyurethane dressing). After noting that the tissue adhesive had degraded under the PAC dressing by day three, the investigators decided to increase the amount of tissue adhesive applied from one drop at the insertion site and under the hub to two to three drops at each of these locations. Reynolds et al (2015) also conducted a four-arm parallel pilot RCT evaluating tissue adhesive against three other dressing and securement options. Tissue adhesive was found to be effective in preventing PAC failure, with a 14% absolute reduction in failure rates with tissue adhesive use. Patient satisfaction with the use of tissue adhesive was the highest of the four dressing products tested. The economic evaluation for this study found that the tissue adhesive method for securement was the most cost effective of the three intervention dressings when compared with the control dressing (simple polyurethane dressing).

### Use of tissue adhesive in central VADs

Central VADs (CVADs) are a range of devices (such as peripherally inserted central catheters (PICCs), tunnelled and non-tunnelled central venous catheters, totally implanted devices), inserted into large veins in the chest, neck, arm or groin, with the catheter terminating in the central vasculature (Ullman et al, 2015a). CVADs are used to support the administration of therapies in a diverse, complex patient group, ranging from short-term inotropes during critical illness, to life-long nutrition. Each of these device types and populations have challenges when using CVAD securement technologies, including tissue adhesive.

For CVADs, tissue adhesive has been used to achieve quicker post-insertion haemostasis at the insertion site, prevent infections, and promote micro- and macro-motion. The four RCTs evaluating tissue adhesive are displayed in Table 3. A four arm pilot RCT (n=221) evaluated the effectiveness of tissue adhesive to secure jugular, non-tunnelled CVADs in the post-cardiac surgical adult population (Rickard et al, 2016). This trial established that tissue adhesive, with a polyurethane dressing but without a suture was not effective to promote CVAD security, with 17% (4/23) of CVADs failing. Tissue adhesive effectiveness was particularly difficult for patients who were diaphoretic, coagulopathic, mobilised early, had large, heavy infusion sets, and with beard regrowth, suggesting that tissue adhesive use in these types of patients may not provide adequate securement. However, when tissue adhesive was added to standard care (sutures and polyurethane dressing), CVAD failures were reduced to 0 (of 30), in comparison to 4% for standard care (2/55). Tissue adhesive was also evaluated for use in PICCs in medical, surgical cancer patients, in a newly published pilot RCT (n=124) (Chan et al, 2017). Comparatively tissue adhesive, in addition to polyurethane dressing, was effective at promoting PICC performance with only 9% (3/35) of PICCs failing. Clinicians reported difficulty with the reaplication of tissue adhesive during the PICC placement, with frequent reports of glue build up on the PICC, which was difficult to remove. Skin complications, including erythema, swelling and tenderness, were also prevalent, with 36% (13/35) of participants receiving tissue adhesive experiencing a skin injury or complication.

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**Table 2. Tissue adhesive removal agents either tested for chemical compatibility with vascular access devices or used in the published evidence**

<table>
<thead>
<tr>
<th>Removal agent</th>
<th>Chemical composition (%)</th>
<th>Compatibility with vascular access devices*</th>
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</thead>
<tbody>
<tr>
<td>Remove™ Universal Adhesive Remover Wipes (Smith &amp; Nephew, North Ryde, NSW, Australia)</td>
<td>(2-methoxymethylethoxy) propanol (50–75) Hydrotreated heavy naphtha (petroleum) (25–50) Aloe Vera, extract (1–10)</td>
<td>Yes†</td>
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<tr>
<td>Paraffin</td>
<td>Paraffin</td>
<td>Yes†</td>
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<tr>
<td>Acetone</td>
<td>2-propanone</td>
<td>No†</td>
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<tr>
<td>Unisolve™ Adhesive Remover Wipes (Smith &amp; Nephew, North Ryde, NSW, Australia)</td>
<td>Dipropylene Glycol Methyl Ether (10–30) Isoparaffin (10–30) Isopropyl Alcohol (10–30) Aloe Extract (&lt;1) Fragrance (&lt;0.1)</td>
<td>Not tested in any published evidence. Use for removal of tissue adhesive in study †</td>
</tr>
</tbody>
</table>

