



## Level 1 Trauma Center Experience Utilizing Negative Pressure Wound Therapy with Instillation: Hypochlorous Acid versus Normal Saline Solution in Complex or Infected Wounds

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### Abstract

Negative pressure wound therapy with instillation and dwell time is widely accepted as adjunct treatment for complex infected wounds; however, results vary by irrigant. This study compared effects of hypochlorous acid versus 0.9% sodium chloride solution on clinical outcomes. We present a single-institution, comparative, observational, retrospective analysis of medically complicated patients with complex or grossly infected wounds. The primary endpoints were length of hospital stay, number of wound-related operating room procedures, and days to wound closure. The study included 24 patients with 27 wounds. Their diagnoses included: necrotizing soft tissue infections, necrotizing fasciitis, infected stage IV ulcers, and multidrug-resistant abscesses. Results indicated a trend towards fewer operating room trips, fewer days to closure, and shorter length of stay when patients were treated with hypochlorous acid compared to sodium chloride solution. (3.3 vs. 4.1,  $p=0.19$ ; 19.4 vs. 22.5,  $p=0.33$ ; and 24.3 vs. 37.9,  $p=0.27$  respectively). Our clinical experience utilizing negative pressure wound therapy with instillation and dwell time with hypochlorous acid has shown favorable outcomes suggesting hypochlorous acid as an effective irrigant in the management of grossly infected and complex wounds. As a result we have standardized our institutional protocol to incorporate hypochlorous acid for challenging or infected wounds.

**Keywords:** Hypochlorous Acids; Vacuum-Assisted Closure; Wound Infection; Wound Infection, Surgical; Wounds and Injury.

### Introduction

Negative pressure wound therapy (NPWT) revolutionized surgical and acute wound management since its inception in 1996 until the earliest attempts to integrate simultaneous instillation therapy in 1998.<sup>1,2</sup> These adjunct modalities have progressed to become part of the armamentarium of the Acute Surgical Wound

Service at [blinded institution], an American College of Surgeons Level 1 trauma center located in the [blinded location]. [Blinded institution] annually encounters nearly 3,000 patients affected by acute complex wounds of various etiologies. These multifaceted wounds are resource-, time-, and labor-intensive; however, NPWT allows efficacious management and closure of these

challenging wounds by stimulating healing through secondary intention or allowing for delayed primary closure. Multiple studies have shown the benefits of augmenting NPWT with instillation liquid and dwell time (NPWTi-d) to accelerate wound healing, decrease wound bio burden, reduce trips to the operating room (OR) and shorten length of stay (LOS).<sup>3-5</sup> Studies have considered different instillation therapies including normal saline solution (0.9%), and commercial products such as polyhexanide + betaine (Prontosan<sup>®</sup>) and hypochlorite solution quarter strength (Dakin's, NaOCl).<sup>3,4,6</sup> At our institution we initially demonstrated the success of NPWTi-d with normal saline and NaOCl as instillation therapies with an increased rate of formation of granulation tissue resulting in reduced wound volumes.<sup>7</sup>

Another commercially available instillation solution is 33% hypochlorous acid (Vashe<sup>®</sup>, HOCl), a non-cytotoxic, non-irritating, wound care product with antimicrobial properties that is a more stable irrigant than other products such as NaOCl. The more neutral pH of the hypochlorous acid solution (5.1-5.5) enables its use on sensitive areas of the body as well as in the pediatric population, making HOCl a universally useful wound cleansing agent.<sup>8</sup> Provider preference influences the choice of NPWTi-d, but the potential benefits have supported the adoption of HOCl NPWTi-d as the standard at our institution. The purpose of this study is to demonstrate the non-inferiority in addition to the clinical advantages of HOCl NPWTi-d therapy compared to normal saline NPWTi-d therapy for large, complex, or infected wounds of a variety of etiologies.

