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Comparison of the effect of negative pressure wound therapy with and without installation of polyhexanide on the bacterial kinetic in chronic wounds

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ABSTRACT

Background: Negative pressure wound therapy (NPWT) has established successfully as a treatment option for acceleration of wound healing in a broad range of clinical indications. Systematic research investigating the bacterial kinetics on wounds is lacking and no studies are available comparing the microbiological difference of repeated instillation of polyhexanide (PHMB) against continuous NPWT without instillation of an antiseptic. The aim of this study was to investigate the bacterial bio-burden on wounds and to measure the bacterial kinetic during application of NPWT with and without intermitted instillation of 0.02% PHMB.

Methods: A cohort of 18 patients with chronic ($n = 16$) and acute ($n = 2$) wounds was treated either with NPWT alone or with additional intermitted instillation of 0.02% PHMB. Wound healing and bacterial load were assessed at every dressing change. All wounds were closed by split-thickness skin grafts or local Reverdin flaps. According to the manufacturer of the investigated NPWT system (V.A.C. therapy unit, Kinetic Concepts Inc. KCI) wounds were filled with a polyurethane sponge (pore size 0.4–0.6 mm) and occluded with a polyurethane foil (KCI Inc., USA). The NPWT-device was connected to the wound and operated at 100 mm Hg sub-atmospheric pressure utilizing an alternating pressure cycle of 5 min of suction followed by 2 min pause. The automated intermittent instillation lasted for 4–20 s, the exposure time was 20 min. After 60 min of NPWT, the instillation was started again.

Results: Seven split-thickness skin grafts, 3 Reverdin-flaps and one combined closure (Reverdin + split-thickness skin grafts) exhibited excellent wound healing after successful transplantation 4 weeks after intervention. The quality of wound granulation was excellent in all wounds, regardless of NPWT application with or without instillation of 0.02% PHMB. The bacterial spectrum remained mostly unchanged after treatment and had no influence on the outcome.

Conclusion: It was demonstrated that management of infected wounds with NPWT, with or without instillation of 0.02% PHMB, did not reduce the number of bacteria on wounds. Bacteria proliferate below a NPWT dressing and increase in numbers. Independently of bacterial kinetics, all wounds showed excellent granulation and healed with no complications. This observation challenges the concept that bacterial bioburden correlates with impaired wound healing.

1. Introduction

One decade after Chariker et al. [1] described topical negative pressure wound therapy (NPWT) using moist gauze over the wound surface with continuous suction ranging from 60 to 80 mm Hg pressure, Fleischman et al. [2,3] introduced a suction drainage system using Redon drainage tubes and a foam dressing instead of

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gauze. Finally, Argenta and Morykwas [4,5] introduced a commercially available vacuum-assisted closure device (VAC) in 1993, set at 20,125 mm Hg pressure using polyvinyl-alcohol (PVA)/and polyurethane (PU) ethylene foam dressings (PVA/PU) together with an integrated tubing system. In the following decades NPWT has established successfully as a treatment option for acceleration of wound healing in a broad range of clinical indications [6].

However, the NPWT systems may not only be used to close a wound and to wick gas and wound fluid out of the wound, but it may also be used in the reverse direction for a controlled instillation of topical drugs into the wound, as proposed by Fleischmann et al. previously [7]. Indeed, some authors [8,9] have investigated the topical application of antibiotics on colonized or infected wounds and have reported significant reduction of microorganisms on wounds [8–10]. There are two aspects making it difficult to set these early reports into today's perspective. First, because of the global increase of bacterial resistance against antibiotics, the topical application of this class of antimicrobial drugs is not recommended today and difficult to predict in presence of resistant pathogens. Second, these experiments have been conducted with in-house developed modified NPWT devices making it difficult to draw any conclusion for the effect of differently constructed devices. Meanwhile two developments have made it possible to reconnect to the earlier described concept of using the NPWT technology as carrier system for controlled local drug administration in wounds for controlling wound colonization and for treatment of wound infection. The instillation of antimicrobial compounds into wounds was made possible by development of a commercially available system, the "VAC instil®" device. This device allows programming of alternating suction and instillation phases in a standardized and reproducible way. Additionally, in parallel to the rapid increase of antibiotic resistance, research on wound antiseptics has made substantial progress during the past decade [11,12]. Particularly, the antiseptic polyhexanide (PHMB) has demonstrated both, a high antimicrobial efficacy on wounds together with excellent tissue tolerability because of its low cytotoxicity [13,14]. The repeated instillation of PHMB during intermitted phases of NPWT may seem to be a promising concept for successful eradication of wounds colonized with pathogenic microorganisms, and was demonstrated to be clinically successful in treatment of wound infection [15]. Yet, up to day systematic research investigating the bacterial kinetics on wounds is lacking and no studies are available comparing the microbiological difference of repeated instillation of PHMB against continuous NPWT without instillation of an antiseptic compound.

