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Antimicrobial Efficacy of Chlorhexidine Gluconate (CHG)-Alcohol Compared with Povidone-Iodine Solution for Patient Preoperative Skin Preparations

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ABSTRACT

BACKGROUND : Skin antisepsis reduces rates of post-surgical infections. In Japan, several types of alcohol-based preparations or Povidone-Iodine (10% PVP-I) solution are most commonly used for preoperative preparation, and Japanese pharmaceutical regulations limit Chlorhexidine Gluconate (CHG) content in antiseptics to a maximum of 1%. To our knowledge, there are no published studies comparing the antimicrobial efficacy of preoperative skin preparation using 1% CHG-ethanol with that of 10% PVP-I when tested according to a standard method, such as ASTM E1173-09.
OBJECTIVE : The study objective was to determine and compare the antimicrobial efficacies of a 79% (v/v) ethanol containing 1% (w/v) CHG (1% CHG-ethanol) and a marketed 10% PVP-I solution when used on healthy human subjects for preoperative preparation.
METHODS : 74 healthy adult subjects meeting criteria for minimum baseline bacterial counts on test sites (potentially multiple per subject) were enrolled to evaluate efficacy of the test products on skin of the antecubital fossa, the abdomen, and the inguina at post-treatment time points of 10 minutes for inguina and abdomen, and 30 seconds for antecubital fossae. In addition, persistent effects were evaluated at all sites 6 hours and 24 hours post-treatment. Testing procedures were performed according to ASTM Standard Method E1173-09.
RESULTS : Relative to baseline microbial populations, both products produced significant reductions in population at all sites (P<0.05), and a blocked, two-factor ANOVA showed the performance of the two products on the three sites to be not significantly different at any time point post-treatment (P>0.05). Subjects experienced no adverse effects over the course of study.
CONCLUSIONS : The 1% CHG-ethanol preparation and the 10% PVP-I solution demonstrated statistically equivalent antimicrobial efficacy at the inguinal, abdominal, and antecubital sites immediate, 6 hours, and 24 hours post-treatment. It is reasonable to expect that the 1% CHG-ethanol preparation will perform well in-use as a preoperative skin preparation and have promising potential as a catheter prep/maintenance preparation.

INTRODUCTION

- Skin antisepsis is the most fundamental and effective treatment for reducing the morbidity and mortality caused by healthcare-associated infections such as catheter-related bloodstream infections (CR-BSI) and post-surgical infections.[1,2]
- Historically, 10% PVP-I solution has most commonly been used for patient preoperative skin preparation or disinfection of catheter sites.
- However, aqueous CHG solutions or tinctures of CHG have become quite common for catheter site care supported by some study data demonstrating both superior immediate antimicrobial effect and a cumulative persistency for hours after product application as well as reducing CR-BSI in the hospitals.[3-12]
- The CDC had been advocated the use of CHG-based preparations in the guideline for the prevention of intravascular catheter-related infections and 2% CHG-alcohol products are widely used for pre-operative skin preparation currently.[5]
- More recently, the CDC`s Guideline for the Prevention of Intravascular Catheter-Related Infections 2011 (the CDC`s new guideline) was issued and it clearly recommended to apply the skin preparation with a >0.5% CHG combined with alcohol for preventing CR-BSI.[13] Herewith, a 1% CHG in alcohol could be used for a skin antiseptic alternatively.
- In Japan, various alcoholic preparations or 10% PVP-I solution are commonly used for skin antisepsis. On the contrary, Japanese pharmaceutical regulations limit CHG content in antiseptics (the leave-on formulation) to a maximum of 1% because of a lack of precedent despite pre-surgical hand scrubs containing 4% CHG are allowed.
- The main purpose of the clinical study reported here was to compare the efficacy of skin preparations between 1% CHG in alcohol and 10% PVP-I formulation according to a standard method, ASTM E1173-09.[14]
- We also aimed to identify an appropriate CHG-alcohol formulation for skin antisepsis that would be effective for pre-catheter insertion/injection or pre-operative use in the clinical settings of Japan as well as meeting with the recommendation of the CDC`s new guideline 2011.[13]

Classification of antiseptics categorized by FDA and each Evaluation Methodology *in vivo*[15,16]

- Healthcare Personnel Handwash
  - ASTM Standard E1174 : *Glove Juice Sampling*
- Surgical Scrub
  - ASTM Standard E1115 : *Glove Juice Sampling*
- Preoperative Skin Preparation
  - ASTM Standard E1173 : *Cylinder Sampling*
    - ① Catheter Preparation/Maintenance
    - ② Preinjection Preparation

METHOD

The Purpose of the Study

The comparative efficacy evaluation *in vivo* by focusing on the immediate antimicrobial activity and persistency within 24 hours post-product application.