## Materials and Methods

### Study Design

The [blinded institution] Institutional Review Board approved this study. We performed a retrospective chart review and observational study of patients who were treated at our institution between December 2015 and December 2017 for

complex infected wounds. The etiology of the wound did not limit inclusion in the study and patients were treated with NPWTi-d for the following wound types: necrotizing, infected surgical, traumatic, compartment syndrome, pressure injury, and vascular insufficiency. Any patient with a necrotic or grossly infected wound underwent aggressive operative debridement of devitalized tissue prior to beginning NPWTi-d. Systemic antimicrobials were implemented according to cultures or hospital-accepted recommendations. Nutritional optimization was also sought to maximize healing potential. Medical records were examined for patient demographics including age, gender, comorbid conditions, hospital LOS, wound etiology, wound location, wound size, and bacterial colonization of the wound. Operative notes and wound care reports were reviewed to determine the number of OR interventions each patient required, and the therapies implemented. Outpatient records were used to evaluate overall wound healing either by secondary intention or delayed primary closure. Patients with incomplete charts or those who were lost to follow-up were excluded from analysis.

### Materials

The solutions used for instillation included hypochlorous acid (Vashe<sup>®</sup>, HOCl) and 0.9% sodium chloride solution (NSS). The amount of solution used for each treatment was dependent on wound size with the volume in milliliters used equating to approximately 20% of the wound area in square centimeters (not accounting for wound depth). The cyclic timing of NPWTi-d therapy was determined by our institutional protocol; 10 minutes of dwell time every four hours. Dressing changes were performed every two-three days to allow close surveillance while utilizing the default setting of -125mmHg. The patients who underwent HOCl NPWTi-d were compared to patients who underwent NSS NPWTi-d.

### Data Analysis

The primary endpoints of the study; LOS, number of procedures requiring the OR, and days to wound closure were evaluated using the Student's

t-test. The significance threshold of the one-tailed test was set at  $p < 0.05$ . Patients with more than one wound were included once when determining length of hospital stay but the number of trips to the OR and time to wound closure was calculated independently for each wound in patients with multiple wounds.

## Results

Between December 2015 and December 2017 thirty-six patients meeting inclusion criteria were treated at our institution. Of these patients, 11 were excluded from the study for incomplete charting data, incomplete wound care records, or loss to follow up. One additional patient was eliminated from the study due to death prior to closure of their wound. Included in the study are 24 patients with 27 wounds. Seventeen patients with 19 wounds were treated with HOCl NPWTi-d and seven patients with eight wounds were treated with NSS NPWTi-d. Three patients, two in the HOCl group and one in the NSS group, had two wounds each, all secondary to fasciotomies for compartment syndrome (Figure 1). The average age of patients in the HOCl group was 49.7 years (standard deviation [SD] 15.1 years) average age of patients treated with NSS NPWTi-d was 36.1 years (SD 19.33 years, Table 1). Male patients were the majority in both groups. The average number of medical comorbidities in the HOCl group was 3.3 (SD 1.9) versus 1.7 (SD 2.6) conditions in the NSS group. Hypertension was the most common medical comorbidity in the HOCl group ( $n=8$ , 47.1%) and tobacco abuse was most common in the NSS group ( $n=3$ , 42.9%). Four patients (23.5%) in the HOCl group had diabetes while only one (14.3%) in the NSS group had diabetes.

The 27 wounds that were treated with NPWTi-d during the study were of a variety of etiologies (Table 2). In the HOCl group, 42.1% ( $n=8$ ) of wounds were related to trauma and in the NSS group 75% ( $n=6$ ) were traumatic. The common causes of wounds treated with HOCl were more

evenly distributed with surgical wound infections ( $n=5$ , 26.3%, Figure 2) and compartment syndrome ( $n=5$ , 26.3%) being most frequent while compartment syndrome was more common in the NSS NPWTi-d group ( $n=4$ , 50%).

The wounds treated with HOCl NPWTi-d were larger with an average wound size of 304.6 cm<sup>3</sup> (SD 292.9 cm<sup>3</sup>) while the average NSS wound was 174.9 cm<sup>3</sup> (SD 174.1 cm<sup>3</sup>), however the size difference was not statistically significant ( $p=0.08$ ). Wound location was most frequently the lower extremity in both groups (HOCl  $n=8$ , 42.1%, NSS  $n=5$ , 62.5%) and most wounds were colonized with bacteria (HOCl  $n=15$ , 78.9%, NSS  $n=5$ , 62.5%). Among the colonized wounds (HOCl  $n=15$ , NSS  $n=5$ ) most had polymicrobial colonization (HOCl  $n=12$ , 80%, NSS  $n=3$ , 60%). The duration of instill days was similar for HOCl and NSS NPWTi-d, with patients undergoing 7.2 days (SD 5.16 days) and 8.6 days (SD 3.93 days) of therapy respectively ( $p=0.22$ ).

