



Antiseptic negative pressure instillation therapy for the treatment of septic wound healing deficits in oral and maxillofacial surgery

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ABSTRACT

Introduction: Impaired wound healing, chronic wounds and extended soft tissue defects present a crucial problem in reconstructive surgery of the head and neck region, even more after radiation therapy. In such cases the standard is a prolonged open wound treatment. The negative pressure instillation therapy might present an alternative therapy option.

Material and methods: In this study the effects of negative pressure instillation therapy on the healing of chronic wounds in 15 patients diagnosed with impaired wound healing were investigated. These based upon infected osteoradionecrosis and osteomyelitis of the jaw. The parameters investigated as markers of the therapeutic success were serum inflammatory parameters i.e. white blood cell counts, wound smear results and wound surface reduction.

Results: The use of negative pressure instillation therapy lead to a reduction of the bacterial load and formation of a stabile granulation tissue in all but one case. The mean inpatient time of the patients was 13.33 ± 4.62 days. Between 2 and 8 dressing changes were needed to reach clinical sufficient wound healing results. Secondary intention wound healing could be obtained in 14 out of 15 cases. The crucial part for the successful application was a watertight enoral suturing as oro-cutaneous fistulae were present in most cases.

Conclusion: The negative pressure instillation therapy poses a good treatment for wound healing problems and extended size soft tissue defects, even when oro-cutaneous fistulae were present. Especially in cases that contraindicate micro-vascular reconstruction, negative pressure instillation therapy could be a good alternative.

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1. Introduction

Complex wounds, wound healing deficits and chronic wounds of the head and neck region can present a challenging task for surgeons. This is even more the case as complex wounds in the field of oral and maxillo-facial surgery may arise as a result of infected osteoradionecrosis of the jaw (IORNJ), osteomyelitis (OM), septic wound healing disorders and oro-cutaneous fistulae. Under such circumstances local or microvascular reconstruction is used as first-

line therapy in accordance with the reconstructive ladder (Boyce and Shokrollahi, 2006). After failure or in the presence of contraindications for the performance of a microvascular reconstruction, open wound therapy is the treatment of choice.

The vacuum-assisted closure (VAC) was introduced to wound therapy by Morykwas et al. nearly 20 years ago (Morykwas et al., 1997). Since then it has become the therapy of choice for complex wounds in near all surgical fields except for head and neck surgery (Acosta et al., 2017; Damiani et al., 2011; Hattori et al., 2017; Robert 2016; Subramonia et al., 2009). VAC works by the application of a constant subatmospheric pressure through a polyurethane sponge that is secured by adherent drape, hence by a vacuum seal (Molnar et al., 2004). Main positive effects of VAC on wound healing

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are an increase in the formation of granulation tissue, a reduction of edema in the surrounding tissue and a reduction of the bacterial load (Orgill and Bayer, 2013). Due to the complexity of head and neck surface structures and the conjunction of head and neck wounds with a heavy bacterial burden due to e.g. oro-cutaneous fistulae, VAC is a seldom performed therapy in head and neck surgery (Satteson et al., 2015; Yang et al., 2013). The addition of an automated instillation of saline solutions such as sodium-chloride 0.9% or antiseptic fluids like polyhexanide make this therapy even more efficient for use in infected wounds (Sibaja et al., 2017; Gabriel et al., 2008). Up to a complete clearance of the bacterial load is described for negative pressure instillation therapy (NPIT) in the literature (Gabriel et al., 2008). In synopsis with reports of orocutaneous fistulae closure by VAC this supports the efficiency of VAC and NPIT in oral and cranio-maxillofacial surgery (Tian et al., 2014).

The purpose of this retrospective clinical trial is to show the effects on impaired wound healing caused by septic diseases of the jaw bone. Therefore the reduction of the wound surface (WS) in cm², pain values, bacterial load evaluated by sore smears and blood work indicating an inflammatory response are analyzed. Furthermore the time of inpatient treatment and number of dressing changes were taken into account. To our best knowledge this is the first investigation regarding the use of NPIT in oral and maxillofacial surgery.

2. Material and methods

This study aimed at investigating the effects of NPIT on inflammation parameters and wound-healing in patients with septic wounds of the head and neck area. Included in this retrospective study were patients that reported to our institution from September 2015 to September 2016 (12 months duration) and had a diagnosis of chronic wounds related to septic diseases of the jaw – IORNJ, OM – in which microvascular reconstruction was excluded as an option for the absence of recipient vessels or health issues. Patients with an ongoing malignant disease were excluded from this study. Informed consent was obtained prior to patients' inclusion. In total 15 patients (n = 15, 7 male, 8 female) were included in this investigation. The mean age of the patients was 63.13 ± 10.02 years. All data regarding the patients gender, age, diseases, irradiation status and co-morbidities as well as exposed structures like anatomical structures and mandible reconstruction plates (MRP) are displayed in Table 1 (Table 1).