To close this gap, the aim of this study was to investigate the bacterial bio-burden on wounds and to measure the bacterial kinetic during application of NPWT with and without intermitted instillation of 0.02% PHMB.

Table 1
Distribution of patients (sex, age, number) and treatment episodes of 18 patients undergoing NPWT with and without instillation of 0.02% PHMB.

	Total	NPWT	V.A.C. instill®
n patients	18	9	9
Mean age patients	70 ± 12	65 ± 13	74 ± 10
n episodes	33	17	16
n sex/patients	10w/8m	4w/5m	6w/3m
n sex/episodes	15w/18m	4w/13m	11w/5m

2. Methods

A cohort of 18 patients, 10 female and 8 male, with a mean age of 70 years were treated either with NPWT alone or with additional intermitted instillation of 0.02% PHMB (Table 1).

Sixteen patients had chronic wounds and 2 patients had acute wounds. Six patients (8 episodes) presented with chronic ulcer wounds on basis of chronic venous insufficiency (CVI, class 6 according to CEAP classification). Three wounds were caused by peripheral arterial occlusive disease (PAOD, 1 episode, 1 patient), diabetes mellitus (3 episodes, 2 patient), or PTS (8 episodes, 3 patients). Two patients (7 episodes) exhibited acute and infected wounds (surgical site infections SSI). Patients' demographic is summarized in Table 2.

One NPWT treatment was defied as one episode. In total, 33 NPWT treatments were performed on 18 patients. Every patient underwent a mean of 2 ± 1 NPWT episodes (Table 3). NPWT was applied as conditioning therapy (30 episodes in 14 patients, wound conditioning) or directly postoperatively on a transplant (6 episodes in 6 patients). One patient underwent one episode with wound conditioning and a second episode with NPWT application directly on the transplant.

2.1. Underlying risk factors for disturbed wound healing

Patients treated with NPWT and PHMB instillation were in average 9 years older compared to patients treated with NPWT alone (Table 1). However, the patients' group treated with NPWT alone included more than 50% diabetics (insulin dependent) and more patients with adipositas (16 vs. 11), yet less patients with arterial hypertension as compared to the patients' group treated with NPWT and PHMB instillation (9 vs. 12). The mean wound surfaces size in patients treated with NPWT alone was 73.5 ± 46.7 cm^2, and in patients treated with NPWT and 0.02% 98 PHMB 95.4 ± 84.4 cm^2 (Table 2).

Table 2
Individual treatment cases by sex (m/f), number of treatment episodes, risk factors, body mass index (BMI), wound surface (cm^2) and localization, after NPWT without 0.02% PHMB instillation.

Nr ID	m/f	nE	[Co-morbidity] (BMI)	Surface [cm^2]/wound localization	Surgical intervention
1 CB	f	1	CVI; [DM, RR, FI] (34)	93.5/Left lower leg	STSG (from left upper leg)
4 FHJ	m	4	SSI; [DM] (34)	12.0/Right lower leg	SD before RFT
6 LI	f	1	CVI; [RR] (19)	36.0/Right lower leg	SD prior STSG (left upper leg)
7 RKP	m	3	SSI; [DM, RR] (51)	72.0/Left upper leg	SD before RFT (left upper leg)
8 RM li	m	1	D; [DM, RR, FI] (73)	90.0/Right lower leg	STSG (left upper leg) of both lower legs
9 RM re	m	1	D; [DM, RR, FI] (73)	104.0/Left lower leg	STSG (left upper leg) of both lower legs
13 SKD li	m	4	PTS; [FI] (34)	39.0/Left lower leg	SD prior to STSG+RFT from left upper leg and S (last intervention)
16 SchB	f	1	CVI; [RR, FI] (46)	133.0/Right lower leg	SD
18 ZR	f	1	DM; [DM, RR, FI] (28)	3.0/Left lower leg	SD
Total		Mean: 17	Mean BMI: 43.6	Mean A: 73.5 (±46.7)	

IDDM, insulin dependent diabetes; FI, increased fibrinogen; RR, hypertension; SM, smoking; D, decubitus; SD, sharp debridement; STSG, split thickness skin graft; RFT, Reverdin flap transplantation; and GD, surgical wound closure scheduled.