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Super-Oxidized Solution (Dermacyn Wound Care) as Adjuvant Treatment in the Postoperative Management of Complicated Diabetic Foot Osteomyelitis: Preliminary Experience in a Specialized Department

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Abstract

Surgery is usually used to treat diabetic foot osteomyelitis (DFO), whether primarily or in cases in which antibiotics are not able to control infection. In many cases, the bone is only partially removed, which means that residual infection remains in the bone margins, and the wound is left open to heal by secondary intent. The use of culture-guided postoperative antibiotic treatment and adequate management of the wound must be addressed. No trials exist dealing with local treatment in the postoperative management of these cases of complicated DFO. We decided to test a super-oxidized solution, Dermacyn Wound Care (DWC; Oculus Innovative Sciences Netherlands BV, Sittard, Netherlands) to obtain preliminary experience in patients in whom infected bone remained in the surgical wounds. Our hypothesis was that DWC could be useful to control infection in the residual infected bone and surrounding soft tissues and would thus facilitate healing. Fourteen consecutive patients who underwent conservative surgery for DFO, in whom clean bone margins could not be assured, were treated in the postoperative period with DWC. Eleven cases were located in the forefoot, 6 on the first ray and the rest in lesser toes, 1 in the Lisfranc joint, and 2 on the calcaneus. No side effects appeared during treatment. Neither allergies nor skin dermatitis were found. Limb salvage was successfully achieved in 100% of the cases. Healing was achieved in a median period of 6.8 weeks.

Keywords

diabetic foot, osteomyelitis, super-oxidized solution, diabetic foot infections

Background

The systematic surgical treatment of bone infection in the feet of patients with diabetes is currently under debate because some patients achieve remission exclusively with antibiotics.[1] However, surgery is the usual approach for treating diabetic foot osteomyelitis (DFO), whether primarily or in cases in which antibiotics are not able to control the infection.[2] The choice of surgical technique to treat DFO is not well standardized, and the goal is to remove the infected bone without reducing the functionality of the foot. Some teams perform amputations to removed the infected bone,[3] whereas others use conservative surgery to conserve the architecture of the foot.[4,5] When infection remains in

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bone and/or soft tissues, the wound should not be closed.[6-8] The open wound caused by surgery will undergo postoperative care to achieve healing by secondary intention or before undergoing reconstructive techniques.

Our approach to treating DFO is to remove the infected bone, leave the wound open to heal by secondary intention, and use culture-guided postoperative antibiotic treatment.[5,9] In many cases, we cannot be sure that all the infected bone has been removed and thus believe that wide drainage through the open wound and postoperative culture-guided antibiotics should be used to eradicate the infection. Theoretically, adjuvant treatment with topical antibiotics or antiseptics could help reduce the bacterial load, which is located in the residual infected bone and soft tissues. This could also help reduce the timing of postoperative antibiotic treatment but this has not been confirmed.

In our experience, management of the postoperative wound following surgery for diabetic foot infections is always determined in an individualized way, and we frequently use silver-based dressings. However, this choice is empiric because no trials exist dealing with local treatment in the postoperative management of DFO. Based on the experience of other groups,[10,11] we decided to test a super-oxidized solution, Dermacyn Wound Care (DWC; Oculus Innovative Sciences Netherlands BV, Sittard, Netherlands), in order to obtain preliminary experience in patients in whom infected bone remained in the surgical wounds. Our hypothesis was that DWC could be useful for controlling infection in the residual infected bone and surrounding soft tissues and could thus facilitate healing.

The aim of this work is thus to present our preliminary experience with a super-oxidized solution as adjuvant treatment in the postoperative wound management of complicated DFO in patients presenting a high risk of amputation in order to establish its safety and usefulness prior to designing a clinical trial.

