The diabetic foot is a common site of infections that frequently result in significant patient morbidity and mortality. Antibiotic treatment is an important component of therapy along with local wound care and pressure offloading. First generation cephalosporins are usually employed for mild infections, whereas more serious cases usually require broad-spectrum IV antibiotics.

In the authors' center, the first generation cephalosporin cephalexin is the usual first line therapy for mild infections, whereas an oral combination of a...
quinolone with clindamycin has been the preferred second line regimen. Hospitalized patients with limb-threatening infections traditionally received IV piperacillin/tazobactam with vancomycin added in cases where methicillin resistant Staphylococcus aureus (MRSA) infection is proved or suspected.

Recently, ertapenem has entered use as primary therapy for moderate to severe diabetic foot infections. Use is based on the study by Lipsky et al who showed equal efficacy of ertapenem and piperacillin/tazobactam. Advantages of this antibiotic include cost effectiveness and once-daily dosing. To the authors’ knowledge the use of ertapenem as salvage therapy in diabetic foot infections unresponsive to traditional antibiotics has not been reported. This prospective study recounts the authors’ experience with this therapy.

Material and Methods
Sixty consecutive patients hospitalized in the authors’ general medicine ward were included in the study. Twenty patients were subsequently excluded from the analysis because of growth of organisms known to be resistant to ertapenem: MRSA, Enterococcus faecalis, or Pseudomonas aeruginosa. All patients were referred from the authors’ hospital diabetic foot clinic after failure of treatment with cephalexin as first line therapy, and a combination of ciprofloxacin and clindamycin as the second line therapy for their diabetic foot ulcers. All ulcers were of IDSA classification moderate or severe.

All patients underwent full evaluation including complete physical examination, baseline laboratory studies, blood cultures; deep wound cultures (obtained from the depth of the ulcer by swabs) and x-rays ruled out osteomyelitis. Anaerobic wound cultures were not obtained.

All patients received standard wound care, which included daily cleansing of wounds with gauze and normal saline, local debridement when clinically indicated, and pressure-off loading using specialized footwear. All patients were then treated with ertapenem 1 g daily/IV. Individuals with soft tissue infections continued antibiotic therapy until significant clinical improvement (resolution of fever, leukocytosis, surrounding erythema and purulent discharge) or ulcer healing. Patients with osteomyelitis continued their therapy on an outpatient basis (home IV ertapenem therapy) for a total of 6–9 weeks according to clinical response.

Results
Characteristics of the 40 individuals with ertapenem-sensitive organisms are shown in Table 1. There were 30 men and 10 women with a mean age of 65 ± 2 years. Thirty patients had moderate and 10 individuals had severe ulcers according to the IDSA classification. Ten patients had fever on admission and all had infection of soft tissue only. Soft tissue infection alone was present in 28 individuals, whereas 12 patients had additional evidence of osteomyelitis. The mean duration of ulceration prior to study entry was 8 ± 2 weeks in the soft tissue group and 7 ± 3 weeks in the osteomyelitis cohort. Twenty percent of patients were insulin dependent and 80% were treated with oral agents only. Mean HgbA1C level was 8.5% ± 2% with a range of 6.3%–15%.

Mean duration of antibiotic treatment was 30 ± 8 days in patients with soft tissue infections and 60 ± 15 days in those with osteomyelitis. Mean hospital stay was 7 ± 2 days for individuals with soft tissue infections alone and
10 ± 2 days for those with concomitant osteomyelitis. Thirty patients completed their treatment in-hospital while 10 patients completed their antibiotic course as outpatients with home IV therapy. None of the patients in the study cohort died. One patient with osteomyelitis failed treatment and underwent amputation of the affected limb. The organisms isolated are shown in Table 2.

Of the 28 soft tissue only patients, all had a favorable response and significant clinical improvement with defervescence and decreased leukocytosis. Of the 12 patients with concomitant osteomyelitis, 3 individuals (25%) required subsequent surgery due to treatment failure while the remaining 9 patients successfully completed 6 weeks of ambulatory ertapenem treatment.

Discussion

This prospective study describes an experience using IV ertapenem for the treatment of moderate to severe diabetic foot ulcers (IDSA moderate to severe) as salvage therapy after treatment failure with both oral cephalexin and a combination of oral ciprofloxacin and clindamycin. Standard practice at the authors’ facility had been to use piperacillin/tazobactam as salvage therapy in these individuals in combination to local ulcer care and off-loading. Following the work of Lipsky et al., it was decided to assess the efficacy of IV ertapenem in this role. All patients were referred to the authors’ general medical ward from the diabetic foot clinic after failure of oral antibiotic treatment.

Ertapenem is a broad spectrum antibiotic which covers 98% of all gram-negative, gram-positive, and anaerobic bacteria present in the flora of diabetic foot ulcers. Intravenous ertapenem was used if the cultured organisms were sensitive to this agent or in case of no growth of organisms in individuals previously treated with antibiotics.

Patients with soft tissue infections alone were discharged after improvement and followed in the authors’ diabetic foot clinic. Individuals with osteomyelitis continued therapy with IV once-daily ambulatory IV antibiotics.

In this study ertapenem as a single agent was efficacious, cost effective, and easy to administer. As reported by others, we saw only mild side effects such as neutropenia, thrombocytopenia, and two patients who developed a confused mental state, which resolved only after stopping the antibiotic.

Conclusion

Ertapenem is an efficacious, easy to use, and a time and cost saving antibiotic for the treatment of diabetic foot infections that have failed therapy with traditional antibiotics. Its use should be strongly considered in individuals with nonhealing diabetic foot ulcers.

References