ALPS

EVALUATION OF LINEZOLID POTENCY ON GRAM-POSITIVE COCCI IN AN AUSTRIAN MULTI-CENTER STUDY

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Revised Abstract

17 laboratories participated in a multi-centre study in Austria to assess the in vitro activity of linezolid, vancomycin, teicoplanin, oxacillin, penicillin G, gentamicin, erythromycin, ampicillin and other antibiotics against gram-positive microorganisms. Strains were isolated from October 2000 until December 2000 from hospitalized and non-hospitalized (only for pneumococci) patients requiring antibiotic treatment. 798 strains from blood, sputum, pus, CSF and nose swab (S. aureus only) were included. MICs were obtained with the E-test. BHI agar and an inoculum of 2.0 McFarland was used for staphylococci and enterococci (glycopeptides only) to support a better growth and clear recognition of hetero-resistant colonies. The NCCLS method was used for all other testing. Results are depicted in Table 2.
Conclusion: Linezolid was 6-fold more active than vancomycin against CNS and 10-fold more active than teicoplanin against CNS. Linezolid was 3-fold more active than teicoplanin and vancomycin against *S.aureus* and 2-fold more active than vancomycin against enterococci. Linezolid has a good potential to treat infections caused by Gram-positive cocci successfully.

Introduction

Gram-positive bacteria have returned as leading cause of infection. In most parts of the world many of these infections are due to multi-drug resistant gram-positive organisms for example methicillin resistant *Staphylococcus aureus* (MRSA), methicillin resistant *Staphylococcus epidermidis* (MRSE), vancomycin-resistant enterococci (VRE) and penicillin non-susceptible *Streptococcus pneumoniae*.
Antibiotic resistance is a complicating factor in the treatment of infected patients. New treatment strategies and new antimicrobial agents can help to cope with this problem.
Linezolid is the first antibiotic of the new class of oxazolidinones. Its spectrum comprises all aerobic Gram-positive bacteria, including MRSA, MRSE, VRE and penicillin-resistant *Streptococcus pneumoniae*.

Aim of the study

To evaluate the in-vitro antibacterial activity of linezolid in comparison to other relevant antibiotics against gram-positive cocci.

Materials and Methods

Study design

17 Medical Microbiology Laboratories from Austria (Fig.1) participated in this multi-centre study.

Bacterial isolates

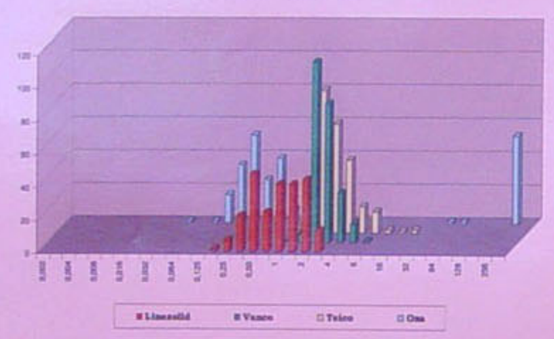
Between October 2000 until December 2000 each laboratory included 10 strains each of *S. aureus*, coagulase-negative staphylococci (CNS), enterococci and *S. pneumoniae*. Strains were isolated from hospitalized and non-hospitalized (only for pneumococci) patients requiring antibiotic treatment.
798 strains from blood, sputum, pus, CSF and nose swab (*S. aureus* only) were included. The strains were identified and tested by each participating laboratory.

MIC testing

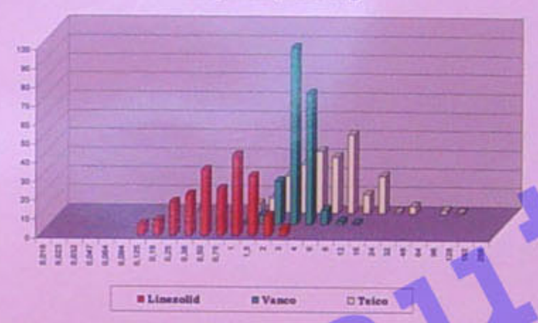
All isolates were tested on site by E-test® (AB-Biodisk) against following antibiotics (Table 1):

- Staphylococcus spp.: linezolid, vancomycin, teicoplanin, oxacillin, gentamicin.
- *S. aureus* was in addition also tested to clindamycin, rifampicin and fosfomycin.
- Enterococci were tested to teicoplanin, gentamicin and ampicillin.
- *S. pneumoniae* were tested against penicillin G, cefotaxime, erythromycin.