NPIT was performed using the V.A.C.UltTM (Acelity Companies, San Antonio, TX, USA) in V.A.C.VeraFloTM-therapy-mode with

polyhexanide 0.04% as an antiseptic wound irrigation solution. The continuous sub-atmospheric pressure was maintained at 125 mm Hg and every 3 h interrupted by an instillation period of 10 min. The instillation volume was chosen according to the soft tissue defect and the decrease in wound volume. The first NPIT device was applied after performing a debridement of the septic wound in endotracheal anesthesia. Osteosynthesis materials (OSM) in our study population mandible reconstruction plates (MRP) were left in situ, if not infected or loosened, or changed. Regarding the saliva leakage from the oral cavity that might occur following enoral suturing, testing was performed using a dyed lavage consisting of 1:1 octenisept[®] (Schülke & Mayr GmbH, Norderstedt, Germany) and Braunol[®] (B. Braun Melsungen AG, Melsungen, Germany). If traces of this solution were found in the wound cavity, irrigation with sodium chloride solution was performed as well as additional enoral suturing. This procedure was repeated until no further traces of the dyed lavage could be found. To ensure the waterproof and airtight sealing of the NPIT dressing the wound margins as well as cutaneous sutures were covered by double-sided adhesive hydrogel pads V.A.C.[®] Gel (Acelity Companies, San Antonio, TX, USA). The following NPIT applications were performed bedside. At least 3 cycles of NPIT were performed, of which each lasted for 3 days past the day of application. If the WS after each therapy cycle was not satisfying, treatment was prolonged until a clinically satisfying result was obtained. Parameters to determine the treatment results were leukocytes counts, C-reactive protein (CRP), bacterial loads and WS reduction. Leukocytes were quantified from EDTA-blood samples. CRP was measured from blood serum. For determination of the bacterial load sore smears were taken each dressing change and the bacterial load was described semi-quantitatively as follows: 0 = no bacterial load, 1 = light bacterial load, 2 = bacterial load that will not fit in 1 or 3, 3 = heavy bacterial load. This method of quantification was performed for each kind of bacteria present in the sore smears. Results were calculated as summary.

Valuation of pain was done by utilization of the numeric rating scale (NRS); 0 means no pain and 10 the worst pain imaginable.

The most important parameter in determining therapy results was the WS reduction. Pictures of the defect were taken prior to the first application of NPIT and every dressing change and surface changes were evaluated. In the case of a deterioration of the wound the NPIT was terminated. The measurement of the WS was performed using ImageJ (ImageJ, NIH) and recorded in cm².

Statistical analysis was performed by use of SPSS 21.0 (IBM, Armonk, NY, USA). Testing for normal distribution was performed by use of a Kolmogorov-Smirnov-test. Dependent t-tests for paired samples were used to determine significance for all data normally

Table 1
Reasons for treatment and co-morbidities.

	Sex	Age	Primary malignant disease	Previous radiation therapy	Primary reason for treatment	Fistulae	Exposed structures	Co-morbidities favoring impaired wound healing
Patient 1	Female	76	Lip carcinoma	Yes	ORNJ	Yes	MRP	-
Patient 2	Male	76	Tongue carcinoma	Yes	ORNJ	Yes	Neck muscles	-
Patient 3	Male	55	-	-	Chronic OM	-	MRP	-
Patient 4	Female	66	Tongue carcinoma	Yes	ORNJ	-	MRP	-
Patient 5	Male	51	Floor of the mouth carcinoma	Yes	ORNJ	-	Neck muscles, external carotid artery	-
Patient 6	Male	56	Floor of the mouth carcinoma	Yes	ORNJ	-	MRP	-
Patient 7	Male	61	Floor of the mouth carcinoma	Yes	ORNJ	Yes	MRP	Diabetes mellitus Type II
Patient 8	Female	63	Floor of the mouth carcinoma	Yes	ORNJ	Yes	MRP	-
Patient 9	Female	63	Floor of the mouth carcinoma	Yes	ORNJ	Yes	MRP	-
Patient 10	Male	80	Tongue carcinoma	Yes	ORNJ	Yes	Neck muscles	-
Patient 11	Female	50	-	-	Chronic OM	-	MRP	-
Patient 12	Female	62	Floor of the mouth carcinoma	Yes	ORNJ	Yes	MRP	-
Patient 13	Female	50	-	-	Chronic OM	-	MRP	-
Patient 14	Male	62	Floor of the mouth carcinoma	Yes	ORNJ	Yes	MRP	Diabetes mellitus Type II
Patient 15	female	76	Lip carcinoma	Yes	ORNJ	Yes	MRP	-

distributed. For non-normally distributed data non-parametric testing by Mann-Whitney-U-test was performed. A p-value of ≤ 0.05 was considered significant, one of ≤ 0.005 as highly significant.

