Original article

EFFICACY AND SAFETY OF LINEZOLID AND AMINOPENICILLIN/BETA LACTAMASE INHIBITORS FOR TREATMENT OF PATIENTS WITH DIABETIC FOOT ULCER: A COMPARATIVE STUDY

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Abstract

Aim:

To compare the efficacy and safety of Linezolid and Aminopenicillin / beta lactamase inhibitors for treatment of patients with diabetic foot ulcer

Materials and methods:

Prospective comparative study was conducted among 60 consecutive patients with diabetic foot ulcer admitted in Department of General surgery of Government Hospital Sarwal, Jammu, India. Patients were randomized to receive both (Group A) linezolid and (Group B) ampicillin-sulbactam (1.5–3 g q6h iv), or amoxicillin-clavulanate. The duration of treatment was 7 days but not >28 days.

Results: Among 60 patients, the clinical efficacy and safety were comparable for patients in both the groups.. Mean age of (group A) 54.29±3.59 and (group B 55.01±2.19). Drug-related adverse events were significantly more common in the linezolid group, but they were generally mild and reversible.

Conclusion:

Study demonstrates that therapy with linezolid is at least as effective as aminopenicillin and b-lactamase inhibitors the most frequently used agents among patients with of diabetic foot ulcer.

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Introduction

Diabetic foot infections are often polymicrobial in nature; however, aerobic Gram-positive bacteria that are multidrug sensitive and multidrug resistant (MRSA, VRE) are frequent causative pathogens. Foot ulcers occur in 5–10% of the diabetic population and are associated with increasing morbidity and mortality, with up to 3% having had a lower limb amputation. Infected diabetic foot ulcers are the commonest cause of admission for diabetic patients, accounting for about 20% of diabetes-related admissions.[1]

Linezolid is a novel oxazolidinone agent that has demonstrated activity against antibiotic-susceptible and antibiotic-resistant gram-positive organisms.[2,3] The oral form of linezolid is 100% bioavailable, allowing for an early switch from i.v. to oral therapy.[4,5]

Linezolid has a unique mechanism of action whereby it selectively binds to the 50S ribosomal unit and prevents formation of the initiation complex. This action is thought to prevent cross-resistance with other antimicrobial agents.[6]

linezolid is expensive, and some clinicians prefer to reserve it for treatment of documented antibiotic-resistant organisms. The aminopenicillin/ b-lactamase inhibitors ampicillin-sulbactam and amoxicillin- clavulanate are broad-spectrum antibiotics that are among the most widely used agents for these infections.[7] Due to paucity of the data in the previous literature the present study was conceived with the

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Key Words:
Aminopenicillin, b-lactamase inhibitors, Linezolid, diabetic foot ulcer

aim to compare the efficacy and safety of linezolid with that of aminopenicillin/beta lactamase inhibitors for treatment of patients with diabetic foot ulcer.

Material & Methods

Study Design

A Prospective comparative study was conducted among 60 consecutive patients with diabetic foot ulcer admitted in Department of General surgery of Government Hospital Sarwal, Jammu, India.

Ethical approval and Informed consent

The study protocol was reviewed by the Ethical Committee of the Hospital and granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained.

Inclusion Criteria

- Patients above 18 years of age and willing to participate in study.
- Patients Diabetes Mellitus (diagnosed on the basis of the American Diabetes Association's definition)[8] and foot ulcers were potentially eligible.

Exclusion Criteria

- Patients who are not willing to give written informed consent
- Patients with critical ischemia of the affected limb
- Patients on antibiotic therapy

Sample selection

The sample size was calculated using a prior type of power analysis by G* Power Software Version 3.0.1.0 (Franz Faul, Universitat Kiel, Germany). The minimum sample size of each group was calculated, following these input conditions: power of 0.80 and P 0.05 and sample size arrived were 60 patients i.e 30 per group.

