Temocillin use as a carbapenem-sparing option in a UK teaching hospital for treating serious Gram-negative bacterial infections

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We read the article about temocillin for the treatment of invasive Enterobacterales infections with interest.1 Temocillin is a narrow-spectrum penicillin with activity against ESBL-producing Enterobacterales (ESBL-PE). It could be used in place of carbapenams for some infections due to these infections (i.e. bacteraemia, pneumonia, urinary tract infection but not meningitis).2 This option is becoming increasingly important in the era of emerging carbapenem resistance. Temocillin has also been shown to have less of an impact on the intestinal microbiota than cephalosporins3 or piperacillin/tazobactam.4

We sought to determine the appropriateness, effectiveness and tolerability of temocillin prescribing in Cambridge University Hospitals (CUH) NHS Foundation Trust. This was considered a service evaluation and ethical approval was not required.

We performed a single-centre retrospective data review of all adult inpatients who received temocillin between 1 October 2016 and 31 July 2017 at CUH. Temocillin was approved for use in CUH when a urine or blood culture isolate was confirmed to be an ESBL-PE and susceptible to temocillin (by BSAC methodology) and resistant to oral agents, in order to preserve carbapenems and piperacillin/tazobactam. Its use was therefore restricted to be only recommended by a microbiology consultant. As part of the formulary submission we were required to analyse its use to confirm it was used appropriately. It was used as monotherapy unless the microbiologist was concerned about polymicrobial infection.

Epidemiological data, duration of therapy and duration of carbapenem-sparing were recorded and analysed. Temocillin was dosed at 4 g/day (2 g IV q12h), except in cases of reduced renal function where dosing followed local guidance.

A total of 24 patients (14 male; 58%) were included. Two patients required two courses of therapy (total 26 courses) due to recurrence (one due to inadequate source control). The age of the patients ranged from 23–96 years (mean 69 years). Sixteen patients were cared by medicine/medicine for elderly, four by urology and two each by transplant and neurosurgery (Table 1).

Two patients (8%) had a rapidly fatal underlying condition, 7 (29%) had an ultimately fatal condition and 15 (63%) had a non-fatal underlying condition. The Charlson comorbidity score ranged from 1 to 12 (median 3). Three required intensive care.

Twenty-one episodes (81%) were bacteraemic; 19 of these were due to an ESBL-PE, whilst one had an AmpC-producing Escherichia coli and one had an E. coli with no ESBL or AmpC identified; three grew ESBL-PE in urine and two were commenced on temocillin as they had previously had ESBL-PE identified from urine/blood cultures.

Fourteen of 21 (67%) bacteraemic episodes were related to a urinary source, three (14%) had a bowel source (who received concomitant metronidazole), three (14%) had healthcare-associated pneumonia and one (5%) had cholangitis.

Duration of therapy varied between 1 and 15 days (mean 6 days). Reasons for stopping temocillin included completion of course (13; 50%), 7 (27%) episodes of switching to ertapenem to facilitate outpatient parenteral antimicrobial therapy, one patient died and 5 (19%) episodes had other explanations. None of the discontinuations were due to intolerance/toxicity and there were no reported side effects. Renal function at the time of commencing temocillin varied greatly during the study, with glomerular filtration rate ranging from 5 to 218 mL/min (median 53 mL/min). There was, therefore, a wide range of doses given. Overall, 19 (73%) had the correct dose, with 6 being underdosed and one being overdosed.

Two patients (8%) had recurrence of disease and one patient died. Patients had received 0–37 g (median 4 g) of meropenem prior to switching. Twenty-five (96%) of the episodes were improving on their previous regimen prior to switching to temocillin; they showed improvement 1 week after switch and 24 (92%) of these episodes showed improvement 1 month after switch. One patient was deteriorating prior to switching to temocillin and continued to deteriorate. Source control and switching back to meropenem occurred in this patient. One hundred and forty-eight days of total carbapenem-sparing was achieved.

