

Skin Antisepsis

Evidence supporting compatibility of chlorhexidine gluconate (CHG) and iodine-based antimicrobial agents when used in combination



Introduction

Many products containing antiseptics are used to reduce the microbial load on the patient's skin throughout the perioperative process. This includes surgical skin preparations with chlorhexidine gluconate (CHG), povidone-iodine (PVP-I) and alcohol. It also includes antimicrobial incise drapes, such as 3M™ Ioban™ 2 Antimicrobial Incise Drapes, which contain iodine in the adhesive layer.

What is the effect of combining these antiseptic agents in a single surgical procedure? For example, what if a patient's skin is prepped with a CHG-based solution and then an antimicrobial incise drape with iodine is applied over the prepped skin?

Chemical interaction between iodine and CHG

CHG, a molecule with two positive charges, is known for being an excellent antimicrobial molecule. The positively charged CHG molecule attacks the negatively charged cell wall of bacteria, disrupting its structure quite easily. Once the cell wall is damaged, the contents can leak out, causing cell death. In addition to its direct effect on microbes, CHG can also bind to human skin cells, helping provide a persistent antimicrobial effect.

The 3M™ Ioban™ 2 Antimicrobial Incise Drape is an iodine-impregnated incise drape made of a breathable plastic film coated with a clear, pressure-sensitive adhesive that contains iodine. The adhesive acts as a reservoir of molecular iodine, slowly releasing the active ingredient at the skin/adhesive interface. Iodine works by attacking the bacterial cell surface where it penetrates the cell membrane and inactivates key molecules like proteins and DNA that are needed to keep the cell alive and functioning.

Iodine and CHG are chemically dissimilar on several fronts. While molecular iodine is uncharged, CHG is a positively charged molecule. As a result, iodine does not have any charge interactions with CHG. Iodine is very poorly water soluble but is very soluble in most organic solvents. CHG is mainly soluble in water and insoluble in most organic solvents. Finally, while iodine is a moderate oxidizing agent, it is not strong enough to oxidize CHG. Consequently, the two active agents will not be chemically influenced by each other when used in combination.

CHG and iodine have different cellular targets and different mechanisms of action. These differences may prove beneficial when using the two antiseptics in combination. CHG damages the outer membrane, which, in turn, would enhance access to the intracellular targets necessary for the bactericidal action of iodine.

References

1. Anderson MJ, Horn ME, Lin YC, Parks PJ, Peterson ML. Efficacy of concurrent application of chlorhexidine gluconate and povidone iodine against six nosocomial pathogens. *Am J Infect Control*. 2010;38:826-831.
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1 Meta-analysis shows bacterial decontamination is more effective when CHG and PVP-I are combined

Davies BM, Patel HC. Systematic review and meta-analysis of preoperative antisepsis with combination chlorhexidine and povidone-iodine. *Surg J.* 2016;2:e70-e77.



Background

Effective preoperative antisepsis is recognized to prevent surgical site infection (SSI), although the definitive antiseptic agent is unclear. Many have compared chlorhexidine (CHG) with povidone-iodine (PVP-I). Emerging evidence indicates that a sequential application of these antiseptics may be advantageous. Following the logic of covering all bases, many surgeons use a sequential combination of CHG preparation and PVP-I preparation. This is a systematic review and meta-analysis evaluating the evidence for combination CHG and PVP-I antiseptics.



Key Findings

- The search strategy identified 18 publications where a combination of CHG and PVP-I had been studied. Four of these publications met the primary and secondary study outcomes (SSI and reduced colonization) for inclusion in the meta-analysis.
- Bacterial decontamination at the operative site is more effective when the combination (CHG and PVP-I) is used.



More effective
bacterial decontamination

2 Sequential application of chlorhexidine/alcohol and PVP-I was shown to be more effective than either alone

Langgartner J, Linde HJ, Lehn N, Reng M, Scholmerich J, Gluck T. Combined skin disinfection with chlorhexidine/ propanol and aqueous povidone-iodine reduces bacterial colonization of central venous catheters. *Intensive Care Med.* 2004;30:1081-1088.