3. Results

NPIT was performed successfully in 14 out of 15 cases. The application lasted for a mean of 13.3 ± 4.6 days. Over the course of the treatment 4.1 ± 1.6 dressing changes were performed, whereas in one case only 2 were needed. The longest treatment lasted for 26 days and a total of 8 dressing changes had to be performed until clinically sufficient results were obtained.

Before the first application of the NPIT the mean leukocyte concentration was $8.55 \times 10^3/\mu\text{L} \pm 2.23 \times 10^3/\mu\text{L}$. After ending of therapy leukocyte concentrations showed a significant decrease to $6.76 \times 10^3/\mu\text{L} \pm 2.26 \times 10^3/\mu\text{L}$ ($p = 0.012$). CRP was calculated by absolute values as well as by percentage. For the first day of treatment CRP values ranged from 55.7 ± 68.0 mg/L. These values decreased to 12.3 ± 10.9 mg/mL and thereby dropped highly significantly ($p = 0.001$) when compared to the initial value. When normalized to percent, a highly significant reduction of the CRP could be observed ($p < 0.001$).

Regarding bacterial loads no significant decrease was found over the course of the therapy. In one case an increase in the bacterial load could be observed to the end of therapy.

The course of the pain value determined via the NRS was highly variable but at the end of the therapy all but 1 patient obtained pain relief.

The mean WS before NPIT was 18.48 ± 12.83 cm² which was highly significantly reduced to 7.6 ± 7.4 cm² ($p = 0.001$) (Fig. 1). A

complete wound closure was obtained by secondary intention in all but one case. An example for a successful negative pressure instillation therapy is shown in Fig. 1. Before the therapy, oro-cutaneous fistulae could be observed in 9 of 15 cases. By therapy-ending no fistulae were present. MRP not covered by soft tissue could be found in 12 out of 15 cases. In 11 cases this did not cause any interference with the NPIT and a complete coverage of the osteosynthesis materials by newly formed granulation tissue could be observed. The NPIT had to be discontinued due to progression of soft tissue loss and skin ulceration in one case with an exposed MRP. In that case the therapy regimen was switched to open wound therapy after MRP removal.

All values prior to and after therapy are shown in Table 2.

4. Discussion

As mentioned previously, complex wound healing deficits pose a severe task for a surgeon. This is even more the case in the head and neck area due to the complexity of the anatomical structure given. There is a lack in literature regarding complex wounds as a complication of therapeutic interventions, i.e. irradiation and surgical procedures in oral and maxillofacial surgery. These can be observed in clinical practice related to ORNJ, MRONJ, OM and osteosynthesis materials in infected soft tissues or as a complication of microvascular reconstruction.

In nearly all surgical fields VAC and NPIT are used as a standard tool in the therapy of complex wounds (Acosta et al., 2017; Damiani et al., 2011; Hattori et al., 2017; Robert 2016; Sibaja et al., 2017; Subramonia et al., 2009)

This therapeutic option has not been added to the standard armamentarium of reconstruction in head and neck surgery due to