Patients and Methods

Fourteen consecutive patients who underwent conservative surgery for DFO, in whom clean bone margins could not be assured, were treated in the postoperative period with DWC. All were assumed to have infected but viable bone remaining in the wounds after removing most of the infected bone. Conservative surgery in this case was defined as a procedure in which only the infected bone and nonviable soft tissue were removed, but no amputation of any part of the foot was undertaken. Conservative surgery preserves the soft-tissue envelope and more distal tissues, which means resection of the infected bone while preserving the soft-tissue envelope.[5] Only cases with osteomyelitis without soft tissue infection were included in this preliminary study. Soft tissue infections were diagnosed either preoperatively or during surgical procedures according to previously published criteria.[12,13]

Diagnosis of osteomyelitis was based on our flow chart comprising a sequential combination of the probe-to-bone test and plain X-rays, as published elsewhere.[14] A neurological examination was undertaken using Semmes-Weinstein filaments (5.07 = 10 g). Neuropathy was diagnosed when the patient did not feel 3 or more sites. Peripheral arterial disease was diagnosed if the patient met the following criteria: absence of both distal pulses and/or ankle brachial index below 0.9. Ulcers in patients diagnosed for neuropathy were defined as neuropathic ulcers. If both neuropathy and peripheral arterial disease were present, the ulcer was defined as neuroischemic.

During surgical intervention, bone samples were extracted for analysis by the microbiology and pathology laboratories. Only aerobic cultures were grown in this study. Surgical wounds were copiously irrigated with DWC in the operating room. DWC was irrigated daily through the wound with the purpose of washing the residual bone. According to our treatment protocol, cases with persistent postoperative infection either in bone or soft tissue that precluded wound healing and/or produced clinical infectious symptoms were reoperated. Reoperations included minor and major amputations if required. Based on our previous experience, infection control was considered successful once the surgical wound and the index ulcer that acted as the point of entry of the infection had healed.[5,9] Patients were followed-up to detect recurrence of the infection, reulceration (whether complicated or not with new osteomyelitis), and the need for amputation. Limb salvage was achieved when the patient did not require a major amputation, which was defined as amputation through or above the ankle joint.

The major endpoint to be evaluated was healing without recurrence of the infection and need for amputation. Any side effect associated with the treatment was assessed.

Patients gave informed consent for surgery, photography, and inclusion in the study. The ethical research committee of the Materno-Insular Hospital of Las Palmas de Gran Canaria reviewed and approved the study protocol and gave consent for publication.

Results

Histopathology reports confirmed osteomyelitis in every case. Eleven cases were located in the forefoot, 6 on the first ray and the rest in lesser toes, 1 in the Lisfranc joint, and 2 on the calcaneus. Cases are presented in Table 1. Eight patients had previously undergone surgery for the same infection, which had not been resolved. Other teams had treated 6 patients, and amputations (2 major) had been indicated. Four patients had undergone surgery in our hospital but infection was not adequately resolved. DWC was not used in the postoperative period following the initial surgery. Cultures were negative in 3 cases, were not available in another one, and bacteria were isolated in the

Table 1. Case Series

	Point of Entry to the Infection	Location of Bone Infection	Previous Surgery Due to the Same Infection	Surgical Procedure	Bacteria Involved	DWC Use	Need for Reoperation and/or Amputation	Postoperative Antibiotic Treatment	Time to Healing	Follow-Up
Case 1	Neuroischemic interdigital ulcer	Proximal phalanx	No	Ostectomy of the phalanx	NA	Lavage of the open wound and soaked gauzes with DWC	No	3 weeks	8.5 weeks	Patient died 1 month after healing following heart attack
Case 2	Spreading of forefoot infection along plantar aponeurosis	Calcaneus. Attachment of plantar aponeurosis to the calcaneus	Yes. Forefoot infection had been operated. Calcaneus osteomyelitis was a consequence of spreading of the infection along plantar aponeurosis. DWC was not applied at the first surgery	Calcaneus curettage	*Escherichia coli*, *Streptococcus* spp.	Close lavage with DWC through the wound	No	7.1 weeks	7.1 weeks	13 months without recurrence
Case 3	Neuroischemic plantar ulcer beneath the first metatarsal–phalangeal joint	Medial sesamoid bone	Yes. DWC was not applied at the first surgery	Sesamoidectomy. Keller's arthroplasty. Internal fixation	*Escherichia coli*, Methicillin-resistant *Staphylococcus aureus*	Infection of the surgical wound. Closed lavage with DWC through the surgical wound and gauzes soaked in DWC	Yes	8.5 weeks	8.5 weeks	Recurrence 2 months after apparent healing. Patient underwent new conservative surgical procedures. No amputation has been required in the year since the first surgery
Case 4	Neuropathic plantar ulcer beneath the first metatarsal–phalangeal joint	Medial sesamoid bone	Yes. DWC was not applied at the first surgery	Sesamoidectomy. Keller's arthroplasty. Internal fixation	*Staphylococcus aureus*	Infection of the surgical wound and reopening of the ulcer. Closed lavage with DWC through the index ulcer and gauzes soaked in DWC	No	8.5 weeks	6.8 weeks	12 months without recurrence
Case 5	Neuroischemic ulcer of the big toe as a consequence of critical ischemia	Distal phalanx of the big toe. Big toe amputation had been indicated by another team	Yes. DWC was not applied at the first surgery	Removal of the distal phalanx. After the first procedure recurrence was found and treated with new curettage and DWC	Methicillin-resistant *Staphylococcus aureus*	Lavage of the open wound and gauzes soaked in DWC	No	4.3 weeks	3 weeks	6 months without recurrence
Case 6	Neuroischemic ulcer on the dorsum of the foot	Osteomyelitis of the Lisfranc joint. Major amputation had been indicated by another team	Yes. Another team performed debridement	Curettage of the Lisfranc joint	*Yersinia enterocolitica*	Close intraosseus lavage with DWC through the wound	No	4.1 weeks	9.2 weeks	8 months without recurrence
Case 7	Neuropathic ulcer on the fifth toe	Osteomyelitis of the proximal interphalangeal joint. Fifth toe amputation had been indicated by another team	No	Curettage of the interphalangeal joint	No growth	Lavage of the open wound and gauzes soaked in DWC	No	0.3 weeks	2.8 weeks	9 months without recurrence

