

Case studies: octenidine in the management of diabetic foot ulcers

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Article points

1. Increased bioburden in chronic diabetic foot ulcers (DFUs) causes a vicious circle of delayed healing. Biofilm, in particular, is a significant issue that needs to be addressed.
2. In the cases described, the addition of octenilin® to the patients' DFU treatment regimen kick-started progression to healing
3. Using a wound cleansing solution in addition to standard care resulted in improved infection control, which improved healing in stalled/chronic DFUs.

Key words

- Bioburden
- Biofilm
- Cleansing

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Diabetic foot ulcers (DFUs) are common and constitute a considerable burden for both patients and healthcare providers. Reducing the length of time to healing reduces the risk of infection and further morbidity. Biofilms delay healing, therefore, they should be treated with a biofilm-based wound care regimen consisting of debridement, topical agents (antimicrobials and antiseptics) and, if appropriate, systemic antibiotics (Cutting and Westgate, 2012). This case series focuses on the use of octenilin®, which contains a broad-spectrum antimicrobial, in the treatment of DFUs to address bioburden, prevent infection and progress healing.

Foot ulcers are a common and disabling condition in people with diabetes, having a global prevalence of 6.3% (Zhang et al, 2017). Men are more likely than women to develop a diabetic foot ulcer (DFU) and people with type 2 diabetes are at greater risk than those with type 1 diabetes (Guest et al, 2015; Zhang et al, 2017). DFUs have a negative impact on patients' quality of life, increase the risk of infection and amputation (Vileikyte, 2001; Ribu et al, 2007; Wukich and Rasporic, 2018), and constitute a considerable economic burden for healthcare providers (Diabetes UK, 2017).

Each year, an estimated 2–2.5% of people with diabetes develop a DFU (Diabetes UK, 2017). In England in 2014–15, the estimated cost of foot ulceration and amputation was £1 billion, and this figure is expected to rise in the future (Kerr, 2017). It is, therefore, essential to identify and treat DFUs promptly to patient improve outcomes and reduce financial pressures on healthcare providers.

Chronic wounds, biofilms and infection

The most common risk factors for DFU formation are diabetic neuropathy and vascular disease (Wounds International, 2013), which slow

healing and increase the risk that wounds will become chronic. Biofilms and infection can also impact the rate of healing.

The number of viable microorganisms present on a surface is known as the bioburden. Increased bioburden has been proposed as an important predictor of poor healing outcomes (Grice and Segre, 2012). Microorganisms (bacteria, fungi and protists) can change from single-celled free-moving forms to a structured community of cells known as a biofilm following attachment, growth and division phases. Mature biofilms are surrounded by a protective matrix, which makes them difficult to remove with antibiotics, antiseptics and disinfectants. At least 60% of chronic wounds have a biofilm (Phillips et al, 2010; Haycocks, 2017). Their presence delays wound healing and they can act as a precursor to infection if not managed effectively (Phillips et al, 2010; Haycocks, 2017).

Infection is the result of disease-causing microbes invading body tissues. Diabetic foot infection is a common complication and is associated with increased risk of hospitalisation and poor clinical outcomes, including increased risk of lower-extremity amputation, reduced

quality of life, and increased risk of mortality (Pickwell et al, 2015). It is, therefore, important to prevent infections or, if present, treat them promptly.

Optimal management

If it is known or suspected that a biofilm is present, a biofilm-based wound care regimen should be implemented to reduce existing biofilms and prevent the formation of new ones. Management generally involves frequent debridement, the application of topical agents (including antimicrobials and antiseptics) and systemic antibiotics (if there is systemic infection) selected based on pathogen sensitivity (Cutting and Westgate, 2012).

Debridement removes debris, necrotic tissue and reduces the bioburden. Various methods can be used and are considered effective in speeding up healing (Edwards and Stapley, 2010).

Patients should be assessed for signs of infection. Wounds without evidence of soft tissue or bone infection do not require antibiotic therapy; however, when infection is present, a post-debridement specimen should be sent for aerobic and anaerobic culture. With acute infection, empiric antibiotics can be narrowly targeted at Gram-positive cocci (Lipsky et al, 2012). Those with chronic, previously treated or severe infection or those at risk of infection with antibiotic-resistant strains often require broad-spectrum antibiotics (Lipsky et al, 2012).

