Comparative Study of Teicoplanin vs Vancomycin for the Treatment of Methicillin-Resistant Staphylococcus aureus Bacteraemia

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Summary

Forty patients with methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia were randomised to receive either teicoplanin or vancomycin therapy to compare the clinical efficacy and safety of these glycopeptides. Treatment was successful in 17 (85%) of 20 patients who were randomised to the teicoplanin group, with 6 cures and 11 improvements, and in 15 (75%) of 20 patients randomised to the vancomycin group, with 8 cures and 7 improvements (p = 0.69). Microbiologically, all MRSA pathogens isolated were susceptible to both glycopeptides by the disc diffusion test. The mean zone of inhibition for teicoplanin was 18 ± 2mm (range 16 to 20mm) and 20 ± 2mm (range 16 to 24mm) for vancomycin. The minimum inhibitory concentration required to inhibit the growth of 90% of organisms in culture (MIC₉₀) for all MRSA isolates was 2.0 mg/L (range 0.5 to 4 mg/L) for teicoplanin and 2.0 mg/L (range 0.5 to 2 mg/L) for vancomycin. The microbiological eradication rate was 85% (17 of 20 isolates) for teicoplanin and 75% (15 of 20 isolates) for vancomycin. None of the failures were due to the emergence of resistant pathogens. Adverse reactions occurred in 19% of patients treated with teicoplanin and 60% of patients treated with vancomycin. There was no significant difference in the occurrence of skin rash (p = 0.60) or in elevation of aminotransferase (p = 0.18). However, nephrotoxicity was significantly greater in the vancomycin group than in the teicoplanin group (50 vs 9.5%, p < 0.05).

In conclusion, the results of this study demonstrate that teicoplanin appears to be a valuable alternative to vancomycin because it is as efficacious as vancomycin, has fewer adverse reactions, and is conveniently administered.
Infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is an increasing problem in many countries, and regardless of whether community-acquired or nosocomial in origin, is usually associated with high morbidity and mortality.[1-5] Options for the treatment of such serious infections are quite limited.[6-7] Only vancomycin has proved to be an effective therapy for infections caused by methicillin-resistant bacteria. In addition, vancomycin remains a major alternative for the treatment of Gram-positive bacterial endocarditis in penicillin-allergic patients.[8]

However, major disadvantages that have been reported with vancomycin include nephrotoxicity, ototoxicity,[9,10] and allergic reactions such as rash, ‘red man syndrome’, and drug fever.[11,12] Furthermore, vancomycin may only be administered by intravenous infusion and is usually given every 6 hours, although twice daily administration may be used for less severe infections.

Teicoplanin is a new glycopeptide antibacterial obtained as a fermentation product of *Actinoplanes teichomyceticus*, and is chemically related to the vancomycin-ristocetin group of antibacterials.[13] Teicoplanin has an antimicrobial spectrum that is very similar to that of vancomycin, including MRSA infections, but it has clear advantages over vancomycin in having a longer plasma half-life, which allows once daily administration, and it can be administered either intramuscularly or intravenously.[14-16] Teicoplanin has also been reported to be less toxic than vancomycin.[17,18]

The purpose of the present study was to compare the clinical results of a prospective randomised comparative study of teicoplanin versus vancomycin for the treatment of severe MRSA bacteraemia.

**Patients and Methods**

**Patients**

Patients over the age of 18 years admitted to the Veterans General Hospital-Taipei with clinical laboratory proven MRSA bacteraemia/septicaemia were enrolled consecutively into this study. All patients consented to the protocol, which was approved by the Pharmaceutical Institute, Veterans General Hospital-Taipei.

Exclusion criteria included a history of hypersensitivity to glycopeptides, pregnant or lactating women, acute and chronic renal failure (serum creatinine in excess of 2.5 g/L), and patients who had already received antibacterials active against MRSA infections.

**Antibiotic Regimens**

Patients were randomised according to a computer-generated randomisation code to receive either teicoplanin (provided by Marion Merrell Dow, Italy) or vancomycin (purchased from Eli Lilly, Indianapolis, USA). Patients randomised to teicoplanin received 400mg intravenously every 12 hours for the first 3 doses, then 400mg intravenously once a day, while patients randomised to vancomycin received 500mg intravenously every 6 hours. The protocol allowed for the concomitant administration of ceftazidime, aztreonam, piperacillin, ticarcillin, quinolones and/or metronidazole for the coverage of proven Gram-negative or anaerobic infections.

**Clinical and Bacteriological Assessments**

We reviewed the patients daily with regard to assessment of their clinical response to therapy and observed them for signs of adverse reactions, which were assessed on the basis of medical findings. Baseline laboratory tests, including complete blood cell count, platelet count, prothrombin time, partial thromboplastin time, direct Coombs’ test, urinalysis, and hepatic and renal function tests were performed and repeated during and after therapy.

Bacteriological assessment including blood culture, Gram stain and culture of the suspected site of infection were performed before treatment and repeated at days 3 and 7 and after discontinuation of therapy. All isolates of MRSA were detected by the agar screening test with Mueller-Hinton agar (Difco Laboratories Inc, Detroit, Michigan, USA) supplemented with 4% sodium chloride and containing oxacillin (6 mg/L) as recommended by