* From Simonova et al (2012)
† Vascular access device chemical compatibility testing performed with Insite™ Autoguard™ (BD, Franklin Lakes, NJ, USA), made of BD Vialon™ Biomaterial with exposure to each removal agent for 1 hour prior to tensile strength testing
‡ Bugden et al (2016)
<table>
<thead>
<tr>
<th>Authors</th>
<th>Vascular Access Device</th>
<th>Setting</th>
<th>Sample size Participants (PIVCs/ PACs)</th>
<th>Products evaluated and outcome measure</th>
<th>Findings</th>
<th>Industry sponsored</th>
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<tr>
<td><strong>Peripheral intravenous catheters</strong></td>
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<tr>
<td>Marsh et al (2015)</td>
<td>PIVC</td>
<td>General medical/surgical wards</td>
<td>85 (85)</td>
<td>TA (with SPU) compared with SPU; BPU; and SSD (with SPU)</td>
<td>Outcome: PIVC failure (composite of pain, blockage, leaking, accidental removal or local or CRBSI)</td>
<td>No</td>
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<td></td>
<td>PIVC failure was lowest with TA group (3/21, 14%) compared with SPU (8/21, 38%), BPU (5/20, 25%) and SSD (5/23, 22%). No infections in any group</td>
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<tr>
<td>Bugden et al (2016)</td>
<td>PIVC</td>
<td>Emergency department</td>
<td>360 (380)</td>
<td>TA (with BPU) compared with BPU</td>
<td>Outcome: PIVC failure at 48 hours (composite of infection, phlebitis, occlusion or dislodgement)</td>
<td>No</td>
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<td>PIVC failure was 10% lower with TA (31/176, 17%) compared with BPU (52/184, 27%), (95% CI -18% to -2%, p=0.02); dislodgment was 7% lower with TA (13/176, 7%) compared with BPU (26/184, 14%), (95% CI -13% to 0%, p=0.04). No infections in any group</td>
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<td><strong>Peripheral arterial catheters</strong></td>
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<td>Edwards et al (2014)</td>
<td>PAC</td>
<td>Intensive care unit</td>
<td>224 (224)</td>
<td>TA (with SPU) compared with SPU; BPU (with SPU); SSD (with SPU)</td>
<td>Outcome: PAC failure (composite of complete dislodgement, occlusion (monitor failure, inability to infuse or leakage), pain, local or blood infection)</td>
<td>No</td>
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<td>PAC failure was highest in the SPU group (10/47, 21%) compared with the BPU (2/43, 5%); TA (6/56, 11%); and SSD (8/49, 16%). PAC failure was significantly higher for SPU compared with BPU (p=0.03). No infections in any group</td>
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<tr>
<td>Reynolds et al (2015)</td>
<td>PAC</td>
<td>Intensive care unit</td>
<td>123 (123)</td>
<td>TA (with SPU) compared with SPU; BPU; and SSD (with SPU)</td>
<td>Outcome: PAC failure (composite of complete dislodgement, occlusion; phlebitis, infection either local or CRBSI)</td>
<td>No</td>
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<td>PAC failure was lowest in the TA group (2/32, 6.3%) compared to BPU (4/30, 13.3%); SSD (5/31, 16.1%) and SPU (6/30, 20%), Infection outcomes not measured</td>
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<td><strong>CVADs in adults</strong></td>
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<tr>
<td>Rickard et al (2016)</td>
<td>JUG-NNT CVAD</td>
<td>Intensive care unit</td>
<td>221 (223)</td>
<td>TA (with BPU and no suture), TA (with BPU and suture), absorbent dressing (AD) and suture, SSD and SPU</td>
<td>Outcome: CVAD failure (premature CVAD removal before completion of therapy including dislodgement, occlusion, local infection, CABSI, breakage)</td>
<td>No</td>
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<td>CVAD failure was lowest in TA with BPU and suture group (0%, 0/30), compared to TA with BPU and no suture (17%, 4/23), BPU and suture (4%; 2/55), AD and suture (2%; 1/56), SSD and SPU (7%; 4/55). No infections in any group</td>
<td></td>
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<tr>
<td>Chan et al (2017)</td>
<td>PICC</td>
<td>Medical, surgical, oncology</td>
<td>121 (124)</td>
<td>TA (with SPU); compared with SPU, SSD, SPU and CHG patch, AD and CHG patch, integrated security dressing (ISD) and CHG patch.</td>
<td>Outcome: PICC failure (a composite of PICC removal for local infection, CABSI, dislodgement, occlusion and/or catheter fracture)</td>
<td>No</td>
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<td>PICC failure were AD and CHG patch 20% (1/5 ~ arm stopped prematurely), SSD, SPU and CHG patch 10% (4/39), TA and SPU 9% (3/35), ISD and CHG patch 7% (3/42). No infections in any group</td>
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<td><strong>CVADs in paediatrics</strong></td>
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<tr>
<td>Kleidon et al (2017)</td>
<td>PICC</td>
<td>Paediatric medical, surgical</td>
<td>95 (101)</td>
<td>TA (with BPU); compared with SSD and BPU, ISD</td>
<td>Outcome: PICC failure (cessation of function prior to completion of therapy)</td>
<td>No</td>
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<td>PICC failure was lowest in TA and BPU (3%; 1/32), compared with SSD and BPU (6%; 2/32) and ISD (6%, 2/31). No infections in any group</td>
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<tr>
<td>Ullman et al (2017)</td>
<td>TUNN-CVF CVAD</td>
<td>Paediatric oncology and medical</td>
<td>48 (48)</td>
<td>TA (with BPU and suture); compared with SSD, BPU and suture, ISD and suture, BPU and suture</td>
<td>Outcome: CVAD failure (cessation of function prior to completion of treatment).</td>
<td>No</td>
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<td>CVAD failure was lowest in TA with BPU and suture (0%; 0/12) and BPU and suture (0%; 0/11), compared to 17% (2/12) ISD and suture, 8% (1/13) SSD, BPU and suture.</td>
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</table>

