be treated, leading to the death of the patient after 5 weeks of treatment in the ICU.

There are scarce data on the dosing of antibiotics in patients undergoing renal replacement therapy.\(^7\) Our data suggest that extended dialysis eliminates colistin effectively and to a larger extent than regular intermittent outpatient haemodialysis. This is in line with recent data on two critically ill patients undergoing a modern type of intermittent dialysis (1.6 m\(^2\) polymethylacrylate membrane, blood/dialysate flow 300/500 mL/min, duration 4 h), in whom a CMS dialyser clearance of 90 mL/min was reported.\(^8\) Li et al.\(^9\) described a dialyser clearance of 11.9 mL/min for colistin and 11.2 mL/min for CMS in one critically ill patient undergoing continuous venous haemodiafiltration, which due to its continuous mode would remove approximately the same amount of the drug. Lastly, dialyser clearance in five patients receiving continuous venous haemodiafiltration was recently reported to be 72 mL/min for colistin and 32 mL/min for CMS.\(^10\)

Thus, dosing colistin as recommended during regular haemodialysis is inadequate and would result in a significant under-dosing, which could be associated with a substantial risk, especially in critically ill patients in the ICU. A dose of 3 million units every 8 h seems to be adequate for patients undergoing daily extended dialysis for ~9 h a day with a high flux 1.3 m\(^2\) dialyser. This dose of 9 million units per day did not lead to accumulation of the drug.

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**Transparency declarations**

None to declare.

**References**


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**Salvage treatment of methicillin-resistant staphylococcal endocarditis with ceftaroline: a multicentre observational study**

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**Keywords:** coagulase-negative staphylococci, cephalosporins, methicillin-resistant Staphylococcus aureus

Sir,

β-Lactam agents have been the main antibacterial agents used for the treatment of infective endocarditis since the discovery of penicillin more than 70 years ago. Indeed, due to their bactericidal activity and a safety profile that allows the use of high doses, this class represents the backbone of most first-line regimens in this indication.\(^1\) However, no β-lactam effective against methicillin-resistant staphylococci was available until recently, and the use of antibacterial agents recommended in these settings (mostly vancomycin and daptomycin) may be limited by dose-dependent toxicity and/or the emergence of resistance. Ceftaroline is a new cephalosporin agent with in vitro and in vivo activity against methicillin-resistant staphylococci, with MIC\(_{90}\)S of 0.5 and 1 mg/L for methicillin-resistant coagulase-negative
<table>
<thead>
<tr>
<th>Age (years)/sex (F/M)</th>
<th>Comorbidity</th>
<th>Bacteria and MICs (mg/L)</th>
<th>Endocarditis characteristics (location, complications)</th>
<th>Antibacterial agents before CPT (duration, days)</th>
<th>Duration of positive blood cultures (days) before CPT</th>
<th>Indication(s) for CPT</th>
<th>Surgery</th>
<th>CPT dose, duration</th>
<th>Combination</th>
<th>Outcome/ follow-up (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>67/F</td>
<td>diabetes chronic renal failure morbid obesity aortic valve replacement</td>
<td>MRSE/MSSE VAN MIC 2 and 1 DAP 0.5 CPT 0.12 and 0.5</td>
<td>bioprosthetic aortic valve vegetation 6 mm</td>
<td>VAN (3) DAP + RIF (23)</td>
<td>2 0</td>
<td>intolerance to DAP (rhabdomyolysis, renal failure)</td>
<td>not considered (early improvement)</td>
<td>400 mg BID, 9 days</td>
<td>RIF</td>
<td>cure/110</td>
</tr>
<tr>
<td>33/M</td>
<td>congenital cardiopathy aortic and pulmonary valve replacement</td>
<td>MRSE VAN 0.5 DAP 0.2 CPT 0.2</td>
<td>aortic and pulmonary mechanical prosthetic valves vegetation 5 mm pulmonary emboli lung abscess</td>
<td>DAP + GEN (5)</td>
<td>2 0</td>
<td>salvage (persistent fever + vegetation enlargement + worsening valvular regurgitation under DAP + GEN)</td>
<td>aortic valve replacement + Bentall procedure (day 9 CPT)</td>
<td>800 mg TID, 42 days</td>
<td>DAP</td>
<td>cure/90</td>
</tr>
<tr>
<td>79/M</td>
<td>morbid obesity aortic valve replacement</td>
<td>MRSA VAN 1 DAP 0.2 CPT 0.2</td>
<td>bioprosthetic aortic valve perivalvular abscess mycotic aneurysm (ilio-femoral) pacemaker vegetation 8 mm</td>
<td>CXA + GEN (3)</td>
<td>1 0</td>
<td>acute renal failure due to CXA + GEN</td>
<td>aortic valve replacement (day 3 CPT)</td>
<td>800 mg TID, 5 days</td>
<td>DAP</td>
<td>failure, death (day 5)</td>
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<tr>
<td>85/F</td>
<td>pacemaker aortic and mitral valve replacement</td>
<td>MRSE VAN 2 DAP 0.5 CPT 0.25</td>
<td>pacemaker vegetation 8 mm</td>
<td>VAN + GEN (2)</td>
<td>2 0</td>
<td>acute renal failure due to VAN + GEN</td>
<td>contraindicated (age, physiological state)</td>
<td>400 mg BID, 6 days</td>
<td>none</td>
<td>failure, death (day 5)</td>
</tr>
<tr>
<td>70/M</td>
<td>leukaemia cirrhosis aortic valve replacement</td>
<td>MRSA VAN 2 DAP 0.5 CPT 0.5</td>
<td>bioprosthetic aortic valve perivalvular abscess vegetation 12 mm lung abscesses stroke</td>
<td>DAP (28) FOF (38) LZD (10)</td>
<td>2 0</td>
<td>salvage (persistent fever + vegetation enlargement under previous regimens)</td>
<td>contraindicated (comorbidities)</td>
<td>600 mg TID, 42 days</td>
<td>none</td>
<td>cure/150</td>
</tr>
<tr>
<td>74/F</td>
<td>cirrhosis cardiac failure</td>
<td>MRSA VAN 1 DAP 1 CPT 0.25</td>
<td>native aortic and mitral valves perivalvular abscess vegetation 25 mm stroke</td>
<td>VAN (28) DAP (7) GEN (14) RIF (7)</td>
<td>5 0</td>
<td>salvage (vegetation enlargement under previous regimens)</td>
<td>contraindicated (comorbidities)</td>
<td>600 mg TID, 17 days</td>
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<td>cure/115</td>
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</table>

