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Review Article

Intrasite vancomycin powder for the prevention of surgical site infection in spine surgery: a systematic literature review

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Abstract

BACKGROUND CONTEXT: Deep surgical site infections (SSIs) following spinal surgery are a significant burden to the patient, patient's family, and the health-care system. Because of increasing pressures to reduce SSIs and control costs, some spine surgeons have begun placing lyophilized vancomycin powder directly into the surgical wound at the conclusion of the procedure. However, the literature supporting this practice remains limited.

PURPOSE: To review the current literature examining the use of prophylactic intrasite vancomycin powder to control SSIs in spinal surgery and determine if any standard recommendations can be made.

STUDY DESIGN: A systematic review.

METHODS: Ovid Medline and PubMed were searched to identify English language articles.

RESULTS: No current guidelines are available for the use of intrasite vancomycin powder in preventing SSIs, and no standard dosage for the drug exists. Based on the limited literature and evidence currently available, there appears to be a protective effect of intrasite vancomycin powder on the incidence of SSI, without evidence of side effects. However, case reports do exist describing the systemic side effects after intrasite vancomycin powder during spine surgery.

CONCLUSIONS: The interpretation of the available evidence supporting the use of intrasite vancomycin powder in surgical wounds is limited, and its extrapolation should be performed with caution. Despite the lack of significant high-quality evidence available in the literature, many surgeons have adopted this practice; anecdotally, it continues to provide protection from infection without apparent significant risk of side effects. Published by Elsevier Inc.

Keywords: Vancomycin powder; Intrasite vancomcyin powder; Topical vancomycin powder; Spine surgery; Spinal deformity surgery; Surgical site infection; Antibiotic prophylaxis

FDA device/drug status: Not approved for this indication (Vancomycin powder).

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The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

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Introduction

Deep surgical site infections (SSIs) are a substantial burden to the patient and the health-care system. Despite the ubiquity of prophylactic antibiotics and aseptic technique, SSIs comprise 22% of all health care-related infections and are the second most common health care-associated infections in the United States [1]. The estimated cost to the United States' health-care system ranges from $1 billion to $10 billion annually [2], and the rates of SSIs vary by the type of surgical procedure being performed [3]. The literature has demonstrated significant morbidity with SSIs after spinal fusion procedures [4–8], as well as adult spinal trauma [9], and the short- and long-term effects of SSI can be devastating. Multiple reoperations, instrumentation removal, long-term antibiotic therapy, and prolonged hospital stays complicate the postoperative period, negatively impact patient reported outcomes and hospitalization costs increase significantly when these complications occur [2,10]. With increasing pressures to control resource utilization, and the curtailed reimbursement for the treatment of ''preventable'' complications, it is imperative that additional techniques to control SSIs and minimize these costs be discovered [10,11].

Traditionally, perioperative prophylaxis for SSIs during spine surgery has included intravenous antibiotic coverage of Gram-positive organisms, such as a 1st generation cephalosporin or clindamycin, given within 1 hour prior to surgical incision and discontinued within 24 hours following the end of surgery [12,13]. Cephalosporins have been preferentially used because of high activity against Gram-positive organisms, particularly *Staphylococcus aureus*, which is the most common cause of SSIs. *S. aureus* has been identified as the causative organism in 30% of all SSIs reported to the National Healthcare Safety Network between 2006 and 2008, including approximately 50% of all orthopedic and neurosurgical procedures [14]. However, rising resistance to common antibiotic medications has led to ineffective prophylaxis against more than half of all SSI-causing organisms; methicillin-resistant *S. aureus* SSIs have seen a significant increase in frequency and are notoriously difficult to treat [15–17]. Because of these concerns, various studies have reported placement of lyophilized vancomycin powder directly into the surgical wound during closure as a form of perioperative antibiotic prophyalxis [18–20]. In doing so, the direct inoculation of the site with high concentrations of the antibiotic will hypothetically overwhelm any residual bacterial load, even those with moderate resistance, and will ultimately decrease the rate of SSIs. Intrasite application of the drug should also theoretically minimize rapid absorption into the systemic circulation, thereby reducing vancomycin-associated side effects [19]. It is also hypothesized that the precipitous concentration gradient between the local wound and the supporting circulation should also curtail the generation of drug resistance [21]. Selection of resistant organisms is thus avoided, as bacteria in the wound are completely eradicated and any other organisms present elsewhere are only exposed to minimal concentrations of antibiotic. However, none of these hypotheses have, to date, been thoroughly evaluated in a clinical setting.

Background and indications for vancomycin

Vancomycin is a glycopeptide antibiotic (branched tricyclic glycosylated nonribosomal peptide, $C_{66}H_{75}C_{l2}N_9O_{24}$) produced by the Actinobacteria species *Amycolatopsis orientalis* and was first isolated in 1953 by Edmund Kornfeld from a soil sample collected in Borneo. Vancomycin was derived from the term ''vanquish,'' and the original indication was for the treatment of penicillin-resistant *S. aureus* [22,23]. The bactericidal mechanism of action of vancomycin is inhibition of cell wall biosynthesis in Gram-positive bacteria and occurs through various methods: inhibits RNA synthesis and formation of long polymers for the bacterial cell wall, for any long polymers that do form, prevents them from cross-linking with each other, and alters bacterial cell membrane permeability [22]. Vancomycin is not active against Gram-negative bacteria (except some non-gonococcal species of *Neisseria*) because they produce their outer membrane and cell walls by a different mechanism. The US Food and Drug Administration (FDA) in 1958 first approved the use of IV vancomycin (initial trade name Vancocin; Eli Lilly, Indianapolis, IN, USA) for the treatment of penicillin-resistant Staphylococci infections and is now widely available in generic versions [22]. Because of its poor oral availability (not absorbed from the gastrointestinal tract into the blood), vancomycin is administered intravenously and is indicated for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant Staphylococci and for penicillin allergic patients who cannot receive or have failed to respond to other drugs, including cephalosporins. The Center for Disease Control has also recommended the use of vancomycin for surgical prophylaxis for major procedures involving implantation of prostheses in institutions with a high rate of methicillin-resistant Staphylococci. A contraindication for use is a patient with known hypersensitivity to vancomycin. In 1986, the US FDA approved an oral form of vancomycin for the treatment of *Clostridium difficile*-induced pseudomembranous colitis, which takes advantage of the poor oral bioavailability by allowing the medication to remain in the gastrointestinal tract to eradicate *C. difficile* [23].

The current topic regarding the use of vancomycin as an intrasite adjunct within a surgical wound uses the IV preparation, which is produced as a white-to-tan lyophilized powder. The unreconstituted lyophilized powder is available in single-dose vials produced by various generic manufacturers and typically contains equivalents of 500 mg, 750 mg, or 1 g. Most importantly, the intrasite administration of vancomycin powder has not been approved by the

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