Continuous versus Intermittent Infusion of Temocillin in Intensive Care Patients

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INTRODUCTION
β-lactams are time-dependent antibiotics and show little gain in activity once their concentration exceeds about 4 fold the MIC, which suggests to promote their administration by continuous infusion (Craig & Elbert, 1992).

In the present study, we have examined the feasibility and safety of this approach for temocillin, a narrow spectrum anti-β-lactam commonly used in combination with an anti-Gram (+) agent in the treatment of nosocomial pneumonia. We followed temocillin the same approach as for cefazidime, i.e.: (i) performing in vitro studies aimed at assessing the drug stability and compatibility under conditions pertinent of its projected clinical use (Servais & Tulkens, AAC 2001); (ii) examining which serum levels can be obtained in patients receiving standard daily doses of temocillin (Lutere et al., ICAC 2003).

METHODS

In vitro studies
Stability studies: Temocillin was prepared in aqueous solutions (4 g in 48 ml) and left at temperatures for up to 37°C. Results were compared with those of other β-lactams obtained previously in our laboratory (Vaeve et al., AAC 2002). A level of 90% intactness was used as a reference (as per the provisions of the European Pharmacopoeia).

Compatibility studies: Temocillin and each of the other drugs of interest (see Results) were mixed at a molar ratio similar to what would take place in a patient’s bloodstream (i.e. 5 g temocillin in 40 ml 24 h; the companion drug following its own administration scheme (see Results).

Analysis: All solutions were first examined visually for pH changes and appearance of precipitates (using a without shaking container). If no change was seen, temocillin was passively identified and quantitatively assayed by HPLC (acetic solvent with Na acetate buffer/acetonitrile [95:5] with fluorescence as internal standard).

Clinical study
Patients and treatment: 5 patients without renal insufficiency but with haemodialysis infection (4 days hospitalization): ethyl suspension of the presence of P. aeruginosa or other temocillin-resistant bacteria were randomly assigned to receive temocillin by continuous infusion (250 ml infused over 12 hours twice a day) or BID (250 ml administered as a 3 h bolus). Plasma was sampled several times for pharmacokinetic evaluation during the first 24 h of administration.

Analysis: Extraction by partition through OXAS®-R (RLE cartridges silica with methanol) followed by HPLC as described above. Each chromatogram was assessed in triplicate. Each patient was his own baseline. All assays were performed in triplicate.

CONCLUSIONS
Administration of temocillin by continuous infusion appears feasible and safe based on the drug stability and compatibility with other commonly used drugs, and allows for sustained levels above breakpoints.