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**The The role of 2 - Octyl-Isocyanacrylate Glue, as a microbial barrier in peripherally inserted central catheter port VADS. A review of the literature**

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## REVIEW

## THE ROLE OF 2 - OCTYL-ISOCYANACRYLATE GLUE, AS A MICROBIAL BARRIER IN PERIPHERALLY INSERTED CENTRAL CATHETER PORT VADS. A REVIEW OF THE LITERATURE

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**Abstract**

**Introduction:** The implanted port catheters in chemotherapy which are connected to a Peripherally Inserted Central Catheter (PICC Ports) are used daily in clinical nursing practice, enabling the administration of intravenous fluids, blood, drugs and Total Parenteral Nutrition. The 2-octyl-isocyanacrylate glue as an alternative intervention in preventing wound infection during PICC port insertion.

**Aim:** The aim of the present review was to explore the use of 2-octylisocyanacrylate glue as a microbial barrier in wound trauma and in peripherally central catheter insertion.

**Methods:** An electronic research was conducted in 4 databases. Sixty five papers focusing on the use of glue in surgical trauma closure and healing were analyzed.

**Results:** The literature demonstrates significant benefits of the 2-octyl-isocyanacrylate glue in comparison to other tissue adhesives, when placed on skin incisions. The 2-octyl-isocyanacrylate glue seems to provide an effective barrier to microbial penetration by Gram-positive and Gram-negative motile and non-motile species.

**Conclusions:** The use of the 2-octyl-isocyanacrylate seems to be an effective method for skin closure and healing in patients undergoing PICC Port implantation whilst causing no side effects such as allergies, skin irritation or pain during the procedure.

**Keywords:** 2octyl-isocyanacrylate, adhesive, picc port, bacteremia, complications.

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## INTRODUCTION

Nowadays, the implanted port catheters in chemotherapy which are connected to a Peripherally Inserted Central Catheter (PICC Ports) are used daily in clinical nursing practice, enabling the administration of intravenous fluids, blood, drugs and Total Parenteral Nutrition (TPN).

However, what is often observed, with high clinical frequency, is the assembly of CRBSI (Catheter-related bloodstream infections), and site infections caused by microorganisms that colonize the incision, through which the port catheter was implanted. Site infections may cause hematogenous infections, CRBSI (Catheter-related bloodstream infections), related to the catheter as well as increased morbidity. CRBSI treatment is a priority for the patient's safety systems and the provision of quality care.

It is estimated that approximately 7.0%-10.0% of patients worldwide develop at least one care-related infection during their hospitalization. The number of hospital infections in Greece is estimated at 200,000 per year, while the majority of them is due to the usage of Vascular Access Catheters (VADs).

Catheter-related infections, and in particular blood-borne infections, are responsible for the high mortality and morbidity rates, ranging from 10% to 20%, in patients with prolonged hospitalization (with an average of 17 days) as well as a higher healthcare cost. It is estimated that 250,000 incidences of hematogenous infections occur in the United States of America each year, with a cost of 25,000 \$ per case.

The PICCPort catheter is a soft catheter, made of polyurethane or silicone, inserted through a peripheral vein (one of the brachials or the basilic vein), with the tip of the catheter reaching the junction between the superior vena cava and the right atrium of the heart (cavo – atrial junction)<sup>1</sup>. Then, the catheter is connected to a port and placed subcutaneously at the middle of the upper limb. The main factors causing catheter infection are various diseases such as AIDS, diabetes and hematological malignancies, poor hygiene and lack of maximal barrier precautions during the implantation, previous operations, multiple attempts for IV catheter insertion and prolonged hospitalization. The most commonly detected microbes are Coagulase-negative staphylococcus, Staphylococcus Aureus, Klebsiella Delezos et al.

pneumoniae and Candida Albicans. The most common cause of hospital bacteremia is the Catheter-associated bloodstream infection (CRBSI). The CRBSIs are not only common and difficult to treat but are also the most expensive of the central venous catheterization complications.<sup>2</sup>

According to a study carried out by Mayetal, catheters with a larger diameter connected to an increased number of tubes were a risk factor as complications were caused by the PICC catheters to adults. This is the first multicenter study that evaluates the complications of PICCs and implanted venous access devices (TIVADs) in children and adults suffering from cystic fibrosis.<sup>3</sup> When placing a central line -no matter if the catheter is advanced centrally or peripherally- maximal barrier precautions (including gloves and full body sterilized gown) are essential.<sup>4</sup> Usage of gloves and changing gloves from patient to patient contribute to the prevention of hospital infections.