AD, absorbent dressing; BPU, bordered polyurethane dressing; CABSI, catheter associated blood stream infection; CHG, chlorhexidine gluconate; CVAD, central venous access device; ISD, integrated securement dressing; PAC, peripheral arterial catheter; PICC, peripherally inserted central catheter; PIVC, peripheral intravenous catheter; SPU, standard polyurethane dressing; SSD, sutureless securement device; TA, tissue adhesive
Tissue adhesive use in CVADs has also been studied in paediatrics, with two pilot RCTs recently completed. When Kleidon et al (2017) evaluated tissue adhesive for PICCs (n=101), there was no reduction in complications or device failure in comparison to standard care (sutureless securement device and polyurethane dressing), however, tissue adhesive was effective at increasing mean time to first dressing change (5.5 days, IQR 3.5–6.5, p<0.01) and reducing non-routine dressing changes (0.1, IQR 0–0.5) by promoting insertion site haemostasis. When Ullman et al (2017) evaluated the effectiveness of tissue adhesive for the securement of tunneled CVAD (n=48), there was no reduction in complications, however it was safe and acceptable to patients, parents and clinicians. Overall, the RCTs evaluating the effectiveness of tissue adhesive for CVADs are small (total n=370) and in specific patient populations and devices, with limited generalisability.

