# 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 dipivoxil fumarate. Generally, RTA is reversible by removing the offending drug. Meropenem and amoxicillin–clavulanate are

TABLE 1 Studies available in the literature reporting on carbapenems for the treatment of drug-resistant tuberculosis

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

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

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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.

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