The high frequency of bacteremias and infections in vascular access practice vary from country to country and hospital to hospital. Studies report extremely high bacteremia rates (<11%, 7-9 cases / 1000 days of catheterization).<sup>5</sup> Most bacteremias (60%) are caused by Gram+ microorganisms that are part of our skin flora (mainly Coag. Neg. Staph. and Staph. Aureus) such as Staphylococcus epidermidis, Staphylococcus aureus, Enterococcus faecium, Enterococcus faecalis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacterbaumannii, Serratiamarcescens, Escherichia coli, Enterobacter cloacae and Candida albicans.<sup>6</sup> A major factor that can help prevent infection is the reduction of infection related risks associated with Vascular Access Devices. Researchers suggest that intravenous catheter bacteremia is responsible for prolonged hospitalization averaging to 20 days and an increased cost of € 3,000 per patient.<sup>7</sup>

## Antiseptic instructions prior to placement of a Vascular Access Device

It is obvious that any type of skin cleansing procedure should remove germs and ensure the safety of the site. However, some researchers argue that the residual antimicrobial activity of an antiseptic (e.g. chlorhexidine) protects both from the presence of non-killed germs and the colonization of new mi-

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crobes between cleansing procedures.

A study that recorded common complications at the site of the application of port peripheral intravenous catheters (sample of 130 catheters) also examined both methods (antiseptic with water - antiseptic with friction) of skin preparation prior to catheterization but it showed no differences.<sup>8</sup> Healthy skin acts as a protective barrier, therefore good cleansing or reduced antisepsis is definitely needed.<sup>9</sup>

The guidelines of international organizations such as the Centers for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC)<sup>10</sup> recommend the following methods:

Regarding the preparation of the patient's skin prior to catheterization, two options are suggested: use of 70% alcohol antiseptic, povidone iodine or chlorhexidine gluconate salt. Alternatively, the use of 0.5% chlorhexidine alcoholic solution prior to the peripheral venous catheterization is also recommended during patch changes.<sup>11</sup>

These guidelines are widely supported by independent studies found amongst a number of scientific papers.<sup>12</sup> The use of >0.5% chlorhexidine solution in combination with 70% isopropyl (an isomer of propyl alcohol with antibacterial properties as well), alcohol prior to the insertion of the central catheter is also suggested as an effective protocol for the preparation of the skin. The back and forth technique is often applied for >30 secs (ideally 60 secs) on the area where the central catheter will be inserted and for >2 minutes on the femoral area. If there is reaction to the use of chlorhexidine, povidone iodine or 70% alcohol solution are used alternatively. The same antiseptic protocols are also proposed for removal of the patches.

### Criticism on the proposed antiseptic protocols

Literature research has brought to the surface several studies that evaluate the efficiency of the antiseptic factors recommended to be applied to the site. Efficiency is evaluated by whether CRBSI is caused, the usage of a range of antimicrobial antiseptics, the possible combinations of antiseptics and whether side effects are noticed on the skin of catheterized patients.

The use of antiseptic solutions with friction (without the use of Delezos et al.

water) has been proved to have high antimicrobial activity.<sup>12</sup>

In a study of 705 neonates, in which peripheral inward catheterization was performed, on the 335 a chlorhexidine patch was placed on the catheterized area, and in the remaining 370 a 10% povidone iodine solution; while in both groups the same low rates causing bacteremias were recorded, in the chlorhexidine group, local dermatitis was recorded in 15.3% of the patients, whilst no dermatitis cases were recorded in the povidone iodide solution patients.<sup>13</sup> The same conclusions were also drawn by a review of studies referring to neonatal catheterization carried out by the Cochrane Neonatal Review Group (CNRG).<sup>14</sup>