There have also been non-randomised evaluations of tissue adhesive use in CVADs. In one of the first publications reporting tissue adhesive use in CVADs, the application of tissue adhesive was found to be less time-consuming than sutures and reported ‘complete success’ in central venous catheter securement (Wilkinson et al, 2007). Pittiruti et al (2016) similarly reported complete success in the application of tissue adhesive to promote CVAD security within adults and paediatrics, with data demonstrating effectiveness in haemostasis, preventing bacterial contamination, and, in paediatrics, a tenfold reduction in central line related bloodstream infection. Likewise, Ariotti (2016) reported applying tissue adhesive to more than 200 patients, and reported a reduction in the need for postoperative dressing change, reduced patient discomfort and economic savings. The role of tissue adhesive to promote site haemostasis was also evident in a report describing tissue adhesive use in PICCs (Scoppettuolo et al, 2013). Comparatively, Lawrence and Hacking (2014) reported that while the application of tissue adhesive in the adult ICU population was achievable and easier than suture, as in the findings of Rickard et al (2016), tissue adhesive without suture was associated with frequent accidental CVAD removal, and tissue adhesive was not adopted after the trial.

**Discussion**

This review of the scientific literature to date, which relate mainly to adult patients, has highlighted the likely benefits of tissue adhesive in preventing VAD complications and device failure. However, the evidence base is still relatively small, and large RCTs testing tissue adhesive use for VAD securement and maintenance are lacking for both peripheral and central VADs and this must be seen as a priority for researchers.

Novel securement approaches are needed, since device dislodgement, occlusion and other failure continue to be highly prevalent despite traditional securement methods. In addition, bloodstream infections are one of the most devastating device complications, and tissue adhesive’s antimicrobial properties likely offer additional protection. Importantly, tissue adhesive’s value appears to be in addition to other products, not to replace them, and nurses should consider implementation of tissue adhesive in suitable patients. However, there are important practical and economic issues for nurses to consider, and more research is needed to understand tissue adhesive’s effect in all patient and device types, as well as to be vigilant for potential adverse events which may not have been detected to date in the relatively small number of trials published.

No one securement method is likely suitable for all patients, but the research to date helps to identify patients for whom tissue adhesive is most likely to be beneficial. In PIVCs, tissue adhesive can significantly reduce failure for adult patients expected to require a PIVC for 24 hours or more (Bugden et al, 2016). This is of benefit since existing products have not been identified in RCTs as significantly reducing complications (Marsh et al, 2015b). Trials have not been done of tissue adhesive for short-term procedural PIVCs (e.g. day surgery), and it is unlikely that the extra time and expense is necessary for these patients. Importantly, there are no published reports of tissue adhesive use in PIVCs or PACs in paediatric patients. Implementing tissue adhesive for PIVCs in a healthcare institution would require inserters to decide the anticipated duration of therapy, and document whether or not tissue adhesive was applied, for example, by a sticker on the dressing and a note in the chart. This would avoid unnecessary use in <24 hour PIVCs, as well as alerting the nurse removing the PIVC that tissue adhesive is in place and needs to be removed first.

For CVADs such as PICCs, tissue adhesive use also appears beneficial to reduce complications, particularly to hasten haemostasis and to avoid early, soiled dressing replacement. Avoiding unnecessary dressing replacements will reduce nursing workload and patient discomfort, and in addition may reduce bloodstream infections (Timsit et al, 2012). Two recent studies (Chan et al, 2017; Kleidon et al, 2017) highlighted that tissue adhesive should only be applied on PICCs at insertion, not at subsequent dressing changes, so as to avoid product build-up on the PICC body itself. More evidence is required before a practice recommendation can be made regarding tissue adhesive reaplication on subsequent dressing changes. In addition, caution is needed for use at jugular sites in hirsute males, as even when applied to clipped skin, new beard growth can be painful and lift the tissue adhesive in some patients. A way ahead may be for jugular CVADs to be inserted lower on the neck (using ultrasound), to facilitate infection prevention and dressing maintenance, issues recognised by nurses but not always by inserters.