Background

Evidence indicates bacterial colonization of the skin at the central venous catheter (CVC) insertion site is strongly associated with subsequent infection. The optimal skin disinfection regimen to reduce CVC-associated infections has not yet been defined. It is theorized more rigorous skin disinfection may be the key to reducing CVC-related infections. This study compares three skin disinfection regimens prior to the insertion of a CVC: (1) Chlorhexidine/alcohol followed by povidone-iodine (2) Povidone-iodine and (3) Chlorhexidine/alcohol, on bacterial skin colonization.



Key Findings

- Skin disinfection using sequential application of chlorhexidine/ alcohol and povidone-iodine was shown to be superior to either of the disinfectants alone in reducing the colonization rates of CVCs (P=.006).
- Skin disinfection with subsequent application of chlorhexidine/ alcohol and povidone-iodine was shown to be safe. No adverse events were observed with a 1-minute application of chlorhexidine/alcohol followed by a 1-minute application of povidone-iodine.
- The results do not indicate a loss of disinfecting activity when chlorhexidine and povidone-iodine are used sequentially.



1 minute application of
chlorhexidine/alcohol



1 minute application
of povidone-iodine



shown to be safe

3 Study indicates that combining CHG and PVP-I has no negative impact on antisepsis

Anderson MJ, Horn ME, Lin YC, Parks PJ, Peterson ML. Efficacy of concurrent application of chlorhexidine gluconate and povidone iodine against six nosocomial pathogens. *Am J Infect Control*. 2010;38:826-831.



Background

CHG and PVP-I are rarely used concurrently despite a lack of evidence regarding functional incompatibility of these agents. Many studies have compared the individual antiseptic activity of these two compounds, but few studies have evaluated the activity of the compounds in combination. This study examined the antimicrobial effects of an aqueous solution containing both CHG and PVP-I. CHG and PVP-I have different cellular targets and different mechanisms of action. These differences may prove beneficial when using these two antiseptics in combination.



Key Findings

- *In vitro* testing indicates that combining CHG and PVP-I has no negative impact on antisepsis. Moreover, data from an *ex vivo* porcine mucosal infection model suggests a potential benefit when combining both antiseptics.
- The study surmised that these two agents would complement one another by creating an initial and rapid kill of resident flora, followed by a sustained antibacterial effect, which could prove quite beneficial in the clinical setting.
- *In vitro* testing using six nosocomial organisms indicated that there is no functional incompatibility when combining CHG and PVP-I. In addition, an *ex vivo* full-thickness mucosal model of infection suggests that there may be a benefit against methicillin-sensitive *Staphylococcus aureus* (MSSA).

4 Using a combination of chlorhexidine with PVP-I is safe and effective

Guzel A, Ozekinci T, Ozkan U, Celik Y, Ceviz A, Belen D. Evaluation of the skin flora after chlorhexidine and povidone-iodine preparation in neurosurgical practice. *Surg Neurol*. 2009;71:207-210.



Background

There are various antiseptics used for disinfecting the skin before surgery, but there is no standard procedure in practice. Chlorhexidine and povidone-iodine are the most preferred compounds among antiseptics. Both have been proven to be safe and effective for skin disinfection. In this study, the aim was to investigate the combined effects of chlorhexidine and povidone-iodine, used consecutively, on the skin's flora before neurosurgical intervention.



Key Findings

- Using a combination of chlorhexidine with povidone-iodine is safe and effective for skin antisepsis. Preoperative scrubbing of the surgical skin area with chlorhexidine for three minutes, followed by cleaning once with povidone-iodine, could be sufficient to reduce skin bacterial flora before neurosurgical intervention. This practice may provide a standard disinfection method in neurosurgical procedures.
- Chlorhexidine and povidone-iodine are each useful agents for skin disinfection when used separately before surgery. Chlorhexidine is a safe and effective skin antiseptic that is more effective than povidone-iodine in diminishing skin colonization with Staphylococci.
- Povidone-iodine like chlorhexidine has bactericidal activity against a wide spectrum of pathogens, including methicillin-resistant *Staphylococcus aureus*. No adverse effects such as skin reaction, allergy or postoperative infection were observed in any patients in the presented study.



Preoperative scrubbing of the surgical skin area with CHG for 3 minutes



followed by cleaning once with povidone-iodine



may sufficiently reduce skin bacterial flora before neurosurgical intervention

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