Journal of Tissue Viability 28 (2019) 223–226

Contents lists available at ScienceDirect

Journal of Tissue Viability

journal homepage: www.elsevier.com/locate/jtv

Oxygen levels during negative pressure wound therapy

Niklas Biermann[a], Edward K. Geissler[b], Eva Brix[a], Daniel Schiltz[a], Lukas Prantl[a], Andreas Kehrer[a], Christian D. Taeger[a,*]

[a] Department of Plastic, Hand- and Reconstructive Surgery, University Hospital Regensburg, Germany
[b] Department of Surgery, University Hospital Regensburg, Germany

ARTICLE INFO

Keywords:
Aerobic
Anaerobic
Negative pressure wound therapy
Oxygen

ABSTRACT

Aim of the study: Negative pressure wound therapy (NPWT) has become an established treatment modality when dealing with chronic and infected wounds. The underlying mechanism of action is still under discussion and remains controversial. Evidence exists showing rather hypoxic conditions as the main reason for the positive results and bacterial clearance. In an attempt to further explain the mechanism of action, we investigated oxygen levels within the foam interface of a NPWT device.

Materials and methods: We used an optical sensor based on the principle of dynamic fluorescence quenching and tested five different commonly available NPWT systems used during our daily clinical routine. All measurements were done in an in vitro experimental design for at least 24 h and multiple vacuum intensities were investigated.

Results: Oxygen levels decreased as much as 22.8% and the amount of vacuum applied inversely correlated with the oxygen reduction. A stepwise increase in vacuum of 25 mmHg showed a linear mean drop of 2.75% per setting. All devices were able to maintain a constant level of negative pressure, and no significant difference between the various dressings was found ($p > 0.05$).

Conclusion: Therefore, oxygen levels are decreased within the foam of NPWT dressings, likely leading to oxygen deprivation effects in the underlying wound tissue.

1. Introduction

Despite general progress in surgical sciences, the treatment of chronic and infected wounds remains quite challenging [1–5]. Although wound-healing complications can sometimes be handled by non-surgical treatments, proper healing of such wounds often requires surgery intervention.

Healing can be promoted by the application of transient negative pressure wound therapy, often in combination with tissue debridement [6–11]. Since its introduction by Argenta et al. NPWT has been used for many medical applications [12,13]. Various NPWT dressings are available with different degrees of semipermeability for wound fluid. Despite undisputed improvements provided by NPWT, the exact mechanism of action remains unclear and controversial. Some speculate that a reduction in interstitial fluid decreases tissue edema and increases oxygenation, thus leading to better healing conditions [12].

Another mechanism could be from a positive influence on the bacterial clearance that has also been described [12,14].

An important component of these effects seems to relate to a reduction in local oxygen availability [12,15,16]. Regarding wound bacteria, a species-dependent suppression of obligate aerobic bacteria is thought to occur as a result of hypoxic wound conditions created by vacuum sealing the surgical entry site. Although changes in the local oxygen content are likely explained by physical application of sub-atmospheric pressure, little is known about the extent of oxygen deprivation within the dressing at the different vacuum intensities. Therefore, we investigated the oxygen content in the foam interface during NPWT, and compared different dressing foils.

2. Methods

The oxygen measurement within the foam interface was performed using an optical sensor (PreSens, Precision Sensing GmbH, Regensburg, Germany). In contrast to previous types of microsensors, using the reductive potential of oxygen at the cathode (Clark-type electrodes), the sensor contains an oxygen sensitive dye and relies on the principle of dynamic fluorescence quenching. This allows oxygen detection through a luminophore light signal with increased spatial resolution. We investigated commonly available vacuum systems used during our daily clinical routine including V.A.C. Ulta™, V.A.C. Prevena™ and V.A.C.

* Corresponding author. University Hospital Regensburg (UKR), Franz-Josef-Strauß-Allee 11, 93053, Regensburg, Germany.
E-mail address: christian.taeger@ukr.de (C.D. Taeger).

https://doi.org/10.1016/j.jtv.2019.09.001
Received 13 July 2019; Received in revised form 29 August 2019; Accepted 2 September 2019

