Safety and Efficacy of Temocillin as a Carbapenem-Sparing Agent

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Background
Antimicrobial prescribing and antimicrobial resistance are inextricably linked, increased rates of extended spectrum beta-lactamases and carbapenemase producing organisms have been directly linked to broad spectrum antimicrobial use. In 2016 a national 3 year CQUIN was set in order to try and reduce the growing number of resistant Gram negative bacteria, one of the primary outcomes was for individual Trusts to reduce total carbapenem consumption. Temocillin is a narrow spectrum penicillin agent with activity against Gram negative bacteria. Licensed for the treatment of bacteraemia, urinary tract infections and lower respiratory tract infections where susceptible Enterobacteriaceae are suspected or confirmed. In 2018 the licenced dose of temocillin for severe infections was increased to up to 6g/day in normal renal function, possibly demonstrating better outcomes however with potential financial implications. To understand current experiences at 4g/day dosing, we undertook a single centre retrospective observational study of the outcomes of patients prescribed temocillin.

Method
All adult inpatient electronic prescriptions of temocillin (3 days or greater) from March 2016 to July 2017 were retrieved at a 400 bed London teaching hospital using a clinical decision support system (ICNET®). ICNET® was then used to retrieve patient demographic and clinical data, including mortality, readmissions, need for antimicrobial escalation, episodes of Clostridium difficile, occurring within 30 days of temocillin ending. Treatment success was defined as survival, no use of broad-spectrum agent for the same indication, no subsequent readmission for infection, and no C. difficile, occurring within 30days of completing temocillin. Treatment was considered empirical if the patient had no positive microbiology results or if results were greater than 30 days old.

Results

Temocillin was used in 148 patient-episodes during the study period. The average patient age was 76.6years (range 20-102years), 45% were female. Pre-temocillin average length of stay was 16.3days (range 0-156days). Prior to temocillin treatment 7 patients were identified as C. difficile carriers. Average temocillin course length was 7.3days (range 3-42days). All patients were dosed at 2g BD, except in cases of reduced renal function where dosing followed local guidance.

Overall temocillin treatment success was 75.6%, highest when used to treat UTIs (82.8%, p=0.01).
110/148 patients had relevant microbiology; there was no significant difference in success observed between patients with Escherichia coli (EC) and other Enterobacteriaceae (EB) infections (82.5% vs 69.8%, p=0.18). Empirical treatment demonstrated a 73.7% success rate (vs 76.4% among targeted treatment, p=0.92).

Conclusions
• Temocillin is an effective an safe alternative to carbapenem agents in treating Gram negative infections.
• Success rate should be considered in the context of age and significant co-morbidities of these patients.
• A dosing strategy of 4g (or renal equivalent) is safe in patients identified as having a infection from a urinary source.
• High dose temocillin or an alternative agent may be considered in patients with a non-urinary source of infection.
• Caution should be exercised when using temocillin empirically for a non-urinary source (such as chest), and an assessment of the need to cover Pseudomonas spp. must be made on a case by case basis.

References