Continued
Table 1. Continued

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<thead>
<tr>
<th>Age (years)</th>
<th>Sex (F/M)</th>
<th>Comorbidity</th>
<th>Cause of E.</th>
<th>ST.</th>
<th>Indication(s) for CPT</th>
<th>Surgery</th>
<th>Duration of CPT (days)</th>
<th>Combination CPT</th>
<th>CPT dose, duration</th>
<th>Outcome/ follow-up (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>73F</td>
<td>F</td>
<td>diabetes</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>none surgery contraindicated</td>
<td>none</td>
<td>7 days</td>
<td>VAN (15)</td>
<td>600 mg TD, 7 days</td>
<td>cure/120</td>
</tr>
<tr>
<td>73M</td>
<td>M</td>
<td>dementia</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>none contraindicated (comorbidities)</td>
<td>none</td>
<td>7 days</td>
<td>VAN (15)</td>
<td>600 mg TD, 7 days</td>
<td>cure/120</td>
</tr>
<tr>
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<td>heart failure</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>contraindicated (comorbidities)</td>
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<td>28 days</td>
<td>VAN (15)</td>
<td>600 mg TD, 28 days</td>
<td>cure/120</td>
</tr>
<tr>
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<td></td>
<td>stroke</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>contraindicated (comorbidities)</td>
<td>none</td>
<td>7 days</td>
<td>VAN (15)</td>
<td>600 mg TD, 7 days</td>
<td>cure/120</td>
</tr>
<tr>
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<td></td>
<td>cardiac failure</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>contraindicated (comorbidities)</td>
<td>none</td>
<td>0</td>
<td>VAN (15)</td>
<td>600 mg TD, 7 days</td>
<td>cure/120</td>
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<tr>
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<td>cardiac failure</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>contraindicated (comorbidities)</td>
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<td>7 days</td>
<td>VAN (15)</td>
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<tr>
<td>7</td>
<td></td>
<td>cardiac failure</td>
<td>native aortic valve vegetation 6 mm</td>
<td>MRSA</td>
<td>contraindicated (comorbidities)</td>
<td>none</td>
<td>7 days</td>
<td>VAN (15)</td>
<td>600 mg TD, 7 days</td>
<td>cure/120</td>
</tr>
</tbody>
</table>

*F, female; M, male; MRSE, methicillin-resistant Staphylococcus epidermidis; MSSSE, methicillin-susceptible S. epidermidis; VAN, vancomycin; DAP, daptomycin; GEN, gentamicin; CPT, ceftaroline; CZA, cloxacillin; RIF, rifampicin; FO, fosfomycin; LZD, linezolid; BID, twice daily; TID, three times daily.*

To the best of our knowledge, this is the second largest series on the use of ceftaroline for the salvage treatment of endocarditis due to methicillin-resistant staphylococci reported to date, and the first that has enrolled patients with MRCoNS endocarditis. Previous observations on the use of ceftaroline for salvage treatment of MRSA endocarditis suggested that the tolerability of this agent is good at high doses (i.e. most frequently 600 mg three times daily for endocarditis, compared with 600 mg twice daily for ABSSSI or CAP) and patients were classified as ‘clinical cure’.
in 18 of the 20 cases reported to date (90%). In conclusion, ceftaroline appears to be well tolerated as a salvage treatment of methicillin-resistant staphylococcal endocarditis, at higher doses than recommended for CAP or ABSSSI. Data available to date do not allow a firm conclusion regarding its efficacy in humans in this indication. Further improvement could arise from: (i) larger international observational studies; (ii) advances in therapeutic drug monitoring, which may allow the use of higher doses, as recommended for most β-lactams indicated for the treatment of endocarditis; and (iii) randomized clinical trials, although these are particularly difficult to set up in the field of endocarditis.

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References

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Unforeseen risk in the treatment of severe community-acquired pneumonia with narrow-spectrum antibiotics

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Keywords: penicillin, clarithromycin, sepsis, Gram-negative bacteraemia, antibiotic policies

Sir,

In October 2011 our hospital adopted a policy of treating severe community-acquired pneumonia with a combination of benzylpenicillin and clarithromycin. This was motivated by concern about the perceived consequences of the previous policy of using benzylpenicillin plus levofloxacin, particularly Clostridium difficile infection and rising rates of fluoroquinolone resistance in Enterobacteriaceae. This change in local policy was a matter of considerable debate because it conflicted with national guidance. Nevertheless the use of penicillin with a macrolide for treating severe pneumonia has been supported by the BSAC and more recently by the Joint Taskforce of the European Respiratory Society and European Society for Clinical Microbiology and Infectious Diseases. We were further reassured by our low local rates of antibiotic resistance amongst respiratory pathogens.

We undertook a prospective audit of the management and outcomes of patients admitted to our hospital with a diagnosis of community-acquired pneumonia, over a 3 month period from November 2011. One hundred and fifty-one patients were