A Brun-Buisson et al<sup>15</sup> study attempting to enhance the antiseptic effect of chlorhexidine by combining it with a silver sulfadiazine catheter did not show a statistically significant difference. Whereas another study reported a decrease of catheter colonization when the same solution was applied it did not result to a lower rate of microbe infection.<sup>15</sup> The review of studies referring to neonatal catheterizations by the Cochrane Neonatal Review Group (CNRG) came to the same conclusions<sup>14</sup>

A study by Brun-Buisson et al<sup>15</sup> in which an attempt was made to enhance the antiseptic effect of chlorhexidine by using a combination of chlorhexidine with silver sulfadiazine on a catheter patch, did not show a statistically significant difference. However, in another study,<sup>10</sup> when the same combination of solutions was used, a decrease in catheter colonization was observed, but the percentage of bacteremias accumulated remained the same.

### Antiseptic side effects

A study with a large sample of patients (2095 eligible patients, underwent 3778 catheterizations in 28,931 Catheter - Days) recommends the use of patches soaked with chlorhexidine as an effective measure to reduce the incidence of infection to 60%, when placing peripherally inserted catheters. The possibility of altering the cleansing of the site from 3 days to 7 days was also examined but this increased the cases of dermatitis due to the residual action of chlorhexidine.<sup>16</sup> In addition, over the last few years cyanoacrylic glue is also used as a microbial

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barrier.

### **The use of the octyl cyanoacrylate glue as a microbial barrier**

The use of the octyl cyanoacrylate glue has recently been introduced into clinical practices in Europe for Vascular Access Devices in order at first to stop the bleeding from the exit site of the PICCs and later at the point of exit of dialysis catheters. The glue has been proven to be 100% effective in preventing bleeding after insertion and in preventing bacterial contamination of the catheter's lumen (or lumens).<sup>17</sup> The glue is cyanoacrylate octyl based.

Octyl cyanoacrylate (OCA), a cyanoacrylate ester, is an octyl ester of 2-cyano-2-propenoic acid. It is a clear colorless liquid with a sharp odor. It is basically used as the main component of medical cyanoacrylate adhesives. OCA, n-butyl cyanoacrylate (n-BCA) and isobutyl cyanoacrylate (ICA) are commonly used in medical and veterinary applications. They provide rapid wound closure, they are bacteriostatic, and minimal pain is caused when used.<sup>18</sup>

### **APPROVALS**

Butyl cyanoacrylate is an intermediate length cyanoacrylate adhesive and was the first product to be broadly used for closing dermal wounds. This compound has been approved for use in Europe and Canada as Histoacryl® Blue (trademark of Aesculap, Inc.) and GluStitch® (trademark of GluStitch, Inc.) for nearly 40 years. It had not been approved by the US Food and Drug Administration (FDA) for use in the United States for a long time. In Europe, Canada, and Japan, it has been used for middle ear procedures, to close cerebrospinal leaks, to repair incisions and lacerations, and to affix skin since the 1970s.<sup>19</sup> 2-octyl cyanoacrylate is one of the most commonly used, commercially-available wound adhesives. It received initial approval in 1998 as an alternative to closure of skin wounds with 5-0 or smaller suture, staples, or adhesive strips by the Federal Drug Administration (FDA) in the United States. Current indications include all easily approximated wounds from surgical incisions or properly cleaned lacerations from trauma in areas that are dry and have minimal friction. Additionally, it was approved for

use in combination with subcuticular sutures for deeper or higher tension wounds.<sup>20</sup>

The wound adhesive 2-octyl cyanoacrylate (Dermabond) is approved by the US Food and Drug Administration (FDA) for the closure of incised skin. In addition to its surgical adhesive indication, 2-octyl cyanoacrylate was approved by the FDA in January 2001 for use as a barrier against common bacterial microbes, including certain staphylococci, Pseudomonads, and *Escherichia coli*.<sup>21</sup>

### **Chemical behavior of cyanoacrylate polymers**

Octane cyanoacrylate (OCA), a cyanoacrylate, is an octyl ester of 2-cyano-2-propenoic acid. It is a clear colorless liquid with a sharp odor as we mentioned before. Its chief use is as the main component of medical cyanoacrylate adhesives. OCA, n-butyl cyanoacrylate (n-BCA) and isobutyl cyanoacrylate (ICA) are commonly used in medical and veterinary applications. Butyl esters provide a stronger bond, but the adhesive is rigid. The octyl ester, while it provided a weaker bond, is more flexible. OCA and n-BCA combinations are available and offer both flexibility and strong bonding.<sup>22</sup>

