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Comparative Antibacterial Activity of Vancocin and Generic Vancomycin

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The in vitro antibacterial activity of generic vancomycin was compared with that of Vancocin (vancomycin hydrochloride; Eli Lilly & Co.) using macrotube dilution testing and subculture. There were no significant differences in MICs or MBCs of the two drugs when tested against a variety of recently isolated hospital pathogens.

Vancomycin is a tricyclic glycopeptide antibiotic that is derived from *Nocardia orientalis*. It is active against staphylococci, streptococci, penicillin-resistant diphtheroids, and *Clostridium difficile* (4). It is available as Vancocin (vancomycin hydrochloride; Eli Lilly & Co.) and Vancoled (Lederle Laboratories) and has been in clinical use for almost 30 years (5). Vancomycin is used extensively in penicillin-allergic patients and for the treatment of methicillin-resistant *Staphylococcus aureus* and *Staphylococcus epidermidis* infections (1). A generic form of vancomycin which is under investigation has physicochemical properties similar to those of Vancocin (R. P. Rapp, R. Diehl, N. De, A. Alan, and J. Kapoor, Abstr. Annu. Meet. Am. Soc. Hospital Pharmacists, abstr. no. P-56R, p. 147, 1986). There are no published data regarding the microbiological activity of generic vancomycin.

The purpose of this investigation was to determine the in vitro antibacterial activity of generic vancomycin and Vancocin against a variety of recently isolated hospital pathogens.

Macrotube dilution testing to determine MICs was performed in Mueller-Hinton broth according to recently revised standards of the National Committee for Clinical Laboratory Standards (2). Commercially available Vancocin and generic vancomycin obtained from the manufacturers (Eli Lilly & Co. and LyphoMed Corp., Inc., respectively) were used to prepare the stock and working solutions. The MIC was recorded as the lowest concentration of antibiotic that completely inhibited growth as detected by the unaided eye. All tests were run in duplicate, and both results were recorded.

To determine the MBCs, all tubes showing no growth at 24 h were vortexed and incubated at 37°C for 4 h. A 0.1-ml sample from each tube was then inoculated onto a Trypticase (BBL Microbiology Systems) soy blood agar plate and incubated at 35°C for 24 h. The MBC was recorded as the lowest concentration of antibiotic showing no growth on the plate at 24 h.

Thirty pathogens recently isolated from clinically infected patients were studied. These included five strains each of the following: methicillin-susceptible *S. aureus* (beta-lactamase positive), methicillin-resistant *S. aureus* (beta-lactamase positive), *S. epidermidis*, alpha-hemolytic streptococci, group B streptococci, and enterococci. Identification was performed by the clinical microbiology laboratory at the San Francisco General Hospital by standard procedures. Reference strain *S. aureus* ATCC 29213 was used as a control. This organism is a weak beta-lactamase producer with an acceptable quality control MIC range of 0.5 to 2.0 μg/ml (1).

Statistical analysis was performed using the Prophet Computer Resource (3).

The MICs and MBCs are shown in Table 1. With one exception (organism 19), the duplicates were within 1 $\log_2$ dilution. In no case were both duplicates more than 1 $\log_2$ dilution different for either the MIC or MBC between Vancocin and generic vancomycin.

With all isolates, the means, geometric means, medians, minimums, maximums, and ranges of MICs and MBCs of both drugs were virtually identical (Table 1). Analysis of the subgroups by organism type also revealed no differences. All pairwise comparisons between the two drugs were made using both the Newman-Keuls multiple-range test and the Friedman test. No significant differences were present ($P > 0.05$).

We conclude that the antibacterial activities of Vancocin and generic vancomycin are indistinguishable by macrobroth dilution testing. If the pharmacokinetics and toxicities of generic vancomycin and Vancocin are also comparable, then generic vancomycin can be considered a useful alternative for the treatment of susceptible pathogens.

Although the number of organisms used in this study was limited, strains representing each of the groups for which vancomycin is commonly used were included. We believe that it is unlikely that testing additional strains would reveal differences not detected in this preliminary study.