We provide data on the use of temocillin as a carbapenem-sparing agent in the management of serious ESBL-PE infections including 21 bacteraemic patients. Safe and effective alternatives are required in order to preserve carbapenems for seriously
| Patient | New/recurrence | Age (y) | Sex | Specialty | Sample | Source | Dose | GFR (mL/min) | Appropriate dose? | Duration of therapy (days) | Reason for stopping Previous antibiotics | McCabe | COMS | Albumin (g/L) | CRP (mg/L) | Peak temperature (°C) | Trends before switch | Outcome at 1 week | Outcome at discharge | Breakthrough infection Organism |
|---------|----------------|---------|-----|-----------|--------|--------|------|--------------|-------------------|----------------------|--------------------------------------|---------|------|-------------|------------|-------------------|----------------------|-----------------|---------------------|------------------------|
| 1       | New            | 53      | F   | Renal transplant | blood | urinary | 1 g twice daily | 36     | y | 5 | completion of course piperacillin/tazobactam, meropenem  | non-fatal | 3 | 32 | 45 | 38.5 | improving improving alive | y | source control | E. coli |
| 2       | Recurrence     | 58      | F   | Renal transplant | blood | urinary | 1 g twice daily | 47     | y | 4 | switch to entepenem piperacillin/tazobactam, meropenem  | non-fatal | — | — | 29 | 98 | 39.7 | improving improving alive | n | E. coli |
| 3       | New            | 83      | F   | Medicine | blood | urinary | 500 mg once daily | 5      | y | 10 | completion of course piperacillin/tazobactam, meropenem | non-fatal | 4 | 21 | 289 | 35.9 | improving improving alive | n | E. coli |
| 4       | New            | 47      | M   | Medicine | blood | urinary | 2 g twice daily | 62     | y | 1 | switch to entepenem co-amoxiclav, gentamicin | non-fatal | 1 | no | 115 | 39.2 | improving improving alive | n | E. coli |
| 5       | New            | 23      | M   | Medicine | blood | bowel | 1 g twice daily | 60     | y | 9 | completion of course meropenem  | ultimately fatal | 7 | 15 | 50 | 40.3 | improving improving alive | n | E. coli |
| 6       | Recurrence     | 70      | M   | Medicine | blood | urinary | 1 g once daily | 50     | y | 2 | switch to entepenem co-amoxiclav, meropenem  | ultimately fatal | 11 | 25 | 174 | 39.0 | improving improving alive | n | E. coli |
| 7       | New            | 77      | M   | Medicine | blood | urinary | 1 g once daily | 20     | y | 9 | completion of course piperacillin/tazobactam, meropenem | ultimately fatal | 6 | 36 | 93 | 39.1 | improving improving alive | n | E. coli |
| 8       | New            | 87      | F   | DME    | urine | urinary | 1 g twice daily | 80     | no, underdose | 2 | switch to entepenem co-amoxiclav, meropenem  | non-fatal | 1 | 25 | 120 | 38.6 | improving improving alive | n | E. coli |
| 9       | New            | 96      | F   | Neuro-surgery | blood | urinary | 1 g twice daily | 74     | no, underdose | 8 | completion of course piperacillin/tazobactam, meropenem | rapidly fatal | 7 | 28 | 95 | 38.0 | improving improving alive | n | E. coli |
| 10      | New            | 60      | F   | Urology | urine | urinary | 1 g twice daily | 72     | no, underdose | 4 | switch to entepenem co-amoxiclav, meropenem  | non-fatal | 2 | na | 38 | 36.0 | improving improving alive | n | E. coli |
| 11      | New            | 69      | M   | Medicine | blood | urinary | 2 g twice daily | 76     | y | 4 | switch to entepenem co-amoxiclav, meropenem  | non-fatal | 10 | 34 | 53 | 38.5 | improving improving alive | n | E. coli |
| 12      | New            | 62      | M   | Urology | blood | urinary | 1 g twice daily | 57     | y | 2 | switch to entepenem co-amoxiclav, meropenem  | non-fatal | 3 | 19 | 49 | 38.7 | improving improving alive | n | E. coli |
| 13      | New            | 80      | M   | Medicine | blood | HAP | 1 g twice daily | 53     | y | 6 | completion of course piperacillin/tazobactam, meropenem  | non-fatal | 3 | na | 70 | 37.8 | improving improving alive | n | E. coli |
| 14      | New            | 74      | M   | Medicine | blood | urinary | 1 g twice daily | 59     | y | 9 | completion of course co-amoxiclav, meropenem  | ultimately fatal | 2 | 38 | 73 | 39.2 | improving improving alive | n | E. coli |
| 15      | New            | 65      | F   | Medicine | blood | HAP | 1 g twice daily | 86     | no, underdose | 10 | completion of course co-amoxiclav, meropenem  | ultimately fatal | 2 | na | 64 | 37.0 | improving improving alive | n | E. coli |
| 16      | New            | 94      | M   | DME    | blood | urinary | 1 g once daily | 26     | y | 10 | completion of course piperacillin/tazobactam, meropenem | ultimately fatal | 12 | 20 | 78 | 37.4 | improving improving alive | n | E. coli |
CCMS, Charlson comorbidity score; CRP, C-reactive protein; DME, Department of Medicine for the Elderly; F, female; GFR, glomerular filtration rate; HAP, hospital-associated pneumonia; M, male; n, no; na, not applicable; y, yes.

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