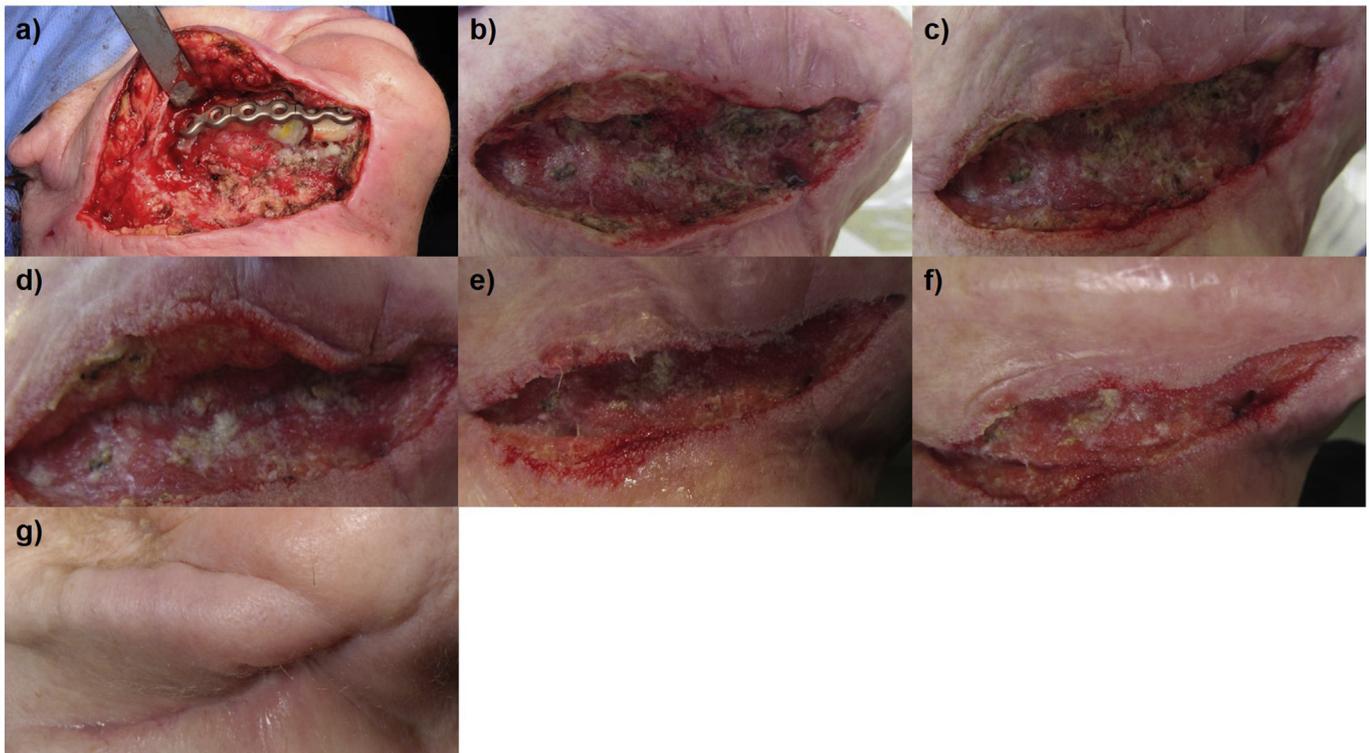


Fig. 1. Changes to a wound over the course of NPIT and the final results obtained. The MRP seen in a) was left in situ and a stable overgrowth of granulation tissue could be observed. a) The intraoperative situs shows the newly placed MRP and the wound after the debridement and before the first application of NPIT. In b) one can see the formation of granulation tissue in on the WS and even granulation tissue coverage of the MRP by the first dressing change 4 days after the initial NPIT application. c) to f) show the complete coverage of the wound by granulation tissue and the gradual approximation and epithelialization of the wound margins up to the point the NPIT was finalized and the patient discharged. The final result obtained after complete epithelialization is illustrated in g) 3 months after discharge for inpatient treatment.

Table 2
Clinical data.

Parameter	Mean \pm SD before NPIT	Mean \pm SD after NPIT	Range before NPIT	Range after NPIT	p-Value
Leukocytes [$\times 10^3/\mu\text{L}$]	8.55 \pm 2.23	6.76 \pm 2.26	3.65–11.38	3.35–12.46	0.012
CRP [mg/L]	55.7 \pm 68.0	12.3 \pm 10.3	8.0–216.0	2.3–36.9	0.001
Wound surface [cm^2]	18.5 \pm 12.8	7.6 \pm 7.4	3.0–50.0	1.0–30.0	0.001
Bacterial load	2.5 \pm 2.0	2.1 \pm 2.1	0–6	0–7	0.6
Pain value	3.1 \pm 2.4	0.1 \pm 0.5	0–8	0–2	0.001

All clinical data regarding investigated parameters (inflammatory blood works, wound surface, bacterial loads and pain values) are displayed here in mean \pm SD as well as ranges.

various reasons, ranging from the complexity of anatomical structures to hair-bearing areas of this region (Satteson et al., 2015). Another factor that needs to be taken into account is the possible communication of complex wounds in oral and maxillofacial surgery with the oral cavity. To ensure the air sealing that is required for VAC a watertight enoral closure is needed (Yang et al., 2013; Tian et al., 2016; Tian et al., 2014). Since NPIT was applied in our study the watertight enoral closure had to be ensured even more, as the necessary air sealing proved harder to obtain than for conventional VAC.