OCA polymerizes rapidly in the presence of moisture. Heating to higher temperatures causes the pyrolysis and depolymerization of the cured glue, producing gaseous products highly irritating to the lungs and eyes.<sup>23</sup>

Cyanoacrylate tissue adhesives combine cyanoacetate and formaldehyde in a heat vacuum along with a base to form a liquid monomer.<sup>24</sup> When the monomer comes into contact with moisture on the skin's surface, it chemically changes into a polymer that binds to the top epithelial layer. This polymer forms a cyanoacrylate bridge, binding the two wound edges together and allowing normal healing to occur below. The conversion from monomer to polymer occurs rapidly, preventing seepage of the adhesive below the wound margins as long as the edges are well apposed. Heat is often generated during the transition from monomer to polymer and this heat can be felt in some cases by patients when applied to the skin.<sup>25,26,27,28</sup> A study by Szanka et al, considers the practical significance that the set time of OCA polymerization can be precisely controlled in the 60–120secs range by the use of appropriate concentra-

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tion of select materials.<sup>29</sup> One of these can be the constructive material of the catheter.

### Historical review

Cyanoacrylate adhesives were first patented in 1949 and the adhesive property of cyanoacrylate was first recognised in the late 1950s.<sup>30</sup> The initial shorter chain cyanoacrylates were found to cause inflammatory reactions,<sup>31,32</sup> which have been reduced with longer chain formulations. The first adhesives were noted to have severe inflammatory effects on tissues. The N-butyl-2-cyanoacrylate, which was developed in the 1970s, was the first adhesive to have negligible tissue toxicity and good adhesion strength, as well as aesthetically acceptable trauma image.

### Applications

Short-chain cyanoacrylates (methyl, ethyl) are toxic to tissues; this is not the case with butyl cyanoacrylate when applied topically. In an experimental model of incision wound healing in hamsters, butyl cyanoacrylate resulted in less inflammation than that caused by 4.0 silk sutures of histological assessment.<sup>33</sup>

N-butyl-2-cyanoacrylate has been used in cartilage and bone transplants, coating of corneal ulcers in ophthalmology, repair of damaged osteosarcoma in otorhinolaryngology, coating aphthous ulcers, embolism of gastrointestinal varices and embolization in neurovascular surgery.<sup>18,25,26,34,35</sup> This adhesive has not been labeled for this use by the FDA but has been used in Canada and many other countries for more than 20 years.

2-OCA has a longer side chain than butyl cyanoacrylate. It was approved by the FDA for use in the United States in August 1998 for certain types of laceration. Its applications have been expanded and it is now marketed as Dermabond® (a trademark of Ethicon, Inc., a Johnson & Johnson Company) topical skin adhesive for closure of lacerations and incisions in place of sutures or staples. Later on, a 2-OCA formulated for greater flexibility, Liquid Bandage, was approved for use in the over-the-counter market in the United States for the treatment of minor cuts and abrasions.<sup>36</sup>

The longer side chain gives 2-OCA several potential advantages over shorter chain cyanoacrylates. 2-OCA, for instance, produces a stronger bond and is more flexible than butyl cyanoacrylate. It has four times higher volumetric break strength than butyl cyanoacrylate. Owing to the increased strength and flexibility and reduced risk of tissue toxicity, 2-OCA is now widely used in the United States for closure of wounds. It is currently one of the best selling bandage brands in the United States.<sup>36</sup>

2-Octyl cyanoacrylate is also extremely effective in immediately controlling air leaks after lung resection, with the results being seen instantly. It dries quickly, does not wash off the lung, and remains intact on the visceral pleura for several weeks.<sup>37</sup>

A meta-analysis by Singer and Thode demonstrates that octylcyanoacrylate can be used successfully in a wide variety of clinical and surgical settings for multiple types of wounds covering most of the surface of the human body. Prior knowledge of the limitations and technical aspects specific to wound closure with octylcyanoacrylate as well as appropriate wound selection and preparation, will help ensure optimal results.<sup>22</sup>

### Application of wound healing

2-octylcyanoacrylate achieves maximum adhesion strength within two and a half minutes and is equivalent in strength to healed tissue seven days after skin resurfacing.<sup>38</sup> The antimicrobial property is particularly relevant to orthopaedic surgery where surgical site infections can have such a devastating consequence.

