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Infusion White Paper

Extreme cost of dehydrated alcohol resulting from FDA Unapproved Drug Initiative:

Impact on catheter lock therapy for home infusion patients with central venous access

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Introduction

Catheter-associated bloodstream infection (CABSI) is a significant risk for patients who require central venous access devices (CVADs). It is associated with high costs, increased length of hospital stay, and morbidity and mortality and may require removal of the access device and treatment with anti-infectives. CABSI is three times more common in pediatric patients and higher in intestinal failure patients than in those with other underlying disease processes.[1]

Alternative lock solutions may be appropriate for patients with long-term CVADs in certain situations, such as when antibiotic lock therapy is not an option. There are significant obstacles to providing alternative lock solutions in the home setting, which limit patient access to therapy. Many of the products used today are not FDA approved or indicated for lock therapy, resulting in zero or minimal reimbursement and prohibitive out-of-pocket cost for patients. The lack of options has created an urgent need in the United States for FDA-approved central line catheter lock solutions.

The lack of options for lock solutions other than antibiotics has created an urgent need in the United States for FDA-approved central line catheter lock solutions.

Purpose

The purpose of this white paper is to 1) address challenges associated with alternative catheter lock therapy and 2) call for change within the FDA, which would allow greater variety of lock options in the U.S. and potentially, more cost-effective access to therapy.

Background

CVADs are necessary for a variety of reasons when peripheral venous access is not possible or appropriate. In the home infusion setting, CVADs are commonly required for therapies such as parenteral nutrition (PN), intravenous antibiotics and chemotherapy.[2]

A serious risk of a CVAD is CABSI, which is associated with a high cost burden: approximately $46,000 per case, with an estimated 250,000 occurrences annually.[2,3]

In particular, the pediatric population is at increased risk for CVAD infection, which is associated with an increased risk of hepatic injury.[4] Prevention of CABSI could potentially decrease the incidence of PN-associated liver disease, which is a life-threatening complication associated with the PN-dependent pediatric patient. In addition, venous access sites are limited in the pediatric population.[5]

Current industry standards and best practice

The primary defense against CABSI is prevention — focusing on adherence to proper catheter care and medication administration technique according to industry best practices and guidelines set forth by the Centers for Disease Control and Prevention (CDC) and Infusion Nurses Society (INS).[6,7]

Catheter/alternative lock therapy

Although not recommended for routine use in the prevention of CABSI, antimicrobial lock solutions are recommended by the CDC and INS in certain situations, such as in patients with long-term catheters who have a history of multiple catheter-related bloodstream infections despite optimal maximal adherence to Aseptic Non-Touch Technique (ANTT®). The goal of lock therapy is to prevent catheter infection by instilling the antimicrobial lock solution for several hours when the catheter is not in use.

> The primary defense against CABSI continues to be prevention. Proper catheter care requires rigorous patient education and training with strict adherence to aseptic catheter handling protocol.[8]

A variety of solutions have been studied for lock therapy, including antibiotics, antiseptics and anticoagulants. The pros and cons are outlined in Table 1.

Ethanol lock therapy

Because it is both bactericidal and fungicidal against a broad range of microorganisms, ethanol has been proposed as an alternative lock solution for more than two decades, with most studies using daily administration of a 70% solution with dwell times of at least two to four hours.[9]

In small observational studies (particularly in the pediatric population), ethanol locks have demonstrated comparable efficacy to antibiotic locks.[9] Use of a daily 70% ethanol lock therapy (ELT) for the prevention of CVAD infections was effective and safe in 15 outpatients in the University of Michigan Children's Intestinal Rehabilitation Program.[5]

Unlike antimicrobial locks (for example, vancomycin or gentamicin), ethanol is not dependent on the antimicrobial sensitivity of the organism. Thus, a potential advantage is to decrease the use of repeated courses of antimicrobial therapy and prevent resistant organisms from infecting or colonizing the patient.

