



An Approach to Linezolid and Vancomycin against Methicillin Resistant Staphylococcus Aureus

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Abstract

In vitro activities of linezolid and vancomycin which were evaluated against methicillin resistant Staphylococcus aureus (MRSA). One hundred clinical isolates of MRSA were collected. The minimum inhibitory concentrations (MICs) of linezolid and vancomycin were determined by the Epsilon-test method. The results showed 100 percent susceptibility of linezolid and vancomycin against MRSA isolates. According to the MIC₉₀ values, linezolid was the most active agent. The heterogeneity of methicillin resistance determined by the dropped plate count revealed homogeneous resistance to methicillin of all isolates.

Introduction

Hospital acquired infections due to methicillin resistant strains of Staphylococcus aureus (MRSA) have been reported worldwide. Among the antibiotics used for gram positive organism, vancomycin is generally recommended as the drug of choice in treating serious MRSA infections. However, since reporting of vancomycin-intermediate Staphylococcus aureus (VISA) from Japan, vancomycin-resistant Staphylococcus aureus (VRSA) from the US, potential adverse effects and relatively high cost of vancomycin, other alternative antibiotics are being investigated. Linezolid has a broad spectrum of activity against gram positive bacteria including drug-resistant strains. Linezolid inhibits bacterial protein synthesis by binding to the 50 S ribosomal subunit near to the interface with the 30S subunit, causing inhibition of 70S initiation complex formations. It is active against both methicillin sensitive S. aureus (MSSA) and MRSA, and inhibits virtually all strains at a concentration of 4 mg/L or less. This study purposed to evaluate the in vitro activity of linezolid compared to vancomycin which have been used in Maharaja Agrasen Medical College, Agroha, Hisar, Haryana, India.

Methods

Bacterial isolates

A total of 100 clinical isolates obtained from patients hospitalized in different clinical wards of Maharaja Agrasen Medical College, Agroha, Hisar, Haryana, India were studied. Each isolate represented a single isolation from each patient. The identification of isolates was confirmed by colonial morphology, catalase test, coagulase test and oxacillin disc diffusion test, as described by the Clinical and Laboratory Standards Institute (CLSI).⁹

Susceptibility testing

Both of the antimicrobial agents, linezolid and vancomycin were tested. The MIC of each isolate was determined by using the Epsilon-test (E-test) method. S. aureus ATCC 29213 was used as a quality control. The MICs of both of the drug were reported as an MIC range, MIC₅₀, and MIC₉₀. The MIC₅₀ and MIC₉₀ were expressed as the nearest log₂ concentration of antibiotic that inhibits 50 percent and 90 percent of the strains.¹⁰ The percentage of susceptibility to MRSA was obtained by using the following breakpoint concentrations: linezolid \leq 4 mg/L and vancomycin \leq 4 mg/L¹¹

Detection of heterogeneity and homogeneity of MRSA

The heterogeneity of methicillin resistance was determined by the dropped plate count method.¹² The number of colonies of MRSA on 50 mg/L-methicillin-containing and methicillin-free plates incubated at 37°C were counted, and interpreted as the efficacy of plating (EOP). EOP was defined as the ratio of the colony forming unit (CFU) on methicillin-containing plates and the CFU on methicillin-free plate. A strain was considered heterogeneity of methicillin-resistance if the EOP was less than 0.1, and homogeneity of methicillin resistance when the EOP was between 0.1 and 1.

Results

The specimens of the 100 MRSA isolates were pus (40), Urine (40) and body fluid (20). The activities of

linezolid and vancomycin against all isolates of MRSA are shown in Table. All isolates were susceptible to linezolid and vancomycin. All isolates had vancomycin MIC < 3 mg/L, and 57 percent were inhibited by vancomycin at concentration of 2-3 mg/L. According to the MIC₉₀ values, linezolid was the most active agent. Phenotypic expression of all isolates showed homogeneous resistance to methicillin with the efficacy of plating of 0.12-1.

Discussion

This study demonstrates that linezolid has an excellent in vitro activity against MRSA. In term of MIC₉₀ values, linezolid is more potent than vancomycin. This high activity of linezolid against MRSA is consistent with various reports^{4,7}. All isolates of MRSA in this study were susceptible to ≤ 1mg/L of linezolid. The MIC of linezolid for MRSA is 0.023-0.75 mg/L whereas the MIC of vancomycin is 0.5-3 mg/L.

Linezolid has a unique mechanism of inhibitory action on the bacterial protein synthesis. It displays in vitro activity against MRSA, vancomycin-resistant enterococci (VRE) and penicillin-resistant *S. pneumoniae* (PRSP). Clinical results showed that linezolid and vancomycin have similar clinical efficacy. Linezolid therapy was shown to be successful for MRSA infection in patient with a severe allergic reaction to vancomycin.¹² Plasma concentrations of intravenous and oral linezolid are equivalent, with average concentration exceeding the MIC for susceptible pathogens throughout the 12 hours dosing interval.⁵ In our study, the MIC range of vancomycin was 0.5-3 mg/L, with a significant proportion of MIC range of 2-3 mg/L. There is no significant difference from the previous MRSA isolates during 2008-09. And all isolates showed homogeneous resistance to methicillin. In conclusion, MRSA isolates in Maharaja Agrasen Medical College, Agroha, Hisar, Haryana, India were still susceptible to vancomycin. Linezolid was found to be very active against the MRSA strains and appears to be a potentially useful drug for MRSA infections.

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Illustrations

Illustration 1

Table

MIC range, MIC₅₀, MIC₉₀ (mg/L) and percentage of susceptibility of 100 clinical isolates of MRSA against Linezolid and Vancomycin

Antimicrobial Susceptibility agents	MIC Range	MIC ₅₀	MIC ₉₀	Susceptibility (%)	Breakpoint
Linezolid	0.023-0.75	0.25	0.5	100	≤ 4
≤ Vancomycin	0.5-3	1.5	2	100	4

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