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Assay of Free and Total Vancomycin Serum Concentrations with E-test-based determination of MICs in patients treated by Continuous Infusion for Severe Staphylococcal and Enterococcal Infections

E. AMPE [1,2], K. BERTHOIN [1], B. DELAERE [2], S. NOIRHOMME [2], P. M. TULKENS [1], J.D. HECQ [2], S. CARRYN [1], Y. GLUPCZYNSKI [1,2]

[1]Université catholique de Louvain, Bruxelles, Belgium, [2]Cliniques universitaires UCL de Mont-Godinne, Yvoir, Belgium.

Mailing address:
P.M. Tulkens
Pharmacologie cellulaire et moléculaire
& Centre de Pharmacie clinique
UCL 73.70 av. Mounier 73
1200 Brussels - Belgium
tulkens@facm.ucl.ac.be

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ABSTRACT (revised)

Background and aims: Only total vancomycin (VAN) concentrations are given in routine TDM, although protein binding varies and it is generally admitted that only free VAN is active. Our aim was to examine the correlation between (i) free and total vancomycin concentrations, and (ii) the corresponding concentration/MIC ratios for patients at risk of treatment failure.

Methods: 13 patients (11 document. infect.) received VAN by CI (target total VAN: 27 mg/L; load. dose: 20 mg/kg; infus.: 2.5 g/day [adapted to renal function and corrected by TDM] for 1 to 43 days (mean: 19 ± 10). Serum samples (70) were analyzed for free (ultrafiltration [Centrifree®; cut-off, 30 kDa]) and total (solid-phase extraction [Oasis® MCX cartridge]) VAN using a validated HPLC method. MICs were measured by E-test.

Results: Organisms and MICs (no.; mg/L) were *E. faecium* (2; 1.5), MRSA (6; 1.5-2), and *S. epidermidis* (3; 1-2). The correlation between free and total VAN conc. was poor.

Conclusion: Total VAN concentration is not predictive of true free VAN concentration. Actual determination of free VAN might be recommended for patients with less susceptible organisms.

INTRODUCTION

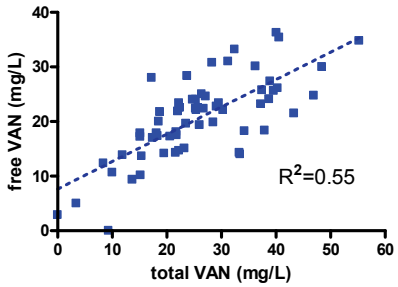
In routine therapeutic drug monitoring, total vancomycin (VAN) concentrations are used to adapt VAN dosing regimens. Although a mean value of 55 % protein binding is usually reported in most textbooks, wide variation has actually been reported (from less than 10 up to 82 % [1]). Yet, protein binding influences antimicrobial activity, although some controversy exists in this context [2].

AIM OF THE STUDY

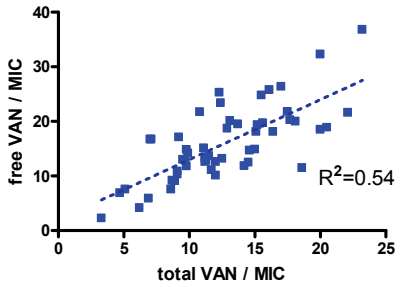
In this study, we wished to examine
(i) the correlation between free and total VAN concentration in order to estimate whether free VAN concentration can be predicted based on total concentration;
(ii) the corresponding free concentration/MIC ratios in order to identify patients at potential risk for treatment failure.

RESULTS

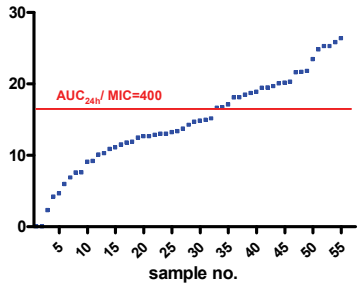
Correlation between free and total vancomycin serum concentrations



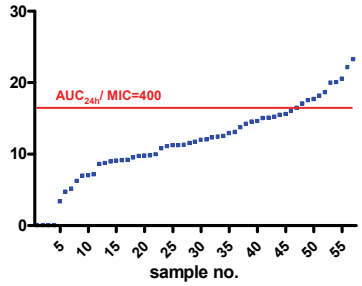
Correlation between free and total vancomycin / MIC ratios



total VAN / MIC ratio



free VAN / MIC ratio



MATERIALS & METHODS

Patients: 13 (11 documented infections)

Treatment: VAN by CI (target total VAN: 27 mg/L; load. dose: 20 mg/kg; infus.: 2.5 g/day [adapted to renal function and corrected by TDM] for 1 to 43 days (mean: 19 ± 10)

Samples:
- Free VAN: ultrafiltration Centrifree® (cut-off: 30 kDa)
- Total VAN: solid-phase extraction (Oasis® MCX cartridge)

HPLC analysis: validated HPLC [3]

MIC determination: Etest (AB Biodisk, Solna, Sweden)

CONCLUSIONS

1. Free and total VAN are poolrly correlated making prediction of free VAN from total VAN very hazardous;
2. An AUC_{24h}/ MIC ratio ≥ 400 (severe infections [4]) was only attained in about 40 % of all samples for total VAN and in about 15 % for free VAN;
3. Actual determination of free VAN might be recommended for patients with less susceptible organisms

REFERENCES

[1] Sun H et al. Serum protein-binding characteristics of vancomycin. Antimicrob Agents Chemother. 1993;37:1132-1136.
[2] Tsuji BT et al. Evaluation of daptomycin, telavancin, teicoplanin, and vancomycin activity in the presence of albumin or serum. Diagn Microbiol Infect Dis. 2008; 60:441-444.
[3] Denooz R. & Charlier C. Simultaneous determination of five beta-lactam antibiotics (cefepim, ceftazidim, cefuroxim, meropenem and piperacillin) in human plasma by high-performance liquid chromatography with ultraviolet detection. J Chromatogr B Analyt Technol Biomed Life Sci. 2008 Mar 15;864(1-2):161-7
[4] Moise-Broder PA et al. Pharmacodynamics of vancomycin and other antimicrobials in patients with Staphylococcus aureus lower respiratory tract infections. Clin Pharmacokinet. 2004;43(13):925-42.