Methodology

Patients were randomized to receive either linezolid and ampicillin-sulbactam (1.5–3 g q6h iv), or amoxicillin-clavulanate. The duration of treatment was 7 days but not >28 days.

Group-A

Patients received linezolid (600 mg q12 h either iv or po).

Group-B

Patients received ampicillin-sulbactam (1.5–3 g q 6h iv), or amoxicillin-clavulanate (500–875 mg every 8–12 h po).

Methodology

Detailed history of the patients was obtained including the demographic, clinical and associated problems. Each patient provided a medical history and underwent a physical examination. The ulcer site was assessed for drainage, erythema, fluctuance, warmth, pain or tenderness, and induration.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages.

Results

Table 1: Demographic details of the study population

Variables	Group A	Group B
Gender		
Male	13 (52.0%)	14 (56.0%)
Female	12 (48.0%)	11 (44.0%)
Age (Years)		
Mean±SD	54.29±3.59	55.01±2.19
Ulcer Size		
<2.5 cm	13 (52.0%)	11 (44.0%)
>2.5 cm	12 (48.0%)	14 (56.0%)
Duration of ulcer		
< 5 months	14 (56.0%)	13 (52.0%)
> 5 months	11 (44.0%)	12 (48.0%)
Ulcer site		
Fore foot	8 (32.0%)	7 (28.0%)
Mid foot	11 (44.0%)	10 (40.0%)
Hind foot	6 (24.0%)	8 (32.0%)

Table 2: distribution of adverse effects

Adverse Effects	Group A N=25	Group B N=25
Diarrhea	8 (32.0%)	7 (28.0%)
Nausea	4 (16.0%)	3 (12.0%)
Vomiting	3 (12.0%)	3 (12.0%)
Abdominal Pain	2 (8.0%)	2 (8.0%)
Anemia	2 (8.0%)	2 (8.0%)
Rash	2 (8.0%)	1 (4.0%)

Table 3: treatment outcome at follow-up

Outcome	Group A	Group B
Ulcer Healed	17 (68.0%)	14 (56.0%)
Ulcer not Healed	8 (32.0%)	11 (44.0%)

Discussion

Many organisms may cause foot infections in diabetic patients, but aerobic gram-positive cocci are the most frequent and virulent pathogens.[9,10] Thus, therapy for these infections requires an antibiotic active against staphylococci and streptococci.

The increasing prevalence of antibiotic resistance among these species (especially MRSA) is disconcerting, because infections with these organisms may have a worse outcome and necessitate selecting from a smaller group of antibiotics.[11,12] Traditionally, diabetic foot infections have been treated intravenously to assure adequate antibiotic concentrations, especially in patients with severe infection or peripheral vascular disease .[13] Newer agents (e.g., linezolid and the fluoroquinolones) with therapeutically equivalent intravenous and oral formulations allow initial treatment to be oral for persons who are clinically stable and allow an early switch from intravenous to oral antibiotics for those who are responding to therapy.[14]

The few previous antibiotic trials of diabetic foot infections have differed in their designs, drug regimens, efficacy end points, and types and severities of infections included, making their results difficult to compare.[15] Overall, however, outcomes with various antibiotics have been similar, with no one drug or combination being superior.[16]

Linezolid was associated with more drug-related adverse events than were aminopenicillin/the b-lactamase inhibitors, but most of these events were mild, reversible, and did not require drug discontinuation. Few adverse effects like Anemia might associated with linezolid therapy were related to the duration of therapy

Conclusion

This study demonstrates that therapy with linezolid is at least as effective as aminopenicillin and b-lactamase inhibitors (plus vancomycin for treatment of MRSA), the most frequently used agents among patients with various types of diabetic foot infections. There is less clinical experience with linezolid, and it was associated with more adverse effects; however, it has excellent pharmacokinetic properties and offers additional coverage against drug-resistant gram-positive organisms. Linezolid would be appropriate to consider for patients with diabetic foot infections that are known or suspected to be caused by MRSA.

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