2-octylcyanoacrylic polymer is marketed as a substitute for sutures having a diameter of 5-0 or less. Properly selected wounds to the face, limbs and trunk can be closed with glue. The use of adhesive, rather than suture, depends solely on the discretion of the health professional and will reflect his or her level of comfort and experience. Wounds tend to heal better when the subcutaneous sutures are first placed. If the adhesive is selected for use in areas of high mobility (such as joints), this area should be immobilized on the splint to avoid premature peeling of the adhesive. Scalp wounds may be closed with adhesive using meticulous care so as not to allow excess adhesive to run through the hair. 2-octylcyanoacrylate should be kept dry in this area for at least five days for normal healing.<sup>27</sup>

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Wound closure with the 2-octylcyanoacrylic polymer is achieved in several steps. Smaller ruptures can often be cleaned with an antibacterial compound and rinsed with sterile saline prior to closure. Minor facial injuries usually heal well with this preparation. One study showed that only one in five children needed local anesthesia to repair minor facial injuries with 2-octylcyanoacrylate.<sup>29</sup> Since the glue is removed within five to 10 days, deeper injuries to the trunk and limbs must have subcutaneous sutures positioned to enhance wound closure. Deep wounds without subcutaneous sutures appear to have a higher percentage of discoloration.<sup>27</sup>

It is indicated for use in holding easily approximated skin edges of wounds from surgical incisions and thoroughly cleansed trauma-induced lacerations. It may also be used in conjunction, but not in place of deep dermal sutures. 2-octylcyanoacrylate has demonstrated superiority over subcuticular sutures<sup>40</sup> and staples<sup>41</sup> with regard to closure time, cosmetic appearance and patient satisfaction, without an increase in wound dehiscence,<sup>42</sup> and with a reduction in infection rates.<sup>43</sup>

This tissue adhesive should not be used on animal bites, seriously infected wounds, ulcers, puncture wounds, mucous membranes (including mucosal dermal connections) or areas with high moisture content, such as groin or armpits. Though, it may be used on selected hand, foot and joint wounds, if these areas are kept dry and immobilized.<sup>29,34</sup>

The availability of adhesive tissue in no way eliminates the need for good irrigation and wound cleaning. Deeper wounds should undergo detailed wound preparation as with traditional repair methods to reduce the risk of infection. This will often include the need for topical or local anesthesia. Good wound management should not be compromised for a quick repair with a tissue adhesive.<sup>27</sup>

Finally, bibliography demonstrates a superiority of 2-OCA in correlation with other cyanoacrylate tissue glues, when it is placed after skin incisions, in wound bursting skin or tensile situation. A meta-analysis by Robertson et al, presents a comparison between 2-OCA itself and a blend of butyl-2-octylcyanoacrylate with 2-OCA, when they're placed in the skin of 433 knee arthroscopy patients. There is no difference observed concerning wound dehiscence, or cosmetic outcome. Delezos et al.

Additionally, in the same study, it is demonstrated that 2-OCA yields a higher wound bursting strength and the ability to withstand greater tensile strength compared to other commercially available cyanoacrylate adhesives.<sup>45</sup>