■ Test Products
① 1% CHG-ethanol : A pre-operative skin preparation used in Japan and meets with the recommendation of the CDC`s guideline
② 10% PVP-I : A conventional product used in Japan

Patient Preoperative Skin Preparation ASTM Standard E1173

Study Design

- 74 healthy adult subjects at least 18 years of age meeting criteria for minimum baseline bacterial counts on test sites (Antecubital fossae : ≥ 2.0 log_{10} CFU/cm^2, Abdomen : ≥ 2.6 log_{10} CFU/cm^2, Inguina : ≥ 4.5 log_{10} CFU/cm^2) following a 14-day restriction period were enrolled.
- No bathing was allowed within 72 hours before the microbial testing day.
- Sampling sites were randomized using a computer-generated schedule.
- The immediate antimicrobial efficacies of the test products on the skin at post-treatment time points of 10 minutes for inguina and abdomen, and 30 seconds for antecubital fossae were measured.
- In addition, persistent effects were evaluated at all sites 6 hours and 24 hours post-treatment.
- Testing procedures were performed according to ASTM Standard Method E1173-09.
- The mean (± SD) log_{10} reduction in colony-forming units (CFU) produced after treatment was measured.

Microbiological Methods

- Samples were taken according to the standard Cylinder Sampling technique (Scrub-cup method), using neutralizers in the sampling fluid (3mL), which was tested and shown to effectively inactivate the antimicrobial activities of the test products (ASTM E1054-08).[17]
- Triplicate spread plates (1mL) were prepared from each of serial dilutions on trypticase soy agar (TSA) with neutralizer and incubated at 30 ˚C ± 2 ˚C for approximately 72 hours.
- The number of microorganisms in each sample was counted and the mean (± SD) log_{10} reduction in colony-forming units (CFU) produced after treatment was measured.

Pass criteria

PreCatheter/Maintenance Preparation

- 2 Log_{10} reduction on the dry site (abdomen) within 10 minutes
- 3 Log_{10} reduction on the moist site (inguina) within 10 minutes
- Maintenance of bacterial counts below baseline for at least 6 hours after product application

Preinjection Preparation

- 1 Log_{10} reduction in normal bacterial flora within 30 seconds

Description of the study

Preoperative Skin Preparation ①

Catheter Preparation/Maintenance

- Tests efficacy of a product versus normal skin bacteria on the body
- Two test sites: Moist (Inguinal site) and Dry (Abdomen)
  - Emphasis on residual efficacy
- Product application: one time
- Cylinder samples taken at each of 4 sites within the test area
  - Baseline
  - 10 minutes after product application
  - 6 hours after product application
  - Additional sample times (e.g., 30-second or 24-hour efficacy)

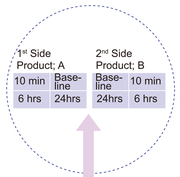
Preoperative Skin Preparation ②

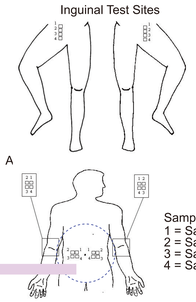
Preinjection Preparation

- Typically conducted in conjunction with Preoperative Skin Preparation testing
- Single Test Site: Antecubital fossa (Forearm)
- Cylinder Sampling 30 seconds after product application

A Diagram of Sampling Sites

e.g.) Abdomen samples
*Sampling sites were randomized using a computer-generated schedule.