Table 1: Snapshot of various alternative lock solutions[6,9]

Solution	Pros	Cons
Anti-infectives	• Bactericidal	• Antibiotic resistance
Concentrated sodium chloride	• Alternative for hemodialysis catheters with high bleeding risk	• High-alert medication — not appropriate for use in home setting
Ethanol	• Bactericidal • Fungicidal	• Not FDA indicated for catheter lock • Can alter catheter integrity
Sodium bicarbonate	• Prevention of hemodialysis catheter loss due to bloodstream infection and catheter-related thrombosis	• Studies limited to hemodialysis catheters
Sodium citrate	• Anticoagulant • Antimicrobial	• Insufficient evidence to demonstrate efficacy for non-hemodialysis catheters • Risk of hypocalcemia leading to cardiac arrest • Protein precipitate with concentration >12%
Taurolidine	• Bactericidal • Fungicidal	• Not FDA approved • Not available in the U.S.
4% Tetrasodium EDTA	• Anticoagulant • Antimicrobial • Prevent and eliminate biofilms	• Available in the U.S. via FDA Compassionate Use protocol only

The use of ELT should take into consideration:

- Prior catheter-related bloodstream infection episodes caused by different organisms for which a single prophylactic antibiotic agent may not be effective, or caused by drug-resistant pathogens[9]
- The consensus that ELT should not be used for treatment of catheter-related bloodstream infection[9]
- Adverse effects associated with ethanol lock flushing, such as nausea, dysgeusia, alcoholic taste, dizziness, and skin flushing, as well as an increased risk of catheter thrombosis[9]

Ethanol lock challenges in the home infusion setting

Many challenges prevent the routine use of ELT in the home infusion setting today. The ethanol lock solution must be compounded using dehydrated alcohol injection, USP. There is only one commercially available dehydrated alcohol product (Ablysinol®), for which there is no equivalent product substitution. Ablysinol is a sterile, preservative-free solution of ≥99% by volume ethyl alcohol. Although it is FDA approved, it is not indicated for catheter lock therapy, so use in this manner would be "off label," making reimbursement a formidable challenge.[10]

The current cost of $800 to $1,000 per 5ml vial of Ablysinol has made it virtually impossible for any provider to offer ethanol locks without reimbursement.

The FDA Unapproved Drug Initiative and its impact on ethanol lock

The Unapproved Drug Initiative (UDI) is a program launched by the Food and Drug Administration in 2006 with the intent to remove unapproved drugs from the market. This initiative has historically been controversial because price increased significantly for newly branded drugs and for parenteral nutrition (PN) ingredients like electrolytes and trace elements that were previously generic, along with adjunctive PN products like ethanol and L-cysteine.

Generic dehydrated alcohol historically used in the compounding of ethanol lock solution was denoted as an "unapproved drug" by the FDA. In 2018, unless manufacturers were willing to go through the FDA approval process, these generics were pulled from the market and are no longer available.

The UDI was discontinued in late 2020 after a coalition meeting with the FDA outlining unintended consequences of the initiative but was then reinstated in May 2021. The result of the rebranding of ethanol is an astronomically higher price (an 800% to 900% increase) and only one manufacturer with an exclusive patent.[11,12]

Reimbursement for ethanol locks in conjunction with home infusion therapy has always been minimal or non-existent, but some providers offered to supply it when the cost of generic ethanol was low. The current cost of $800 to $1,000 per 5ml vial has made it virtually impossible for any provider to offer ethanol locks without reimbursement.[13] As a result, access to this critical adjunctive therapy, effective in decreasing CABSI for many patients requiring long-term central venous access, has been greatly affected.

With an increase in cost from ~$10 a day to anywhere from $100 to $500 a day, one major health care system in the U.S. concluded that at this price point, CLABSI reduction with ethanol lock prophylaxis is not cost-effective.[13]

Now that home infusion and hospital providers are subject to a tenfold price increase for dehydrated alcohol and only one branded product on the market, the majority of providers no longer provide ethanol lock therapy for home PN patients.

Recommendations and conclusions

Clinicians and prescribers involved in the provision of home infusion need to be aware of the impact of policies such as the FDA's UDI that may inadvertently limit access to safe and appropriate home infusion therapy.

Recommendations and conclusions (continued)

Having only one branded – and cost-prohibitive – product available with very limited or non-existent insurance coverage, along with minimal alternative options prevents patients from receiving adjunctive therapy that could prevent further episodes of CABSI and its associated costly complications.

Lowering the cost of ethanol lock solution and approving alternative lock products could create significant cost savings and would improve quality of life for children with intestinal failure.[13]

Clinicians and organizations like the American Society for Parenteral and Enteral Nutrition, the National Home Infusion Association, the Intravenous Nursing Society, Oley Foundation and others should continue to lobby for significant changes and approval of alternative lock solutions and devices that would facilitate cost-effective therapy with appropriate reimbursement, enabling patients to receive alternative lock therapy when clinically indicated.

Lowering the cost of ethanol and gaining FDA approval for alternative lock products could create significant cost savings and would improve quality of life for children with intestinal failure.[13]

Learn more about home infusion therapy and Optum Infusion Pharmacy services by contacting your local Optum representative.

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