The primary end points of the study; LOS, OR trips, and days to wound closure were decreased in patients treated with HOCl compared to patients treated with NSS NPWTi-d, though none of the differences were statistically significant. LOS for the 17 patients in the HOCl group was 24.3 days (SD 16.6) compared to the seven patients treated with NSS at 37.9 days (SD 53.74,  $p=0.27$ ). Time to final wound closure by either secondary intent or delayed primary closure occurred at 19.4 days (SD 9.0) for the patients treated with HOCl and at 22.5 days (SD 18.0,  $p=0.33$ ) for the patients treated with NSS. Lastly, patients with HOCl NPWTi-d required an average of 3.3 trips to the OR (SD 2.3) while those who underwent NSS therapy required an average of 4.1 trips (SD 2.0,  $p=0.19$ ). Despite the lack of statistical significance at these primary endpoints, the clinical significance of the decreased LOS, trips to the OR, and time to wound closure in more medically complex patients is encouraging and prompts further study with larger and more homogenous groups of patients.

**Table 1.** Patient Summary Statistics

Variable	HOCl NPWTi-d <sup>a</sup> (n=17)	NSS NPWTi-d <sup>b</sup> (n=7)
Age (yrs.), avg. (SD <sup>c</sup> )	49.7 (15.1)	36.1 (19.3)
Male, no. (%)	13 (76.5)	6 (33.3)
Medical history		
<i>Smoking, no. (%)</i>	1 (5.9)	4 (42.9)
<i>Intravenous drug abuse, no (%)</i>	2 (11.8)	1 (14.3)
<i>Diabetes, no (%)</i>	4 (23.5)	1 (14.3)
<i>Comorbid conditions med. (IQR<sup>d</sup>)</i>	4 (2-5)	0 (0-3)
Length of stay (days), avg. (SD)	24.3 (16.6)	37.9(53.7)

<sup>a</sup>HOCl NPWTi-d – Hypochlorous acid (Vashe®) negative pressure wound therapy with instillation and dwell time;

<sup>b</sup>NSS NPWTi-d – normal saline solution negative pressure wound therapy with instillation and dwell time;

<sup>c</sup>SD – standard deviation; <sup>d</sup>IQR – interquartile range.

**Table 2.** Wound Summary Statistics

Variable	HOCl NPWTi-d <sup>a</sup> (n=19)	NSS NPWTi-d <sup>b</sup> (n=8)
Traumatic wound, no. (%)	8 (42.1)	6 (75)
Underlying wound cause, no (%)		
<i>Compartment syndrome</i>	5 (26.3)	4 (50)
<i>Open traumatic wound</i>	4 (21.1)	2 (22.2)
<i>Infected surgical wound</i>	5 (26.3)	1 (11.1)
<i>Necrotizing wound</i>	3 (15.8)	0 (0)
<i>Pressure ulcer</i>	1 (5.3)	1 (11.1)
<i>Vascular insufficiency</i>	1 (5.3)	0 (0)
Wound location, no. (%)		
<i>Lower extremity</i>	8 (42.1)	5 (62.5)
<i>Upper extremity</i>	2 (10.5)	1 (0.13)
<i>Abdomen</i>	5 (26.3)	1 (0.13)
<i>Perineum/Sacrum</i>	4 (21.1)	1 (0.13)
Wound size (cm <sup>3</sup> ), avg. (SD <sup>c</sup> )	304.6 (292.9)	174.9 (174.1)
Bacterial colonization, no (%)	15 (78.9)	5 (62.5)
Trips to operating room, avg. (SD)	2.2 (2.3)	4.1 (2.0)
NPWTi-d duration (days), avg. (SD)	7.2 (5.2)	8.6 (2.9)
Time to wound closure (days), avg. (SD)	19.4 (9)	22.5 (18)

<sup>a</sup>HOCl NPWTi-d – Hypochlorous acid (Vashe®) negative pressure wound therapy with instillation and dwell time;