Patient Preoperative Skin Preparation ASTM Standard E1173

Procedures of the test (Flowchart)

Abdomen Test Sites

1) Dispense 10 mL of product into a sterile Petri dish
2) Don sterile gloves
3) Dip a sterile gauze sponge (USP) into the product until fully absorbed
4) Apply the product to the test site using repeated back-and-forth strokes for 30 seconds; ensure the treatment area (4"×4") is thoroughly wetted
5) Allow the fully prepped area to air-dry for a minimum of 30 seconds
6) Sampling : Into a sterile cylinder (φ3.46 cm^2) , 3mL of sampling solution (+neutralizer) was added and massaged with a sterile rubber policeman (1 minute) ➡ TSA incubate 30℃、72hrs ➡ Colony count

1. Product application 2. Scrubbing 3. Sample taking

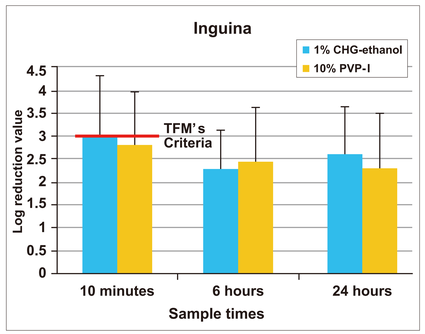
Inguinal Test Site

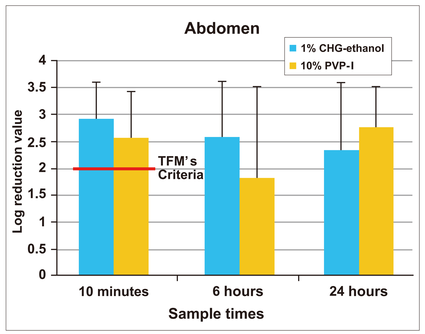
1) Dispense 10 mL of product into a sterile Petri dish
2) Don sterile gloves
3) Dip a sterile gauze sponge (USP) into the product until fully absorbed
4) Apply the product to the test site using repeated back-and-forth strokes for 2 minutes; ensure the treatment area (2"×5") is thoroughly wetted
5) Allow the fully prepped area to air-dry for a minimum of 1 minute
6) Sampling : Into a sterile cylinder (φ3.46 cm^2) ,3mL of sampling solution (+neutralizer) was added and massaged with a sterile rubber policeman (1 minute) ➡ TSA incubate 30℃、72hrs ➡ Colony count

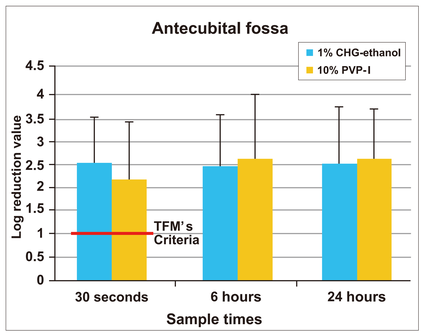
1. Product application 2. Scrubbing 3. Sample taking

RESULTS

- **Both 1% CHG-ethanol and 10% PVP-I products demonstrated significant reductions at all sites relative to baseline microbial populations (P<0.05).**
- **A blocked, two-factor ANOVA showed the performance of the two products on the three sites to be not significantly different at any sample times post-treatment (P>0.05).**







Summary Table of the Study
(Log reduction value)

Site	Sampes time	1% CHG-ethanol	10% PVP-I
Inguina		n=12	n=20
	10 minutes	2.93±1.41	2.81±1.15
	6 hours	2.24±0.92	2.46±1.20
	24 hours	2.63±1.04	2.29±1.23
Abdomen		n=12	n=11
	10 minutes	2.90±0.71	2.56±0.90
	6 hours	2.58±1.03	1.83±1.71
	24 hours	2.33±1.26	2.76±0.77
Antecubital fossa		n=14	n=18
	30 seconds	2.55±0.97	2.18±1.23
	6 hours	2.45±1.12	2.61±1.39
	24 hours	2.48±1.24	2.63±1.08

※Statistics: A blocked, two-factor ANOVA showed the performance of the two products on the three sites to be not significantly different at any time point post-treatment (P>0.05).

CONCLUSIONS

- The 1% CHG-ethanol preparation and the 10% PVP-I solution demonstrated statistically equivalent antimicrobial efficacy on the inguinal, abdominal, and antecubital sites at immediate, 6 hours, and 24 hours post-treatment.
- It is reasonable to expect that the 1% CHG-ethanol preparation will perform well in-use as a preoperative skin preparation and have promising potential as a catheter prep/maintenance preparation.
- It also could be an appropriate CHG-alcohol formulation for skin antisepsis that would be effective for pre-catheter insertion/injection or pre-operative use in the clinical settings of Japan as well as meeting with the recommendation of the CDC`s new guideline 2011.[15]
- In the next step, we are planning to conduct an additional comparative efficacy study among some skin preparations focusing on much longer sample times at 72 or 168 hours post-product application that representing the real world of catheter preparation/maintenance in clinical practice.

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