Topical agents can be used to treat infection, as well as reduce or prevent biofilms, although not all agents do both. Antimicrobials can be incorporated into dressings, irrigation solutions or gels. Ideally, antimicrobial preparations should have a broad spectrum of activity, be fast-acting, stable and non-cytotoxic (Apelqvist et al, 2017). Silver and octenidine, for example, have demonstrated antimicrobial activity against a number of planktonic organisms known to form biofilms, including *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Percival and McCarty, 2015; Apelqvist et al, 2017).

Silver-containing dressings have been shown to combat infection in chronic wounds and DFUs while minimising dressing-related pain (Richards and Chadwick, 2011). Antiseptic or antibiotic

irrigation solutions, based on octenidine, polyhexanide or doxycycline, can be used with or without negative pressure wound therapy to treat chronic wounds and DFUs (Apelqvist et al, 2017). In negative pressure wound therapy with instillation (NPWTi), solutions saturate the foam and bathe the wound, which is then cleansed for the recommended soak time before the fluid is removed and negative pressure restored. There is also evidence to favour NPWTi over conventional NPWT in DFUs as it promotes formation of granulation tissue and is the more cost-effective option (Gupta et al, 2016).

Octenidine dihydrochloride: a broad-spectrum antimicrobial

Octenidine dihydrochloride is an antimicrobial with broad-spectrum efficacy and no known microbial resistance. It is a safe and effective agent that prevents bacterial growth (Cutting and Westgate, 2012). It is well tolerated, has no side effects and is not absorbed systemically. Octenidine also has deodorising properties, is active in as little as 60 seconds, and its biocidal activity lasts at least 48 hours.

octenilin® wound irrigation solution (schülke) is a colourless, alcohol-free solution containing octenidine, which has been designed to cleanse and moisturise chronic wounds and burns. octenilin® has been shown to inhibit the formation of biofilm material for up to 3 days (Cutting and Westgate, 2012). It can also be used to loosen encrusted dressings and cleanse hard-to-reach areas, such as small fissures and wound pockets (schülke, 2015; Haycocks, 2017). octenilin® irrigation solution contains ethylhexylglycerin, which has surfactant, emollient, skin-conditioning and antimicrobial properties. Ethylhexylglycerin reduces the surface tension of aqueous solutions, enhancing its wetting behaviour (Cutting and Westgate, 2012). The presence of ethylhexylglycerin therefore optimises the spread of octenilin® irrigation solution into all wound fissures.

octenilin® wound gel is a hydrogel that can be used to reduce the risk of microbial colonisation of the wound. In a prospective randomised study of 61 patients with superficial skin graft donor site wounds, it significantly lowered microbial

colonisation compared to placebo (Eisenbeiss et al, 2012). In a prospective open-label study of 49 chronic venous leg ulcers, wound size reduction was significantly greater in patients treated with octenilin® wound gel or octenilin® wound gel plus modern phase-adapted dressings compared to those treated with modern dressings alone (Hämmerle and Strohal, 2016). The overall cost per patient was about 27% lower in the octenilin®-alone group due to earlier wound healing and the higher costs associated with phase-adapted dressings (Hämmerle and Strohal, 2016).

octenisan® wash mitts (schülke) are soft octenidine-impregnated cloth wipes that can be used to decontaminate the skin around the wound to reduce risk of bacteria migrating into the wound before the application of a new dressing (schülke, 2015). The mitts should be used to decontaminate an area at least as large as the dressing. Dressings can be securely applied once the area is dry.

Case studies

Case study 1: patient with cellulitis, infection and osteomyelitis

This 49-year-old male patient had a history of type 2 diabetes, neuropathy, retinopathy and transient ischaemic attack. He has history of minor amputation of his left second toe. He presented with osteomyelitis of the second toe distal phalanx and ulceration to the apex of the right second toe. He attended urgent care as a result of cellulitis in his right second toe and was

given oral flucloxacillin 500 mg, to be taken four times daily. Five days later, he was referred to the community intravenous team as his cellulitis was advancing. At this time treatment with ceftriaxone 2g per day for 7 days, this treatment was extended to 6 weeks on confirmation of osteomyelitis, and povidone iodine-impregnated gauze was commenced. The dressing was changed twice weekly.

He was referred to podiatry from the community intravenous team and seen within 1 working day. On review by podiatry, the patient had an ulcer on the apex of his right second toe covering a 5 cm² area (2 cm × 2.5 cm). Bacterial infection was diagnosed based on the clinical symptoms of redness, swelling, heat and cellulitis (Lipsky et al, 2012) and the wound bed consisted of bone, slough and granulation tissue (*Figure 1a*). Assessment of the ulcer gave a Site, Ischaemic, Neuropathy, Bacterial infection and Depth (SINBAD; Ince, 2008) score of four out of six — an indication for poor healing — and a Texas grade (Lavery, 1996) of B3 (a wound penetrating to bone or joint with infection). A probe-to-bone test suggested the presence of osteomyelitis (Lipsky et al, 2012). The patient was diagnosed with neuropathic DFU with soft tissue infection and suspected osteomyelitis. Intravenous antibiotic therapy was prescribed to treat the infection.