### **Antimicrobial properties of 2-octylcyanoacrylate**

Cyanoacrylates have also been shown to have antimicrobial properties.<sup>46</sup> The adhesive provided an effective barrier to microbial penetration by Gram-positive and Gram-negative motile and non-motile species.<sup>47</sup> A study by Rushbrook et al, demonstrates that octylcyanoacrylates have antimicrobial properties with regards to Gram-positive bacteria. Standardised pellets of cyanoacrylate product were created by dropping the glue into the mould and allowing it to set. The inhibition rings around the pellets persisted following 10 days of culture. Swabs taken from these inhibition rings then produced no further culture, suggesting that octylcyanoacrylate has a bactericidal mechanism of action. The pellets were placed directly on standardised agar dishes containing methicillin-resistant *Staphylococcus aureus* (MRSA), Oxford *Staphylococci*, Group G *Streptococci*, *Enterococcus faecalis*, coagulase negative *Staphylococcus* (CNS), *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*. This was to simulate placing the glue directly onto the skin rather than onto an interface such as filter paper. Each petri dish was divided into quadrants, with a pellet placed in three of the quadrants, and the fourth left as a control. The agar dishes were incubated at 37 degrees centigrade for 10 days, and were examined at day 1 and day 10. A swab was taken at day 1 and day 10 from the inhibition ring, if present, and each cultured on agar plates at 37 degrees centigrade for 24 hours. Inhibited growth of Gram-positive organisms was observed, with constant inhibition rings being displayed at day 1 and day 10.<sup>48</sup> It is thought that this is due to the strong electronegative charge on the cyanoacrylate monomer that reacts with the positively charged carbohydrate capsule of Gram-positive organisms.<sup>49</sup>

It must be noticed, that the cyanoacrylates present wider antimicrobial action, when they act as a liquid-glue formula. A study investigates the polymerization reaction which contributes additionally to the antibacterial effects of two commonly

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used cyanoacrylate tissue adhesives. It was found that the cyanoacrylates extend their bacterial inhibitory, not only to Gram positive such as *Staphylococcus aureus* or *Streptococcus pneumoniae*, but also to Gram negative strains like *Escherichia coli* or *Pseudomonas aeruginosa*.<sup>50</sup>

The antimicrobial capacity of the n-butyl-2-cyanoacrylate form has been studied in a corresponding letter examining tissue adhesion in surgical trauma. Strains of *Streptococcus pyogenes*, *Streptococcus mitis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, failed to contaminate the adhesive patch in tissues used in surgical trauma.<sup>51</sup> In another study, again for surgical trauma, a successful bacteriostatic effect was recorded on *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, or *Mycobacterium chelonae*, on patches of Methoxypropyl cyanoacrylate and Methoxypropyl cyanoacrylate.<sup>52</sup>

Sealing the outside of the catheter with adhesive also reduces the risk of contamination of the outer lumen, possibly by microbial transport from the sealing point.<sup>53</sup>

In another study, evaluating the antimicrobial activity of a product based on N-butyl cyanoacrylate (Histoacryl) as a skin adhesive, the product exhibited specific inhibitory activity against all gram+, but not against gram-, or *C. albicans*.<sup>54</sup>

The antimicrobial property of octylcyanoacrylates have been demonstrated in vitro. Other studies demonstrate the barrier properties of octylcyanoacrylates and found it to be an excellent barrier to bacteria with the exception of *P. aeruginosa*.<sup>55</sup> Clinical studies have demonstrated reduced infection rates associated with its use.<sup>56,57</sup>

Randomized controlled clinical trials 4–8 showed that infection rates did not differ significantly between stapled and closed wounds with octylcyanoacrylate. Ilker studied the effects of closing lacerations with suture or with cyanoacrylate tissue adhesive on staphylococcal counts in inoculated guinea pig lacerations. Wounds closed with adhesive alone had lower counts than wounds containing suture material ( $P < 0.05$ ). The results of a time-kill study were consistent with a bacteriostatic adhesive effect of the adhesive against *Staphylococcus aureus*.<sup>58</sup>

Colonization of central venous catheters (CVCs) by microor-  
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ganisms is an event that precedes central line associated bloodstream infection (CLABSI). It is possible that sealing the skin insertion site of CVCs with 2-octyl cyanoacrylate adhesive may reduce catheter colonization by creating a sterile barrier and minimizing subsequent extraluminal colonization of the catheter. Dahl studied 19 patients who underwent the application of 2-octyl cyanoacrylate adhesive to the CVC insertion site, followed by daily inspection for visual signs of 2-octyl cyanoacrylate sealant integrity with skin / catheter interface. 2-OCA succeed to seal the insertion point of CVC for an average of 7 days.<sup>59</sup>

Another study by Simonova investigated the in vitro use of tissue adhesives in securing Vascular Access Devices (VADs). They compared two adhesives for interaction with VAD material, comparing skin glues with current securing methods in terms of their ability to prevent IVC dislodgement and inhibit microbial growth. Two tissue adhesives (Dermabond, Ethicon Inc. and Histoacryl, B. Braun) and three removal agents (Remove™, paraffin and acetone) were tested for interaction with IVC material by use of tensile testing. Neither TA weakened the IVCs ( $P > 0.05$ ).<sup>60</sup>