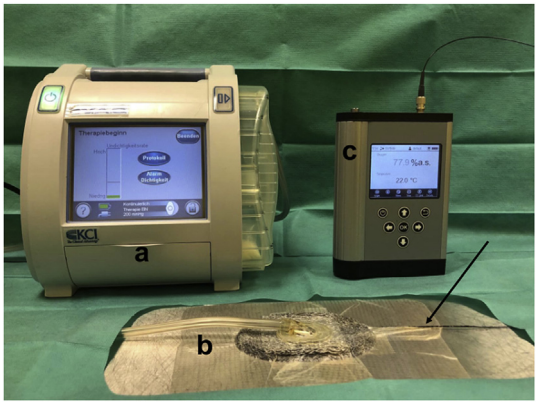

Fig. 1. Test setup using the standardized vacuum application system(KCI Medizinprodukte GmbH, Wiesbaden) **(a)** in combination with the dressing (IV3000^{Tm} Smith and Nephew, London, UK) **(b)** and the measurement device (PreSens, Precision Sensing GmbH, Regensburg, Germany) **(c)** beneath the foam **(arrow)**. All devices were tested in vitro and measurements were performed on a metal laboratory table under constant thermal conditions (22°C).

SNaP™ all purchased from KCI Medizinprodukte GmbH, Wiesbaden, Germany. (Fig. 1).

Furthermore, two different vacuum coating foils were tested including 3M^{TM}Ioban^{TM} (3 M. St. Paul, MN, USA) and IV3000™ (Smith and Nephew, London, UK). The same microsensor was used to test all units and all were gauged at 22°. Values given by the sensor were in "% a. s." meaning "area saturation". This is in relation to the baseline oxygen (100% a. s. is gauged to 21% true oxygen). The measurements were performed on a metal laboratory table under constant thermal conditions. Systems were tested for at least 24 h at 125 mmHg and, if possible, at 200 mmHg. All data are presented as arithmetic means. The Kolmogorov-Smirnov test was used to test for probability distribution of the variables. Parametric data of linear variables were compared using Student's t-test or the analysis of variance (ANOVA). A p-value < 0.05 was set to indicate significance for all tests. The software used to perform the statistical analysis was the "Statistical Package for the Social Sciences" (SPSS Inc., Chicago, IL, USA) Version 25.0 and Graph Pad PRISM, Version 5.0.

3. Results

A total of five different dressing foils were tested using a standardized vacuum application system (Fig. 1). After applying 125 mmHg of vacuum for 24 h, oxygen levels dropped by a mean of 14.5% ± 0.14 considering data from all devices. There was no statistical difference in the oxygen levels at 125 mmHg in any of the devices tested. The range of oxygen level decrease was between 14.2% and 14.6% ($p < 0.05$). Except for the V.A.C. SNaP™, which has a separate portable vacuum pump with a maximum capacity of 125 mmHg, all other devices were also tested at 200mmHG. After 24 h of NPWT at 200 mmHg, a mean drop in oxygen of 22.8% ± 0.19 was observed. There was no statistical difference in the oxygen levels at 200 mmHg in any of the devices tested. The range of oxygen level decrease was between 22.5% and 23.1% ($p < 0.05$). To test for the correlation of vacuum intensity and decrease in oxygen, a stepwise increase in vacuum of 25 mmHg every 2 min showed a linear mean drop of 2.75% per setting (Fig. 2).

4. Discussion

Recent explanations for the underlying mechanism of action regarding NPWT have evolved from those initially described by Argenta et al. [12,17]. It remains particularly controversial as to the role oxygen content plays in adjacent wound tissue [15,16]. In an attempt to further contribute to the understanding of NPWT, we measured the oxygen levels within the dressing interface.

Oxygen levels show decreases by nearly 25% at the interface of the dressing and wound, and this decrease is the same in the different NPWT dressings we tested. Also, we could show that the initial vacuum level and resulting loss of oxygen was constant over at least the first 24 h, indicating establishment of a good seal with these dressings. Furthermore, measurements at different vacuum pressures show that the level of vacuum applied inversely correlates to the oxygen level. We can therefore confirm that NPWT devices set up an environment in the wound that deprives potentially infective bacteria of oxygen.

Moues et al. compared NPWT to conventional moist gauze therapy in acute and chronic wounds in a prospective, randomized clinical trial, but no significant change in the overall bacterial bioburden was found. However, they did find a significant reduction in gram-negative and aerobic rods with NPWT. A possible explanation for the decrease in these aerobic species was the hypoxic wound environment. Interestingly, the author found an increase in *S. aureus* that they suggested could have been a nosocomial colonization without infective potential [18].

As might be expected from our data, Glass et al. described another five studies suggesting a species-dependent suppression of obligate aerobic bacteria and an increase in obligate anaerobic bacteria [19–28]. However, the author also describes eight studies, including another two randomized clinical trials, suggesting no change in the bacterial bioburden and four studies showing even an increased overall number of bacterial colonies during NPWT.