TABLE 1. MICs and MBCs of Vancocin and generic vancomycin

Organism and no.	MIC (μg/ml)[a]				MBC (μg/ml)[b]			
	Vancocin		Generic vancomycin		Vancocin		Generic vancomycin	
	Expt 1	Expt 2	Expt 1	Expt 2	Expt 1	Expt 2	Expt 1	Expt 2
Staphylococcus aureus (methicillin susceptible, beta-lactamase positive)								
1	2.0	2.0	2.0	2.0	8.0	8.0	4.0	8.0
2	1.0	1.0	2.0	2.0	8.0	16.0	16.0	8.0
3	1.0	1.0	2.0	2.0	8.0	8.0	16.0	16.0
4	1.0	1.0	1.0	1.0	8.0	4.0	4.0	4.0
5	1.0	1.0	1.0	2.0	4.0	4.0	4.0	8.0
Staphylococcus aureus (methicillin resistant, beta-lactamase positive)								
6	2.0	2.0	2.0	2.0	4.0	4.0	4.0	8.0
7	2.0	1.0	2.0	1.0	8.0	8.0	8.0	4.0
8	4.0	2.0	2.0	2.0	16.0	8.0	8.0	16.0
9	2.0	2.0	2.0	1.0	8.0	16.0	16.0	16.0
10	4.0	2.0	1.0	2.0	16.0	16.0	8.0	16.0
Staphylococcus epidermidis								
11	8.0	8.0	8.0	4.0	16.0	32.0	16.0	32.0
12	2.0	2.0	2.0	2.0	8.0	8.0	4.0	8.0
13	4.0	4.0	2.0	2.0	32.0	16.0	16.0	16.0
14	2.0	2.0	2.0	2.0	8.0	8.0	16.0	16.0
15	1.0	1.0	2.0	1.0	8.0	8.0	4.0	4.0
Alpha-hemolytic streptococci								
16	0.1	0.1	0.1	0.1	1.0	1.0	1.0	1.0
17	1.0	0.5	1.0	0.5	16.0	8.0	8.0	8.0
18	0.1	0.1	0.1	0.1	1.0	1.0	1.0	1.0
19	0.25	0.1	0.25	0.1	2.0	1.0	2.0	1.0
20	0.25	0.25	0.25	0.25	4.0	2.0	4.0	4.0
Group B streptococci								
21	1.0	1.0	1.0	1.0	8.0	4.0	8.0	16.0
22	1.0	0.5	0.5	0.5	8.0	4.0	8.0	16.0
23	0.5	1.0	2.0	1.0	16.0	8.0	4.0	8.0
24	1.0	1.0	1.0	1.0	16.0	16.0	8.0	8.0
25	1.0	1.0	1.0	1.0	8.0	8.0	8.0	16.0
Enterococci								
26	4.0	4.0	4.0	4.0	16.0	16.0	16.0	16.0
27	1.0	1.0	1.0	1.0	16.0	16.0	8.0	8.0
28	8.0	8.0	8.0	8.0	64.0	64.0	64.0	64.0
29	1.0	1.0	1.0	1.0	8.0	8.0	16.0	8.0
30	1.0	1.0	1.0	1.0	8.0	8.0	4.0	8.0
Staphylococcus aureus control (ATCC 29213)	1.0	1.0	2.0	1.0	16.0	16.0	16.0	16.0
Mean	1.91	1.73	1.85	1.60	11.87	11.13	10.32	12.23
Median	1.00	1.00	2.00	1.00	8.00	8.00	8.00	8.00
Geometric mean	1.21	1.07	1.23	1.07	8.56	7.48	7.15	8.56

[a] Minimum MIC, 0.10 μg/ml; maximum MIC, 8.00 μg/ml; range, 7.90 μg/ml.
[b] Minimum MBC, 1.00 μg/ml; maximum MBC, 64.00 μg/ml; range, 63.00 μg/ml.

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