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Temocillin: A Meropenem-Sparing Agent for Treating Infections Caused by ESBL-Producing *Enterobacterales*

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Dear Editor,

Carbapenems have traditionally been the drugs of choice for treating infections caused by extended-spectrum β-lactamase- (ESBL) and AmpC producers. Use of carbapenems increases the risk of patients being colonized or infected with Carbapenemase-producing *Enterobacterales* (CPE) and therefore alternative treatments are needed.[1]

Temocillin has resistance to both classical and extended-spectrum β-lactamases and AmpC enzymes and some activity against KPC-producing *Enterobacterales*.[2] Temocillin is licensed for treatment of septicaemia, urinary tract infection and lower respiratory tract infection where susceptible Gram-negative bacilli are suspected or confirmed.[3] A number of review articles have noted the potential of temocillin as an meropenem-sparing agent for ESBL/AmpC –producing organisms, however there is limited published literature regarding temocillin usage and clinical efficacy.

As part of an institutional antimicrobial stewardship initiative temocillin was introduced as a meropenem-sparing agent. A record was kept of all patients who were prescribed temocillin over a 6-month period. These patient's healthcare records and laboratory results were retrospectively reviewed.

Sixteen patients were included in this study. All patients received temocillin for a temocillin-susceptible ESBL-producing isolate detected in a clinical sample. The maximum dose prescribed was 2g BD. Temocillin susceptibility testing was done on the VITEK using BSAC breakpoints. Nine patients (56.25%) treated had urinary tract infections. Other infections were intra-abdominal (n=2), respiratory (n=2), biliary (n=1), wound site (n=1) and unclear source (n=1). Eight patients (50%) had an associated blood stream infection with the ESBL-producing organism isolated from blood cultures. The majority (87%) of the ESBL-producing organisms isolated were *Escherichia coli* and the remainder were *Klebsiella pneumoniae*.

There was resolution of infection in 15 of the 16 cases reviewed. One patient developed breakthrough bacteraemia while on temocillin with a temocillin-resistant ESBL-producing isolate. This patient had intra-abdominal sepsis with inadequate source control. There were no documented side-effects attributed to temocillin nor were there any reported cases of *C. difficile* infection.

When this study was carried out there were no EUCAST breakpoints for temocillin. The BSAC guidelines were used. The newly released EUCAST criteria define MICs >0.001 and <16mg/L as susceptible with increased exposure for *E. coli, Klebsiella* species (except *Klebsiella aerogenes*) and *Proteus mirabilis*. These breakpoints apply to a high-exposure dosing regimen of 2g 8 hourly.[4] The standard dose as listed in the drug summary of product characteristics is 2g twelve hourly.[3] All patients in this study received a lower dose of temocillin than currently recommended by EUCAST and notably 93.8% had documented resolution of their infection. They state there are insufficient data to recommend breakpoints and dosing regimens for pneumonia or other invasive infections.[4] In this study temocillin was used to treat patients with pneumonia and intra-abdominal sepsis. Both patients with pneumonia had good clinical outcomes. One of the patients with intra-abdominal sepsis had a poor outcome.

This study, despite small sample size, adds to the literature and supports the use of temocillin as an effective meropenem-sparing agent for the treatment of infections caused by temocillin-susceptible ESBL-producing isolates. Larger scale studies are needed, particularly to evaluate temocillin use in patients with deep-seated infections.

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