We attempted to further explain the working mechanisms of NPWT, and found a decrease in the oxygen partial pressure as high as 22.8% for several commonly available NPWT systems. As known from the hyperbaric oxygenation therapy of clostridium species, obligate anaerobe or aerobe bacteria sensitively react to changes in the oxygen partial pressure, and thus bacterial growth selection seems possible [29]. In vitro measurements by Van Unnik et al. showed a rapid halt in spore and alpha-toxin production of *C. perfringens* under hyperbaric oxygenation [30]. This emphasizes, that changes in the oxygen content around the skin may contribute to the bacterial bioburden.

Although our measurements were performed outside the tissue, we support the findings of Kairinos et al. [15,16] who described that decreased capillary perfusion and partial hypoxia result in the formation of proliferation hormones, which provides an essential explanation for the working mechanism of NPWT. Other hypothesis about the mechanism of action involve a direct increase of the capillary perfusion as shown by Timmers et al. [31]. Limited by the in-vitro setting of our study we were not able to proof these findings and may not address the response of the wound to the NPWT device. However, an oxygen-deprived wound environment most likely negatively influences diffusion into the cells, and thus contributes to less intracellular oxygen availability. The extend of oxygen deprivation may not be assessed by our results as we did not measure the transcutaneous oxygen flux (tcJ_{o2}). According to Stücker et al. the transcutaneous oxygen uptake is about 1 ml O2 m^{-2} min^{-1} and intracutaneous profiles of oxygen partial pressure show, that the upper layers of the skin up to a depth of 0.4 mm are almost exclusively supplied by external oxygen [32]. This diffusion capacity might even be intensified when capillary oxygen supply is reduced or parts of the epidermis are damaged or missing. An additional wound sealing by the NPWT dressing thus might possibly depict an oxygen exchange barrier [32,33]. Other limitations of our study are the in-vitro experimental design and the small number of tested devices. Furthermore, no tests involving bacterial microorganisms were made. However, based on basic physical laws, the in vivo setup of NPWT should not significantly vary from our methods. Further studies investigating partial hypoxia and the influence on species-individual growth under NPWT are needed to more fully understand the exact working mechanism of this important treatment option.

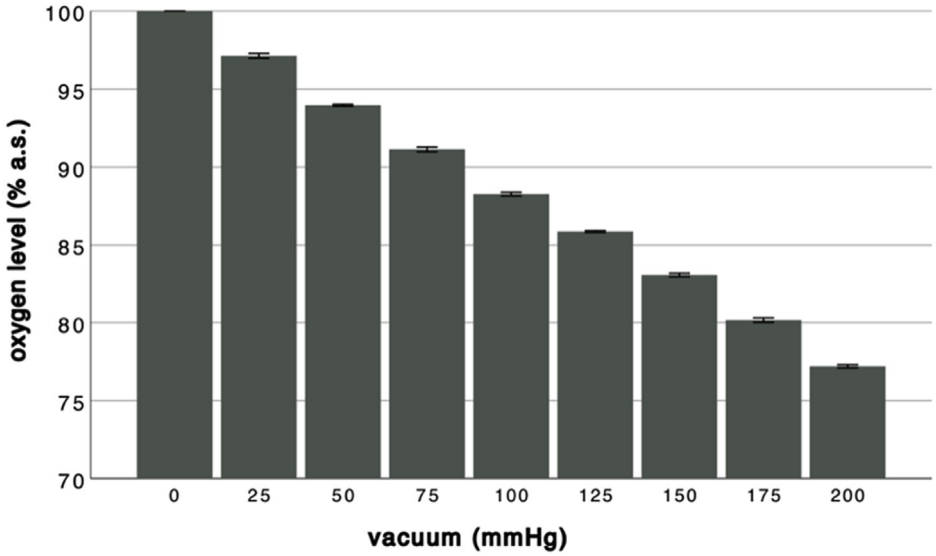

Fig. 2. Graphic demonstration of the oxygen level (y-axis) and the applied vacuum (x-axis) for the V.A.C. Ulta™. The vacuum intensity was increased in steps of 25mmHG up to 200 mmHg.

5. Conclusion

We attempted to further explain the working mechanisms of NPWT, and found a decrease in the oxygen partial pressure as high as 22.8% for different NPWT systems used during our clinical routine. Therefore, oxygen levels are decreased within the foam of NPWT dressings, likely leading to oxygen deprivation effects in the underlying wound tissue. An influence on bacterial growth selection and oxygen exchange with the adjacent tissue seems possible and needs further investigation.

Financial interest

Dr. Taeger is a consultant for Kinetic Concepts, Inc. The other authors have no financial interest to declare in relation to the content of the article.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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