(continued)

Table 1. (continued)

	Point of Entry to the Infection	Location of Bone Infection	Previous Surgery Due to the Same Infection	Surgical Procedure	Bacteria Involved	DWC Use	Need for Reoperation and/or Amputation	Postoperative Antibiotic Treatment	Time to Healing	Follow-Up
Case 8	Neuropathic ulcer on the big toe	Osteomyelitis of the interphalangeal joint of the hallux. Big toe amputation had been indicated by another team	No	Curettage of the interphalangeal joint	*Escherichia coli*	Lavage of the open wound and gauzes soaked in DWC	No	5.4 weeks	6.1 weeks	8 months without recurrence
Case 9	Neuropathic ulcer over the first metatarsal–phalangeal joint	Osteomyelitis of the first metatarsal-phalangeal joint. Transmetatarsal amputation had been indicated by another team	Yes. Another team performed debridement during admission in another hospital	Curettage of the first metatarsal-phalangeal joint. External fixator. The index ulcer was left open to allow joint lavage	*Proteus morganii, Staphylococcus aureus*	Lavage through the ulcer and gauzes soaked in DWC	No	4.4 weeks	7.1 weeks	8 months without recurrence
Case 10	Neuropathic ulcer on the tip of the third toe	Osteomyelitis of the distal phalanx	No	Ostectomy of the distal phalanx	No growth	Lavage of the wound and gauzes soaked in DWC	No	2.7 weeks	4.3 weeks	9 months without recurrence
Case 11	Interdigital neuroischemic ulcer	Osteomyelitis of the middle phalanx of the fourth toe	No	Open arthroplasty	*Acinetobacter baumanii*	Lavage of the open wound and gauzes soaked in DWC	Yes. Progressive involvement of soft tissue with necrosis requiring amputation of the fourth toe	NA	NA	NA
Case 12	Neuropathic ulcer on the heel	Osteomyelitis of the calcaneus and Chopart joint. Major amputation had been indicated by another team	Yes. Another team performed debridement. Negative pressure with silver was applied during admission in another hospital	Curettage of the calcaneus and Chopart joint	No growth	Close intraosseus lavage with DWC through the wound	No	7.1 weeks	11.4 weeks	Three months without recurrence
Case 13	Interdigital neuropathic ulcer	Osteomyelitis of the proximal interphalangeal joint of the fourth toe	No	Open arthroplasty	*Serratia marcescens*	Lavage of the open wound and gauzes soaked in DWC	No	4.8 weeks	3.8 weeks	Five months without recurrence
Case 14	Neuropathic plantar ulcer on the big toe	Osteomyelitis of the distal phalanx of the big toe	Yes. DWC was not applied at the first surgery	Partial distal phalanx removal	*Serratia marcescens*	Debridement of the ulcer. Lavage of the open wound and bone exposed and gauzes soaked in DWC for 5 days. Bone surgery and closure of the wound	No	3 weeks	2.1 weeks	Three months without recurrence

Abbreviation: DWC, Dermacyn Wound Care (DWC; Oculus Innovative Sciences Netherlands BV, Sittard, Netherlands); NA, Not available.

