



# Use of Highly Purified Synthetic Calcium Sulfate Impregnated With Antibiotics for the Management of Diabetic Foot Ulcers Complicated by Osteomyelitis

Diabetes Care 2015;38:e79–e80 | DOI: 10.2337/dc14-3100

Rajesh M. Jogle,<sup>1</sup> Deborah E. Modha,<sup>2</sup> Kaustubh Nisal,<sup>1</sup> Rachel Berrington,<sup>1</sup> and Marie-France Kong<sup>1</sup>

Diabetic foot osteomyelitis can be managed medically with systemic antibiotics alone or surgically by removing infected bone (1,2). Localized delivery of antibiotics directly to the bone offers a way to achieve an optimal concentration of chosen antibiotics at the site of infection. Antibiotics have been delivered directly into wounds using various vehicles, such as methyl methacrylate and absorbable antibiotic-impregnated gauze, in other clinical settings (3). Highly purified synthetic (HPS) calcium sulfate-based antibiotic therapy offers advantages of being biodegradable, having predictable elution characteristics to deliver antibiotics in concentrations far exceeding the minimum inhibitory concentration of the infecting organism, and having an ability to fill dead space (4,5). We report our experience of using HPS calcium sulfate impregnated with vancomycin and gentamicin in the management of osteomyelitis in the diabetic forefoot.

Over 18 months, 20 patients (15 males) with diabetic foot ulcers attending our multidisciplinary foot clinic were treated with minimal surgical intervention and local delivery of vancomycin and gentamicin using HPS calcium sulfate. The median age was 59 years (range 25–74). Mean HbA<sub>1c</sub> was 8.4% (68 mmol/mol) (range 6.5–11% [48–97 mmol/mol]). All patients had forefoot ulcers with underlying osteomyelitis

(all confirmed radiologically and 11 had earlier bone samples confirming osteomyelitis) and had failed to respond to regular wound debridement, systemic antibiotics, and off-loading. Eighteen patients had no evidence of peripheral vascular disease. Median ulcer duration prior to intervention was 11.5 weeks (range 3.6–104). Vancomycin and gentamicin were selected as the antibiotics of choice based on in vitro sensitivities of isolates obtained from diabetic foot infections in our laboratory. All surgical procedures were carried out by the same individual. HPS calcium sulfate powder was mixed with 1 g of vancomycin hydrochloride and 80 mg of gentamicin sulfate to form pellets. Sequestrae were excised, the bone was fenestrated and packed with the pellets, and primary closure was carried out. The ulcer was defined as fully healed when epithelization was complete and the intervention was considered successful when there was no reoccurrence for 12 months.

Intraoperative bone samples showed all the gram-positive isolates were sensitive to vancomycin. All but two gram-negative isolates were sensitive to gentamicin. Two patients grew *Candida* species in addition to their bacterial isolate and received an oral antifungal agent postoperatively. The need for postoperative antibiotics was decided individually as per clinical assessment

and the median duration was 2 weeks (range 0–9). All patients achieved healing with a median time span of 5 weeks and no recurrence within 12 months after intervention (Fig. 1).

We have found this technique to be safe and effective for the treatment of forefoot diabetic osteomyelitis and believe that this has prevented more radical surgery. No adverse reactions were noted in these patients or indeed in any of our additional patients over the past 36 months. We now also offer this treatment to patients with midfoot and calcaneal osteomyelitis.



Figure 1—Foot X-ray of one of the patients 16 months postoperatively.

<sup>1</sup>Department of Diabetes, University Hospitals of Leicester NHS Trust, Leicester, U.K.

<sup>2</sup>Department of Microbiology, University Hospitals of Leicester NHS Trust, Leicester, U.K.

Corresponding author: Marie-France Kong, marie-france.kong@uhl-tr.nhs.uk.

© 2015 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered.

We acknowledge limitations of our case series given the small number of patients and suggest a randomized controlled trial to further evaluate this technique.

---

**Acknowledgments.** The authors thank Professor William Jeffcoate (Foot Ulcer Trials Unit, Nottingham University Hospitals Trust, U.K.) for his helpful comments and time spent reviewing the manuscript.

**Duality of Interest.** D.E.M. received sponsorship from Biocomposites, the manufacturer of Stimulan (purified synthetic calcium sulfate), to attend a microbiology and infectious disease

conference. No other potential conflicts of interest relevant to this article were reported.

**Author Contributions.** R.M.J. wrote the manuscript. D.E.M. researched data and reviewed and edited the manuscript. K.N. and M.-F.K. reviewed and edited the manuscript. R.B. researched data and reviewed the manuscript. D.E.M. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

## References

1. Game FL, Jeffcoate WJ. Primarily non-surgical management of osteomyelitis of the foot in diabetes. *Diabetologia* 2008;51:962–967

2. Aragón-Sánchez FJ, Cabrera-Galván JJ, Quintana-Marrero Y, et al. Outcomes of surgical treatment of diabetic foot osteomyelitis: a series of 185 patients with histopathological confirmation of bone involvement. *Diabetologia* 2008;51:1962–1970

3. Gogia JS, Meehan JP, Di Cesare PE, Jamali AA. Local antibiotic therapy in osteomyelitis. *Semin Plast Surg* 2009;23:100–107

4. Bistolfi A, Massazza G, Vernè E, et al. Antibiotic-loaded cement in orthopedic surgery: a review. *ISRN Ortho* 2011;2011290851

5. Gauland C. Managing lower-extremity osteomyelitis locally with surgical debridement and synthetic calcium sulfate antibiotic tablets. *Adv Skin Wound Care* 2011;24:515–523