Following sharp debridement, he was started on a treatment regimen including cleansing the wound bed with octenisan® wash mitt and octenilin® irrigation solution, followed by application of a foam dressing. After sharp debridement, the wound was cleansed with the octenisan® wash mitt. The wound was then flushed with octenilin® irrigation solution and octenilin®-soaked gauze swabs were placed over and, where possible, in to the wound bed for 5 minutes. This process was conducted at the weekly dressing review with podiatry for 2 weeks. During this time period, the patient was also on the once daily treatment of ceftriaxone 2g.

The right distal phalanx was loose a week after the patient's podiatry review, so the majority of the bone was removed and sent to microbiology. The podiatrist continued to use octenilin® irrigation solution and octenisan® wash mitt as part of the patient's treatment regimen. Oral metronidazole

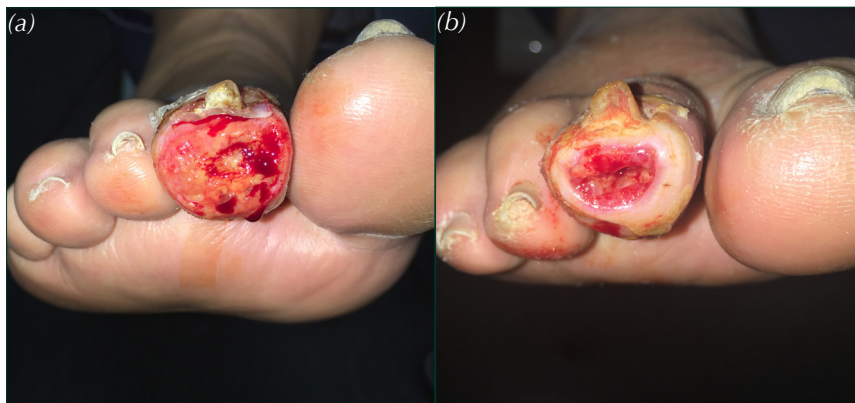


Figure 1. Case 1, patient with cellulitis, infection and osteomyelitis (a) 17.05.18; (b) 31.05.18.

400mg three times per day was introduced following microbiology test results, which showed presence of anaerobic bacteria. Seven days later, the wound measured 1 cm × 1.5 cm, 85% of the wound bed comprised granulation tissue, and there was evidence of epithelisation (*Figure 1b*). The ulcer had a SINBAD score of two and a Texas grade of A1. At this time, the octenilin® irrigation solution was discontinued.

Case study 2: older patient with chronic kidney disease and DFU

An 85-year-old male with type 2 diabetes, stage 3 chronic kidney disease and peripheral arterial disease presented with ulceration of the right lateral fifth metatarsophalangeal joint. The patient's peripheral arterial disease had recently been assessed by duplex ultrasound, which had revealed vessel disease distal to the popliteal fossa, and he was awaiting a review of his duplex results and a treatment plan. The metatarsophalangeal joint ulcer initially measured 0.2cm × 0.4cm and assessment revealed monophasic pulse signals and active ulceration. The patient was referred to the vascular service. Infection was present 17 days later; as a result, flucloxacillin 500mg four times per day for 7 days was prescribed. He was treated topically with dialkylcarbamoylchloride (DACC)-coated gauze. At this time, the ulcer measured 0.8cm × 0.6cm and was continuing to deteriorate (*Figure 2a*).

There was no soft tissue infection present 6.5 weeks later but the presence of biofilm was suspected due to the chronic nature of the wound. The wound bed consisted of 95% slough and 5% granulation, and had extended to 1cm × 1cm (*Figures 2b; 2c*). On assessment, the ulcer was classed as Texas grade C1 and had a SINBAD score of two. Post-debridement, octenisan® wash mitt was used to topically clean debris. octenilin® wound gel was also used to reduce the risk of infection and avoid the possibility of prolonged antibiotics use in this patient due to his advanced age and kidney disease. The wound was dressed with a non-adhesive foam dressing throughout treatment.