Figure 1. Case 2. Abscess on the heel after undergoing debridement of the plantar central compartment. Bone could be probed through the incision

Figure 3. The wound was closed after new curettage of the calcaneus, leaving a Foley's catheter inside for performing instilation with DWC

Figure 2. X-ray of the case 2. Yellow arrow shows cortical defect where the abscess was drained

Figure 4. Total healing of the surgical wound

remainder, as illustrated in Table 1. Gram-negative bacteria were isolated in 8 cases and methicillin-resistant *Staphylococcus aureus* (MRSA) in 2 cases. Postoperative antibiotic treatment was given for a median of 4.4 weeks.

DWC was used in different ways: closed lavage through a catheter inserted in the cavity or by inserting the tip of a syringe between the stitches, open lavage, or by placing gauzes soaked in DWC. Case 2 is shown in Figure 1. The patient had undergone debridement of the plantar central compartment and was readmitted for abscess on the heel. X-ray showed signs of osteomyelitis in the calcaneus (Figure 2, yellow arrow). He underwent debridement and bone curettage, which did not resolve the infection. He underwent a reoperation consisting of new curettage of the calcaneus and the wound was closed, leaving a Foley's catheter inside (Figure 3). Postoperative culture-guided antibiotics were administered and lavage with DWC was carried out 3 times a day. The catheter was removed and healing was achieved without complications (Figure 4). Lavage through the stitches due to wound infection in case 3 is shown in Figure 5. The Kirschner wire was not removed due to infection. The Kirschner wire was removed 6 weeks after surgery, and the patient was discharged with only a minor defect in wound healing in order to undergo outpatient care (Figure 6A, white arrow). However, recurrence 3 months after apparent healing was found in case 3 (Figure 6B). The latter patient underwent new conservative surgical procedures using DWC in the postoperative period. No amputation has been required in the year since the first operation. One patient (case 11, Figure 7) required amputation of the toe due to uncontrolled infection by *Acinetobacter baumanii* and progressive destruction of the soft tissue envelope. Neither recurrence of

Figure 5. Lavage through the stitches due to wound infection in case 3

the infection nor subsequent amputation was found in the rest of the patients. Limb salvage was successfully achieved in 100% of the cases. Healing was achieved in a median period of 6.8 weeks.

No side effects appeared during treatment. Neither allergies nor skin dermatitis were found. Pain was not evaluable because of the neuropathic etiology of the ulcers.

Discussion

The role of antiseptics in wound care is controversial because in vitro studies have shown the cytotoxicity of such products.[15,16] Despite these in vitro studies, the clinical relevance of this cytotoxic effect on wound healing is unknown and could be compensated for by their control of bacterial burden.[17] Recently, the cytotoxic effect of 12 commonly used antiseptics on topical application in vitro to 2 human skin substitutes and a full-thickness autograft was assessed. Dermacyn was not cytotoxic in that study.[18] Cytotoxicity was not assessed in the present study. However, we consider that time to healing could be considered as an indirect way to test the possible deleterious effect of DWC on wound healing. In our first series dealing with DFO, open wounds healed by secondary intention over a median period of 12.8 weeks. The median wound healing time in patients with successful conservative surgery was 11.4 weeks compared with 17.1 weeks for those who had minor amputations ($P = .003$).[5] Wound healing was achieved by secondary intention after a median of 8 weeks in our more recent series.[9] Healing time in cases of wide postsurgical wounds was 10.5 ± 5.9 weeks in the group treated with DWC versus 16.5 ± 7.1 weeks in the group treated with povidone iodine ($P = .007$).[11] The median time to healing in the current investigation using DWC was 6.8 weeks, and this figure can be considered favorable. Even though we cannot state categorically that the improvement in healing time was due to the use of DWC, at least the healing time was not prolonged due to possible cytotoxicity.