However, if adequate cleaning and preparation of wounds deteriorates due to ease of use of a tissue adhesive, infection rates may increase.<sup>27,39,44,56</sup>

## Complications

Despite the reported safety, studies report complications with the use of cyanoacrylate in the form of N-butyl cyanoacrylate (Histoacryl). When using Histoacryl in a sample of 20 patients with KFC, the second day after application, detachment was observed in 6.<sup>61</sup>

A special study of vascular access, dealing only with peripheral inlet central catheters, noted a large reduction in hospitalization costs and a large decrease in the incidence of complications in patients with cyanoacrylic glue use. Suspicious infection under the glue can be treated with oral antibiotics. The natural reaction to a real infection generally pushes the dried polymer away from the skin. In these rare cases, the adhesive should be removed and standard wound care measures should be initiated.<sup>62</sup> 2-octylcyanoacrylate, as a key ingredient in the

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latest formulations in cyanoacrylate technology, has less toxicity and almost four times the potency of N-butyl-2-cyanoacrylate. To the above-mentioned, chemical polymer, special plasticizers were added to provide flexibility.<sup>38</sup> 2-octylcyanoacrylate use is not without complication. It has been known to cause a localized inflammatory reaction following its use for wound closure for patellofemoral joint replacement in a patient with a history of atopic eczema. Blisters formed around the incision site four weeks postoperatively, and on close inspection it was noted that 2-OCA was still present on the skin. There was improvement following removal of the ingredient.<sup>63</sup> Complications have also resulted from misplacement of Dermabond® in the eye and mouth, but this was following surgery in close proximity to these structures.<sup>64</sup>

A study by Puccio et al, investigated the possibility of damage to the VAD, secondary to a long-term contact with a two-component skin glue (N-butyl + octyl cyanoacrylate). Twelve PICCs of different brands and types were selected (11 made of polyurethane and one made of silicon). PICCs were glued onto artificial skin pads. No chemical reaction between the glue and the material of the catheters was evident. The long-term use of N-butyl + octyl cyanoacrylate glue on polyurethane PICCs is not expected to be associated to any damage to the catheter.<sup>64</sup>

## CONCLUSIONS

2-octylcyanoacrylate is a commonly used tissue adhesive that demonstrates bacteriostatic properties against Gram-positive bacteria and certain types of Gram-negative bacteria. It is used for wound closure following procedures with high risk of infection by Gram-positive bacteria thus reducing postoperative wound infection. This would be best assessed with a randomized control trial. 2-octylcyanoacrylate has demonstrated superiority over traditional subcuticular skin sutures in terms of closure time, cosmetic appearance, and patient satisfaction. This technique provides a novel method of wound closure after CABG. Cyano-acrylate glue was 100% effective in preventing post-insertion bleeding from the exit site. Also, in PICCs, the glue was effective in preventing extra-luminal bacterial contamination of the catheter. In pediatric CICC, a specific insertion bundle including glue as one of the main recommendations was effective in achieving a tenfold reduction of the incidence of CRBSI. However, it presents specific complications which can be overcome through careful choice of materials and procedures. Reusing the adhesive in such cases is not recommended.

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## ANNEX

## CHEMICAL INFORMATION OF CYANOACRYLATE

<b>Octylcyanoacrylate</b>	
<b>NAMES</b>	
Suggesting name according to IUCAS	
Octyl 2-cyanoprop-2-enoate	
Others names	
Octyl	2-cyanopropenoate
Octyl	2-cyanoacrylate
Ocrylate	
<b>IDENTIFICATION</b>	
CAS Number	•6701-17-3 ✖
3D model (JSmol)	Interactive image
ChemSpider	•21678 ✔
ECHA InfoCard	100.027.045
PubChem CID	•23167
Chemical formula	C <sub>12</sub> H <sub>19</sub> NO <sub>2</sub>
Molecular weight	209.29 g·mol <sup>-1</sup>
Appearance	Liquid transparent
Solubility in water	Reaction
Information are given for the ingredients according to 25 °C [77 °F], 100 kPa.	