Implementing tissue adhesive into routine clinical practice requires institutions to plan and support a tailored education and change management initiative. The inserter workforce requires education so as to ensure the correct amount of tissue adhesive is applied, at the correct place (1–2 drops each at the device entry point, and under the device hub). Around 80% of PIVC insertions globally are undertaken by nurses, although this varies by country (Alexandrou et al, 2015). CVAD insertions are increasingly undertaken by advanced practice nurses, particularly for PICCs (Krein et al, 2017). However, even within the same institution, insertion procedures cross nursing, medical and other health workforce boundaries, and a trans-disciplinary, integrated approach to education and practice change is vital. Institutional insertion policies also require updating to include tissue adhesive, with pharmacists and purchasing departments...
involved in trialling and stocking the chosen brand. Nurses predominantly remove vascular access devices, and educational, policy and product updates also need to focus on tissue adhesive removal with commercially available adhesive remover wipes, prior to withdrawing the device.

Barriers to uptake of tissue adhesive for device securement include the excessive volume of many current products designed for wound use, compared to the very small volume (ideally approximately 0.15–0.2 ml) needed for device securement. If hospitals stock larger volume ampoules, this risks unfamiliar inserters applying excessive amounts, leading to tissue adhesive run off to unintended areas of the body, risk of unpleasant heat sensations as the tissue adhesive cures (sets), and even thermal injury. The purchase costs of many traditional tissue adhesive packaging is cost-prohibitive for PIVCs, since adding tissue adhesive to the billions of these devices used each year would substantially increase healthcare costs. Smaller-volume products, at lower cost, are urgently needed and could be included in insertion packs. In addition, while tissue adhesive use for device securement is covered by the current regulatory approvals for use on internal and external tissue, specific listing of the VAD securement indication would likely increase inserter uptake.

It must be noted that the majority of studies cited in this narrative review tested Histoacryl (B.Braun, Melsungen, Germany) tissue adhesive, which limits generalisability to other tissue adhesive types. This NBCA formulation lacks the flexibility that the newer formulation of cyanoacrylate glue (OCA) possesses thereby making it more brittle and possibly more prone to causing skin tears and build-up on the catheter hub. It is plausible that the use of OCA may not be associated with tissue adhesive build-up on devices, or with adverse skin events due to its more flexible formulation, but this is not yet known.

Current clinical practice guidelines will need to be updated in line with evidence as it emerges (Pittiruti et al, 2009; O’Grady et al, 2011; Lovey et al, 2014; Chopra et al, 2015; Bodenham et al, 2016; Gorski et al, 2016). To the authors’ knowledge, only two existing guidelines mention tissue adhesive use in securing VADs: the Michigan Appropriateness Guide for Intravenous Catheters (MAGIC), whose authors concluded in 2015 that there was insufficient evidence or experience upon which to make a recommendation at that time (Chopra et al, 2015); and the Infusion Nurses Society Standards of Practice, which state that the use of tissue adhesive in combination with a standard transparent dressing shows a slight trend towards less VAD failure but that larger trials are needed in the area and particularly to identify in which patients tissue adhesive use is inappropriate (Gorski et al, 2016).

Conclusion

The use of tissue adhesive to prevent complications and failure in VADs appears to be promising however more evidence is required to guide its clinical usage, particularly in the paediatric population. Tissue adhesive appears to reduce failure in adult patients with PIVCs; and be useful in achieving haemostasis and preventing the need for early dressing change in adult and paediatric patients. However, while tissue adhesive may be of use at CVAD insertion, it may not be practicable at subsequent dressing changes; and there is a need to identify patients for which tissue adhesive is safe so as to avoid the risk of skin injury. As global interest in this indication for tissue adhesive use increases, new studies are expected to add to the body of knowledge on this subject. Two RCTs on its use in PIVCs and CVADs are currently registered on the World Health Organization’s international clinical trials registry (apps.who.int/trialsearch/Default.aspx). These will add to the existing knowledge reviewed in this article and will further inform nurses in the appropriate and safe use of tissue adhesive to secure VADs. BJT
Are current vascular access device (VAD) securement options adequate for your patients needs or are innovations necessary to reduce VAD failure? Think about what innovations might be useful to your patients.

Could tissue adhesive be a useful securement option for your patients to prevent failure and early dressing change, and provide haemostasis? Which patients in particular would these be useful for and why?

From the evidence available, are you able to ascertain if tissue adhesive is a safe for your type of patient?