Our approach to dealing with DFO is to remove the infected bone if possible and leave the wound open to healing by secondary intention in most cases.[2,5,19-21] We hypothesized that using a product that reduces the bacterial burden in bone and soft tissues could be beneficial. Two small single-center randomized controlled trials showed that super-oxidized solution was useful for treating foot infections and wide postsurgical lesions.[10,11] Another group reported that super-oxidized solution was at least as effective as oral levofloxacin for mild diabetic foot infections.[22]

In this small series, DWC was always in contact with the residual infected bone. It was applied by means of pulse irrigation or by filling the wound cavity with soaked gauzes. We also used closed lavage in cases in which the surgical wound had been closed; in 2 of these cases a wire had been inserted. Intraosseus lavage with DWC was used in midfoot and calcaneus osteomyelitis. This is a novel approach in our experience and the outcomes were favourable. Limb salvage was achieved in 100% of patients and only one required a minor amputation. Infection was eradicated in every patient included in this series and every wound healed. Only 1 recurrence was detected but the patient was treated with new conservative procedures, including the use of DWC through the wound. No amputation has been required to date in this complicated case.

One of the possible advantages of using DWC as adjuvant treatment to surgery and antibiotics could be its potential to reduce the period of postoperative antibiotic treatment. IDSA guidelines recommend that in cases in which residual infected (but viable) bone remains, antibiotics should be administered for 4 to 6 weeks initially parenterally but possibly switching to oral administration depending on conditions.[23] Definitive conclusions cannot be drawn from our preliminary experience but 4.4 weeks seems to be a short period compared with other investigations. Moreover, the microbiological isolates in this series were a little atypical. They included a high proportion of MRSA and gram-negative bacteria unlike most series in which Methicillin Sensitive Staphylococcus aureus (MSSA) was the most frequent isolate.[1] Postoperative antibiotic treatment was given for a median of 5.1 weeks in our previously reported prospective series.[9] The duration of antibiotic therapy was 10.1 ± 6.1 weeks in the group treated with DWC compared with 15.8 ± 7.8 weeks in the group treated with povidone iodine ($P = .016$) reported by Piaggesi's group.[11]

The weaknesses of this study were the following: there was no control group, only short-term follow-up was conducted in 3 cases, and in our experience, at least 6 months should be considered to state that the bone infection has been eradicated. No bacteriological postoperative controls

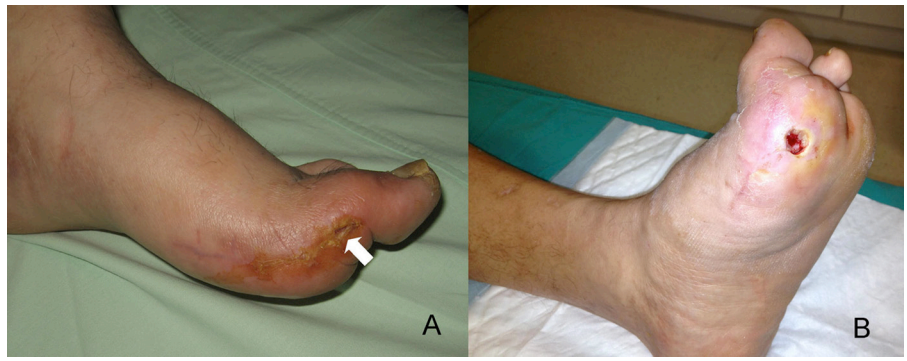

Figure 6. (A) Minor defect in wound healing when the patient was discharged from hospital. (B) Recurrence of osteomyelitis after apparent wound healing was detected after 3 months of follow-up

Figure 7. Progressive destruction of the soft tissue envelope and necrosis in case 11 requiring toe amputation

were carried out. The strengths of the study are that it is the first time that DMC has been used in cases of residual bone infection after surgery for DFO, bone infections were always histopathologically confirmed, and patients underwent specialized treatment in cases with a high risk of amputation. Indeed, other teams had indicated several amputations, including 2 major. The good outcomes obtained in this preliminary study have encouraged us to design a trial to test the use of DWC in cases of bone infection.

In conclusion, using DWC as adjuvant treatment in the postoperative period of surgery for DFO when the wound is open and bone margins may have residual infection is safe and may help eradicate the infection when combined with antibiotic treatment. Additional controlled studies are necessary to determine the precise role of DWC in the management of patients who have a high risk of amputation.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Free samples of Dermacyn Wound Care (Oculus Innovative Sciences Netherlands BV, Sittard, Netherlands) were received from the company to be tested in a series of patients. No payments or grants were received from the company.

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