The wound was similar in size and appearance when the patient attended the service 8 days later. Three weeks after starting treatment with



Figure 2. Case 2, older patient with chronic kidney disease and diabetic foot ulcers (top left and clockwise). (a) 19.03.18; (b,c) 02.05.18; (d) 23.05.18

octenilin® wound gel, however, there was a noticeable improvement in the wound bed, which consisted of 60% granulation and 40% slough. There was evidence of epithelialisation and the ulcer had reduced in size by 25% (*Figure 2d*), as such, octenilin® wound gel was discontinued.

Case study 3: diabetic foot with severe infection and multiple DFUs

This 64-year-old male patient initially presented with a 4-day history of redness and swelling of the foot to the emergency room. He had chronic alcoholism and was diagnosed with type 2 diabetes a year ago, but was not taking any medication. Erythema and oedema of the left instep were present. The patient was diagnosed with erysipelas and *Tinea pedis*, and discharged on oral flucloxacillin. His temperature was slightly raised and he was tachycardic (105 beats per minute) 2 days later. The inflammation had extended towards the lower leg and there was a spontaneously draining abscess on his left



Figure 3. Case 3, Diabetic foot with severe infection and multiple diabetic foot ulcers (top left and clockwise). (a) initial assessment; (b) Six days; (c) Three weeks; (d) Two months; (e) Twelve weeks.

instep. The patient's antibiotic was changed to amoxicillin with clavulanic acid and he was discharged.

Five days later, a GP sent the patient to the emergency room with symptoms of confusion, fever (38°C), tachycardia (101 beats per minute), leukocytosis, high C-reactive protein and hyperglycaemia. There were ulcers on the first metatarsal, on the base of the third, fourth and fifth toes, and on the anterior face of the tibial–tarsal transition (Figure 3a). The tendons were exposed and there were several abscesses containing purulent, foul-smelling exudate. The patient was admitted to hospital, a biopsy tissue collection for bacteriologic study ordered, and linezolid 600 mg IV every 12 hours was commenced. He was referred to the multidisciplinary leg ulcer and diabetic foot team. Although his HbA_{1c} was high (10.7%), the patient's vascular status was considered normal for his age. The wound was considered a condition of neuropathic diabetic foot complicated by a severe soft tissue infection. Initial treatment involved

aggressive surgical debridement with drainage of the abscesses, followed by debridement using mechanical hydrodissection technique. NPWTi using intermittent instillation of octenilin® irrigation solution (125 mmHg, 10 minutes dwell time every 8 hours) were instigated and the patient's dressings changed every 3 days. *Serratia marcescens*, methicillin-sensitive *Staphylococcus aureus* and *Enterobacter hormaechei* were present, so he was started on clindamycin and piperacillin plus tazobactam.

Nine days later there was a marked improvement; the ulcers were shallower and the wound beds contained granulation tissue (Figure 3b). The ulcers were packed with sterile swabs moistened with octiset®, which was changed every 2 days. After 3 weeks (Figure 3c), the patient was discharged to primary care, where a dressing soaked in octenilin® solution was applied to his foot three times a week. The wounds continued to improve (Figure 3d), and had fully healed 12 weeks after local treatment with octenilin® irrigation solution was initiated (Figure 3e).

Declaration of interest

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Disclaimer

octenilin® and octiset® are official brand names used in the UK and Portugal respectively.

Summary

The addition of octenilin® to the patients' DFU treatment regimen kick-started progression to healing in the cases described. Its broad-spectrum antimicrobial action makes it suitable for use where biofilm is suspected, when the organisms colonising a biofilm are unknown (as in case 2), and in situations when multiple organisms are present (as in case 3), some of which may be resistant to antibiotics. octenilin® is also useful in the prevention of infection when the use of long-term systemic antibiotics is undesirable, such as in case 2 where the elderly patient had chronic kidney disease.

Appropriate classification of patients with ulcers is important when selecting treatment and monitoring progress to healing from baseline. The University of Texas system is both flexible and descriptive and the SINBAD score is useful in predicting ulcer outcome (Ince et al, 2008). DFU classification provided a clear guide to the progression of healing in case 1, for example, with the SINBAD score improving from four to two and the Texas grade from B3 to A1.

Conclusion

In the case studies described, the addition of octenilin®, with its broad-spectrum antimicrobial action, to the patients' treatment regimens contributed to the DFUs progressing to healing. Used in conjunction with debridement and systemic antibiotics as part of biofilm-based wound care, octenilin® irrigation solution, octenilin® wound gel and octenisan® wash mitts are capable of managing bioburden in chronic wounds and aiding healing. ■

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