By the application of NPIT we aimed for a reduction of the bacterial load. However we could not observe a complete clearance of bacterial load as reported by Gabriel et al., (2008) (Gabriel A et al., 2008). This may be explained by the prevalence of oro-cutaneous fistulae in our study group. Hence bacteria from the oral cavity may have migrated into the wound cavity through micro-leakages in the watertight enoral closure that however did not affect the air sealing. A possible solution for this problem was presented by Tian et al., 2016. By utilizing a patch fashioned from a sterile surgical glove they achieved a watertight enoral wound closure that completely seals and protects the wound from saliva and intraoral secretions leakage to the soft tissues (Tian et al., 2016). Despite the non-statistically significant reduction of bacterial load observed, a reduction of bacterial load can still be contemplated as a positive effect on wound healing as all but one therapy results showed efficiency by the end of therapy. In the case where NPIT fell short, this could not be tied to an increased bacterial load but to a progressing loss of soft tissues.

Regarding pain values we found a decrease when pre-therapeutic were compared to post-therapeutic values. Nearly all patients showed relief from pain at the end of therapy. Inter-individual variations in pain perception could have influenced the results. Additionally patients with septic diseases of the jaw report severe pain and require light to sometimes strong opioids for pain control medication according to the WHO analgesic ladder (Eisenberg et al., 2005; Dietrich et al., 2017).

Satteson et al. reported a good clinical outcome for the use of VAC in patients with head and neck wounds. In their study the anatomical locations of the soft tissue defects were not specified and there were no details on bacterial load or fistulae associated with wounds treated like in this study (Satteson et al., 2015). Because in our patients the prevalence of oro-cutaneous fistulae was one of the main problems and besides the damaged bone one of the main reasons for wound formation, we faced a different set of problems. Yang et al. published a similar study on patients with head and neck wounds utilizing VAC without instillation (Yang et al., 2013). Their findings showed close similarity to ours. The average duration of the therapy was 10.8 d, ranging for 4 d to 24 d, which is significantly shorter than the average therapy duration needed for satisfying clinical results documented in our study. This may well be due to the differences in the underlying diseases, as the patients reported by Yang et al. had received free or local flaps that had completely or partially failed because of infection, saliva

leakage and fistulae (Yang et al., 2013). In comparison our patients presented with septic diseases of the lower jaw, which resulted in large infected soft tissue defects and were commonly (9/15 cases) accompanied by oro-cutaneous fistulae. We also reaffirm the latter authors' understanding that watertight closure of the enoral wound side is a crucial part in VAC of the head and neck region. This is even more the case for NPIT as we found that even the smallest leakage of the mucosal suturing may result in failure to obtain the air sealing needed. Yang et al. reported fistulae in about 62% of the patients. No prevailing fistulae were found after VAC and 11 out of 13 patients had wound healing by secondary intention (Yang et al., 2013). These results are consistent with ours for NPIT, as no fistulae could be observed after therapy ending and secondary intention wound healing was achieved in 14 out of 15 cases. The major difference in the results is the severe wound infection reported by the latter authors for one case, which could not be reported for any of our patients. This may be due to the adjunction of instillation to VAC in NPIT.

A limitation of the presented study is its nature as a retrospective study that lacks the evidence of a randomized controlled trial (RCT). This is the case for nearly all cited work regarding the use of VAC/NPIT and can in accordance with Palm et al. be stated for nearly all publications regarding VAC and NPIT in head and neck surgery (Palm et al., 2011).

5. Conclusion

The astonishing results of NPIT regarding WS reduction in complex wounds of the head and neck region support the opinion that VAC and especially NPIT are good therapeutic options in the treatment of such soft tissue defects. This is even more the case as the results were obtained under septic circumstances and the prevalence of oro-cutaneous fistulae. Even in exposed OSM a complete overgrowth by granulation tissue could be observed. NPIT can be used to prepare a wound bed for further reconstruction with split thickness skin grafts or a free flap (Satteson et al., 2015; Yang et al., 2013). Furthermore our results suggest that this therapy is a feasible option for wound closure, even without secondary reconstruction, for soft tissue defects where microvascular reconstruction is not possible.

Further investigation by means of RCTs are a given necessity for the investigation of the efficiency of VAC and NPIT in oral and maxillofacial surgery. However the results of our study regarding WS reduction and elimination of oro-cutaneous fistulae by NPIT are very promising.

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Conflicts of interest

The authors declare that there are no conflicts of interest related to this study.

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