<sup>b</sup>NSS NPWTi-d – normal saline solution negative pressure wound therapy with instillation and dwell time;

<sup>c</sup>SD – standard deviation

FIGURES

Figure 1. 58 year old male treated with HOCl NPWTi-d after compartment syndrome



A. Post-operative day 8

B. Post-operative day 22

58 year old male presented with a self-inflicted stab wound to the left upper extremity that was sustained in a dirty body of water. The patient subsequently developed compartment syndrome following revascularization. Wound cultures were positive for *Acinetobacter baumannii* complex, *Pseudomonas putida*, *Enterococcus faecium*, and *Bacillus cereus* group. Hypochlorous acid NPWTi-d was applied until grafting on post-operative day 15.

Figure 2. 54 year old male treated with HOCl NPWTi-d for an infected surgical wound



A. Day of wound care consult

B. 2 weeks later

C. 4 months later

54 year old male undergoing chemotherapy for multiple myeloma presented with a recurrent right medial thigh abscess status postsurgical debridement. On the day of the wound care consult, the initial measurement was 5 x 3.2 x 1.8 cm (28.8 cm<sup>3</sup>). After two weeks of hypochlorous acid NPWTi-d wound measurements were reduced to 3 x 1 x 0.8 cm (2.4 cm<sup>3</sup>), accounting for a 91.7% decrease in size. By four months, the patient's wound was completely healed and has not recurred for greater than one year at the time of this report.

**Discussion**

In this retrospective chart review and comparative observational study we found that medically complicated patients with large, complex, often infected wounds of a variety of etiologies

clinically required shorter hospital LOS, fewer wound-related trips to the OR, and shorter times to wound closure when treated with HOCl compared to NSS NPWTi-d. As a trauma-affiliated acute care wound service, our patients

have vast dissimilarities in their baseline health status and presentations. This multifaceted patient population was well-represented in our study where the patients comprising the two cohorts were heterogeneous. Patients in the HOCl cohort were on average older, with more medical comorbidities and a higher rate of diabetes which is one of the most studied detriments to wound healing. For diabetic patients, in particular, NPWT serves to increase granulation tissue and wound vessel density thus promoting wound healing and should be a commonly used tool in the management of diabetic wounds.<sup>9</sup>

Standardized between the HOCl and NSS cohorts is our institutional protocol for instillation and dwell time. The addition of instillation and dwell time has been monumental in facilitating wound healing with Gabriel et al. demonstrating that the use of saline or commercial wound cleanser products decreases LOS, time to healing, and trips to the OR.<sup>5</sup> These findings were previously demonstrated in our earlier comparative studies of different irrigation solutions: HOCl, NSS, NaOCl, but can be further evaluated as a cost-saving strategy as patients with fewer OR trips and shorter lengths of stay have decreased medical bills.<sup>5,7,10</sup>

Our study has several limitations. First, this study was conducted at a single institution with standard wound care protocols and therefore may not be applicable to other institutions that follow different wound care protocols. Second, our small sample size limits the statistical power of the study, however due to the time-intensive care required for these wounds it is challenging to quickly increase our sample size. Since our original research on irrigants, we have nearly eliminated our use of sodium hypochlorite 0.125% (Dakin's, NaOCl) due to its cytotoxic properties. We also increased our reliance on HOCl due to the propensity of our trauma patients' injuries toward infection. These measures were based on our clinical observations. However, this ultimately reduced our sample size for comparison. Finally, heterogeneity of the patient population also served

to complicate the analysis as medical comorbidities and wound etiology factor into wound healing time regardless of the wound care method used.

In summary, HOCl NPWTi-d was successful in treating the large complex wounds of medically challenging patients. The treatment led to shorter hospital stays, fewer trips to the OR, and decreased time to definitive wound closure. Normal saline NPWTi-d also showed success in the management of these wounds; however, the patients were in general less comorbid and with smaller wounds. The success of HOCl NPWTi-d in enabling the closure of large complex wounds has resulted in a standardization of protocol at our institution, making HOCl our wound irrigant of choice for challenging or infected wounds. In the future, a randomized control trial with a homogenous patient population will serve to show the success of HOCl NPWTi-d that we demonstrated in our small single institution study and validate cost savings to the patient, improved outcomes, and patient satisfaction.

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