Cost avoidance using linezolid for methicillin-resistant Staphylococcus aureus infections in a specialist diabetes foot clinic

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Objectives: An audit was performed to determine whether linezolid (Zyvox, Pharmacia Limited, Sandwich, UK) was being used in accordance with local guidelines and if this had an effect on admissions for diabetes foot ulceration.

Methods: Seven hundred and four patient records from 2005 to 2010 in the Diabetes Foot Clinic, Royal Infirmary of Edinburgh were audited for methicillin-resistant Staphylococcus aureus (MRSA) infections, admissions and antibiotic use.

Results: Seventeen percent (n=119) of patients had proven MRSA infections. Of these, 28% (n=33) were prescribed linezolid, 94% (n=31) for up to 14 days and none for 28 days. Eight (24%) had repeated courses. Ninety-one percent (n=30) either avoided admission or were discharged early with resolution of infection. Four out of 33 patients had reversible blood abnormalities. The total cost for linezolid over this period was £58000. However, 420 bed days, costing £500/day, were avoided, producing a total saving of £210000 on inpatient costs.

Conclusions: Linezolid guidelines reduced lengths of stay, inpatient costs and overuse of this expensive but effective treatment.

Keywords: antibiotics, foot ulceration, MRSA, outpatient therapy

Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) infection is a significant problem in the management of diabetes foot ulceration with reported prevalence rates of up to 47% of Gram-positive isolates.1 These infections can lead to admissions, and, if uncontrolled, to limb loss.2 Therefore, it is imperative that effective antibiotic therapy is implemented to minimize complications. However, oweruse, and misuse, of antibiotics is also common in diabetes foot clinics.3 The antibiotic linezolid (Zyvox, Pharmacia Limited, Sandwich, UK) is the first oxazolidinone antibiotic and is licensed in the UK for complicated skin and soft tissue infections (SSTIs) including those caused by MRSA.4 It is equally effective by intravenous and oral routes. It is relatively expensive as a daily cost in comparison with other antibiotics, but is said to be cost-effective in clinical use.5-6 Previous audits in our hospital have found that most admissions related to the diabetic foot were for uncontrollable infection, were Infectious Diseases Society of America (IDSA) grade 3 (moderate) or 4 (severe)2 and that more than 60% were MRSA infections requiring treatment with intravenous vancomycin or teicoplanin.3 The average length of stay for these patients was 20 days.

Linezolid has been used to provide oral follow-on treatment for serious diabetes foot infections due to susceptible organisms, but its use has been questioned by pharmacists, due to the high daily cost, and limited by microbiologists, due to the fear of increasing bacterial resistance to linezolid.7,8

Methods

Linezolid usage was audited to determine the effect of treatment in routine clinical practice in a large multidisciplinary diabetes foot service in a teaching hospital.

A case record review was performed of 704 patients attending the Diabetes Foot Clinic, Royal Infirmary of Edinburgh, Scotland, UK from 2005 to 2010. Admission rates, microbiological culture results and antibiotic usage were recorded. As per current recommended guidance for diabetes foot infections, microbiological samples were only collected where clinical infection was suspected and were mainly tissue samples or deep swabs of purulent exudate.9

Linezolid usage was deemed appropriate if it was used within the license as defined in the summary of product characteristics.4 The audit standards for treatment were that there was proven MRSA SSTI without osteomyelitis and no patient received more than 28 days of treatment as a single continuous treatment course, although repeat courses were allowed. Our unit policy also restricted linezolid to outpatients with no suitable oral alternative. Inpatients were not to be treated with linezolid as the local antibiotic policy, adapted from Leese et al.,9 has other, less expensive, intravenous alternatives.
Admissions were defined as a period of inpatient hospital stay. Admissions were classed as avoided if the use of oral linezolid as an outpatient was chosen rather than admission to hospital for intravenous antibiotics. Reductions in length of stay were calculated as the difference between the length of hospital admission for patients discharged on linezolid treatment and the inpatient duration of stay for patients with standard treatment.

Blood monitoring was performed during linezolid treatment. Any blood abnormalities developing during treatment were followed until resolution.

Resolution of infection was a clinical decision based upon the end of systemic symptoms or downgrading of the ulcer to grade 1 or 2 infection by the IDSA classification. Further microbiological samples for culture were not collected unless there was a clinical indication to do so.

**Results**

Of the 704 patients, 17% (n = 119) had confirmed MRSA SSTI and of these 28% (n = 33) were prescribed linezolid; 8 patients (24%) had two courses. All were IDSA grade 3 (moderate) or 4 (severe). In 94% of patients (n = 31) linezolid was prescribed for a maximum of 14 days and no patient had more than 28 days as a course. However, 4/33 patients had reversible blood abnormalities including anaemia during this period. The blood abnormalities all resolved on cessation of linezolid treatment. Three of the patients with blood disorders were transferred to other antibiotics. Two had improved clinical infection levels, but required further treatment and were managed with oral alternatives, namely doxycycline and co-trimoxazole. In one patient the infection had completely resolved and one was admitted to hospital for intravenous vancomycin.

In 91% of patients treated with linezolid (n = 30) admission was either avoided or early discharge facilitated with cessation of intravenous antibiotic therapy with resolution of infection. Sixteen patients were not admitted and the remaining 14 were discharged after a mean length of stay of 8 days. Over this period the total cost for linezolid was calculated as £58 000. Compared with the previous length of stay (mean of 20 days) over 420 bed days were avoided at a basic hotel cost of £500/day resulting in an estimated inpatient cost saving of £210 000.

Three patients, including one of the blood abnormality patients, had to be admitted despite linezolid treatment, spending a total of 62 days in hospital at a nominal cost of £31 000. This reduced the inpatient saving to £179 000. The net saving, allowing for linezolid costs, was estimated at £121 000 for hotel costs alone. There were no major amputations in the linezolid group.

**Discussion**

Linezolid is not a first-line treatment for diabetes foot infections and should be used where no alternative oral antibiotic is available and to avoid or minimize inpatient admission. Our audit suggests that devising guidelines for linezolid use can limit expenditure whilst producing excellent clinical outcomes. Linezolid treatment was considered effective in 91% of patients as gauged by our criteria of avoiding admission for further treatment and clinical resolution of infection. This is better than the 76.8% treatment success rate reported by Vardakas et al., and is based upon clinical criteria rather than microbiological cure. The rate of anaemia is similar to the rate quoted in the product literature and was reversible on withdrawal of the treatment. On this basis, linezolid, an expensive but efficacious treatment, should be considered as an effective treatment to reduce lengths of stay and reduce inpatient costs in the management of MRSA diabetic foot infections.

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**Transparency declarations**

None to declare.

**Author contributions**

This audit was designed by J. E. M. and M. J. Y. in conjunction with G. H. who performed the main data collection and initial analysis. M. J. Y. is the guarantor for this paper.

**References**