Renal Fanconi syndrome with meropenem-containing regimen in drug-resistant tuberculosis

From the authors:

We read with great interest the correspondence by Abadie et al. [1] describing the case of extensively drug-resistant tuberculosis patient developing renal Fanconi syndrome while receiving a meropenem/amoxicillin–clavulanate-containing regimen.

The International Carbapenem Study Group centres collected data on 96 patients treated with meropenem–clavulanate and 84 patients with imipenem–clavulanate. Carbapenem and β-lactam/lactamase inhibitor combinations were well tolerated; no cases of Fanconi syndrome were encountered [2, 3]. Other groups have also published their experience and there were no cases of Fanconi syndrome (table 1) [11].

Meropenem dosing and duration were heterogeneous in our study group; the majority of patients were administered meropenem for a median of 85 days (range 49–156 days), particularly during the intensive phase or until their sputum culture conversion [2]. Only the Belgian team prescribed a higher dosage of meropenem for more extended periods [10] (table 1 [2–10]). Meropenem/amoxicillin–clavulanate, given its bactericidal qualities, appears ideally placed in the intensive phase until sputum culture conversion occurs.

If required, ertapenem–clavulanate may be used in the continuation phase [8].

Several drugs are known to cause proximal renal tubular acidosis (RTA) with Fanconi syndrome. It can be caused by several drugs including aminoglycosides, rifampicin, cisplatin and tenofovir disoproxil fumarate. Generally, RTA is reversible by removing the offending drug. Meropenem and amoxicillin–clavulanate are

<table>
<thead>
<tr>
<th>First author [ref.]</th>
<th>XDR-TB cases out of the total number of cases studied</th>
<th>Control group</th>
<th>Adverse reactions</th>
<th>Carbapenem and dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chambers [4]</td>
<td>2/10 (20.0%)</td>
<td>No</td>
<td>Not done</td>
<td>Imipenem 1 g twice daily</td>
</tr>
<tr>
<td>Palermo [5]</td>
<td>4/10 (40.0%)</td>
<td>No</td>
<td>0/10 (0.0%)</td>
<td>Meropenem 2 g three times daily then 1 g three times daily</td>
</tr>
<tr>
<td>De Lorenzo [6]</td>
<td>9/37 (24.3%)</td>
<td>Yes</td>
<td>5/37 (13.5%)</td>
<td>Meropenem 1 g three times daily</td>
</tr>
<tr>
<td>Van Rijn [7]</td>
<td>ND</td>
<td>No</td>
<td>2/18 (11.1%)</td>
<td>Ertapenem 1 g once daily</td>
</tr>
<tr>
<td>Tiberi [8]</td>
<td>2/5 (40.0%)</td>
<td>No</td>
<td>0/5 (0.0%)</td>
<td>Ertapenem 1 g once daily</td>
</tr>
<tr>
<td>Tiberi [2]#</td>
<td>47/96 (49.0%)</td>
<td>Yes</td>
<td>6/93 (6.5%)</td>
<td>Meropenem 1 g three times daily</td>
</tr>
<tr>
<td>Tiberi [9]#</td>
<td>57/84 (67.9%)</td>
<td>Yes</td>
<td>3/56 (5.4%)</td>
<td>Imipenem 500 mg four times daily</td>
</tr>
<tr>
<td>Tiberi [3]#</td>
<td>Imipenem 57/84 (67.9%)</td>
<td>No</td>
<td>Imipenem 3/56 (5.4%)</td>
<td>Imipenem 500 mg four times daily</td>
</tr>
<tr>
<td>Payen [10]</td>
<td>15/18 (83.3%)</td>
<td>No</td>
<td>0/18 (0.0%)</td>
<td>Meropenem 2 g three times daily then 2 g twice daily</td>
</tr>
</tbody>
</table>

XDR-TB: extensively drug-resistant tuberculosis; ND: not declared. #: International Carbapenem Study Group cohorts; #: children were included in this study.

not typically given for prolonged periods or in combination. In normal circumstances, Fanconi syndrome has not been regularly reported for either of the two drugs and could be considered rare.

The occurrence of this rare adverse event, related to a drug with well documented toxicity, and the paucity of published evidence on their safety and tolerability advocates for active drug safety monitoring of anti-TB medications [12–14]. Data collection is essential for clinicians and drug advisory bodies to ensure patient safety. Further attention with regards to formulations and preparation of meropenem, as well as its subsequent storage temperature, is also worth considering.

Simon Tiberi1,2,6, Marie-Christine Payen3,8, Giovanni Sotgiu4, Lia D’Ambrosio5,6, Rosella Centis5, Jan-Willem Alffenaar1 and Giovanni Battista Migliori6

1Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University, London, UK. 2Division of Infection, Royal London Hospital, Barts Health NHS Trust, London, UK. 3Division of Infectious Diseases, CIEU Saint-Pierre, Université Libre de Bruxelles (ULB), Brussels, Belgium. 4Clinical Epidemiology and Medical Statistics Unit, Dept of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy. 5World Health Organization Collaborating Centre for Tuberculosis and Lung Diseases, Maugeri Care and Research Institute, Tradate, Italy. 6Public Health Consulting Group, Lugano, Switzerland. 7University of Groningen, University Medical Center Groningen, Dept of Clinical Pharmacy and Pharmacology, Groningen, The Netherlands. These authors contributed equally.

Correspondence: Giovanni Battista Migliori, WHO Collaborating Centre for TB and Lung Diseases, Fondazione S. Maugeri, Care and Research Institute, via Roncaccio 16, 21049 Tradate, Italy. E-mail: giovannibattista.migliori@icsmaugeri.it

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References

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