

Category : **Renal: extracorporeal support**

A131 - Influence of continuous renal replacement therapy on fosfomycin serum levels in critically ill patients.

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Introduction:

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Fosfomycin plays an important role in the therapy of multi-resistant organisms in critically ill patients. To date, no data are available on pharmacokinetics of fosfomycin in patients who require continuous renal replacement therapy. In order to achieve adequate serum levels and avoid overdosing, this knowledge is essential. We hypothesize that dialysis leads to a significant decrease in serum levels and a shortening of elimination half-life.

Methods:

We determined 300 serum fosfomycin levels in 15 critically ill patients using high performance liquid chromatography. Samples were taken before and after 15, 30, 60, 90, 120, 180, 240, 300 and 360 minutes after intravenous administration of 5 g fosfomycin during multi-filtration dialysis and withdrawal of renal replacement therapy, each in the same patient. Using E max model for time-concentration curves we determined peak concentration, time to half-maximum concentration and gamma, each for rise and fall in concentration, elimination half-life as well as area under the curve (AUC) of elimination.

Results:

15 patients had a mean age of 60 (± 8 SD) years, mean weight of 88.5 (± 19.8 SD) kg and mean height of 175.6 (± 19 SD) cm. 13 patients were male. Dialysate flow was 2.4 (± 0.5 SD) l/h, blood flow 110 (± 27 SD) ml/min and ultrafiltration 73 (± 57 SD) ml/h. Fosfomycin peak concentration was significantly lower during renal replacement therapy (117 $\mu\text{g/ml}$; ± 59.9 SD) compared to discontinuation of multi-filtration (143 $\mu\text{g/ml}$; ± 54.7 ; $p < 0.05$).

Elimination half-life was 114 min (25th-75th percentiles 103.5-156.5) for dialysis compared to 570 min (25th-75th percentiles 196-1172; $p < 0.05$). Renal replacement therapy resulted in a 59% (± 37.2 SD) reduction of AUC of fosfomycin elimination.

Conclusion:

Continuous renal replacement therapy results in significant lower fosfomycin serum levels and a significantly shorter elimination half-life, which should be considered in dosing fosfomycin during renal replacement therapy.