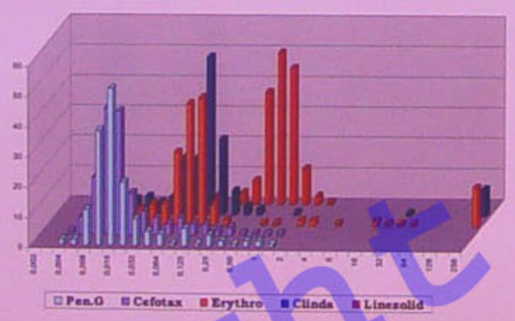
Staphylococcus aureus



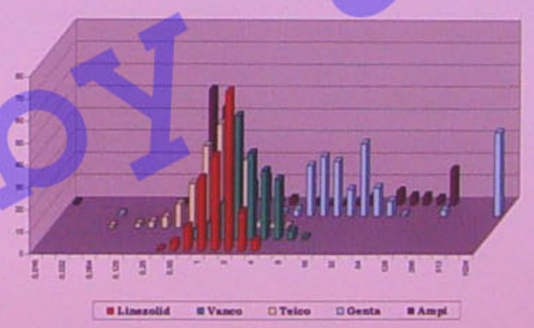
Staph. coagulase neg.



S. pneumoniae



Enterococcus spp



BHI agar and an inoculum of 2.0 McFarland was used for staphylococci and enterococci (glycopeptides only) to support a better growth and clear recognition of hetero-resistant colonies. The NCCLS method was used for all other testing.

Quality Assurance

For quality assurance reference strains of *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619 were included in each run of susceptibility testing. The study coordinator retested all resistant strains.
In addition, the macrolide resistance genes present in the erythromycin-resistant pneumococci and the glycopeptide resistance genes in the VRE were search about with a PCR method (Ref. 1 and 2).

Results and Discussion

The respective MIC 50 and MIC 90 for 241 strains of S. aureus, 204 strains of coagulase-negative staphylococci (CNS), 165 strains of pneumococci and 188 strains of enterococci are depicted in Table 2 and Diagrams 1, 2, 3 and 4.
S. aureus. Upon retesting we found 6 (2,4%) strains of *S. aureus* with vancomycin MIC ≥ 4 mg/L. We intend to submit these strains to population-analysis in order to confirm them as hetero-VISA.
CNS. 40 (19,6%) strains of CNS showed MIC to vancomycin ≥ 8 mg/L and teicoplanin ≥ 8 mg/L or teicoplanin MIC ≥ 12 mg/L.

Table 1.

Staphylococci		
Oxacillin	Mueller Hinton-agar + 2% NaCl	0,5 McFarland 24-48 h
Vancomycin	BHI-agar	2 McFarland 48 h
Teicoplanin		
Linezolid Gentamicin Clindamycin Levofloxacin Rifampicin Fosfomycin	Mueller Hinton-agar + 2% NaCl	0,5 McFarland 24 h
Enterococci		
Vancomycin Teicoplanin	BHI-agar	2 McFarland 48 h
Linezolid Gentamicin Ampicillin	Mueller Hinton-agar + 2% NaCl	0,5 McFarland 24 h
Pneumococci		
All antibiotics	Mueller Hinton-agar + 2% NaCl	0,5 McFarland 24 h

References:

1) J. Sutcliffe, T. Grebe, A. Tait-Kamradt, L. Wondrack. 1996. Detection of Erythromycin Resistant Determinants by PCR. Antimicrob. Agents Chemother. 40:2562-2566.
2) S. Dutka-Malen, S. Evers, and P. Courvalin. 1995. Detection of Glycopeptide Resistance Genotypes and Identification to the Species Level of Clinically Relevant Enterococci by PCR. J. Clin. Microbiol. 33:24-27.

Figure 1.

Table 2. Overall results

No. strains	*S. aureus* 241		S. coag. neg. 204		*S. pneumoniae* 165		Enterococcus 188	
Antibiotic	MIC50	MIC90	MIC50	MIC90	MIC50	MIC90	MIC50	MIC90
Linezolid	1	3	0,75	2	0,75	1	2	3
Vancomycin	3	4	3	8	0,5	0,75	3	6
Teicoplanin	3	8	6	24			1	2
Oxacillin	0,38	256	8	256				
Clindamycin	0,094	256			0,125	0,5		
Levofloxacin	0,19	32						
Rifampicin	0,016	0,016						
Fosfomycin	0,75	12						
Gentamicin	0,5	256	8	256			24	1024
Ampicillin							0,75	192
Penicillin					0,016	0,125		
Cefotaxim					0,016	0,125		
Erythromycin					0,125	32		

S. pneumoniae. 19 (11,5%) strains were penicillin intermediate-resistant and 1 was highly resistant (0,6%). 25 (15,5%) strains were erythromycin-resistant: 13 strains had a MLSB phenotype (8 erm genes and 5 ND) and 12 strains had a M phenotype (3 mef genes and 9 ND).
Enterococci. Overall 19 enterococcal strains showed raised MIC to vancomycin. 15 strains were reidentified and tested with PCR for glycopeptide-resistance genes. Among these we found 3 strains of *E. casseliflavus* (C2/3) and 1 strain of *E. gallinarum* (C1).

Conclusion:

Linezolid was 6-fold more active than vancomycin against CNS and 10-fold more active than teicoplanin against CNS. Linezolid was 3-fold more active than teicoplanin and vancomycin against S.aureus and 2-fold more active than vancomycin against enterococci. Linezolid has a good potential to treat infections caused by Gram-positive cocci successfully.