

Pharmacokinetics of meropenem in intensive care patients receiving continuous renal replacement therapy

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Introduction: This study was conducted to determine the appropriate dose of meropenem in critically ill patients with acute renal failure treated by continuous veno-venous haemofiltration (CVVH) or haemodiafiltration (CVVHDF) who require antibiotic therapy.

Methods: Ten critically ill patients (7 males, 3 females, median age 68 yrs (range: 51-77 yrs), median weight 77kg (range: 51-119kg), median APACHE II 27 (range: 15 - 37)) were included. All patients were receiving CVVH (n=5) (haemofiltration rate 1-2l/hr) or CVVHDF (n=5) (haemofiltration rate 1-1.5l/hr : dialysis rate 1-1.5l/hr) using a polyacrylonitrile (AN69) hollow fibre 0.9m² filter (Multiflow 100, Hospal.) All patients received a meropenem dose of 1g 12 hourly, intravenously over 5 mins. Venous blood samples were taken pre-dose and 5, 15, 30, 60, 90, 120, 240, 360, 480 mins post-dose on day 3 to approximate steady state conditions. Haemofiltrate was collected for determination of a sieving coefficient. Samples were analysed by high performance liquid chromatography.

Results: Sieving coefficient for meropenem with the AN69 filter was 0.93 +/- 0.06 (n=9) indicating free flow across the membrane. Mean (+/- SD) serum concentrations at pre-dose, 5, 15, 30, 60, 90, 120, 240, 360, 480 mins post-dose were: 7.6 (5.1), 90.9 (23.9), 66.0 (13.0), 53.9 (15.7), 40.0 (10.3), 39.0 (9.2), 31.0 (10.4), 21.1 (6.9), 17.2 (6.2), 13.8 (6.4) mg/l respectively. Actual pre-dose (C_{trough}), 5 mins (C_{peak}) and 480 mins (C₄₈₀) post-dose levels are given below. Serum concentrations remained above the MIC₉₀ for *Ps. aeruginosa* (4mg/l) in all patients for two-thirds of the dosage interval which is the target recommended for β -lactam antibiotics. A lower dose may not have been sufficient for all the patients.

Conclusion: An intravenous meropenem dose of 1g 12 hourly is adequate in patients treated with CVVH or CVVHDF using an AN69 HF 0.9m² filter.

Table

Patient	1	2	3	4	5	6	7	8	9	10
Weight	70kg	82kg	80kg	74kg	67kg	51kg	95kg	70kg	90kg	119kg
Renal replacement	CVVH					CVVHDF				
Haemofiltration rate (l/hr)	1	1.5	2	2	2	1	1	1	1.5	1.5
Dialysis rate (l/hr)						1	1	1	1.5	1.5
C _{trough} (mg/l)	13.3	4.2	3.4	7.2	14.6	13.3	2.5	6.3	0.5	10.8
C _{peak} (mg/l)	90.1	127.7	85.2	73.2	81.7	116.3	101.2	115.0	63.1	55.3
C ₄₈₀ (mg/l)	19.4	10.5	14.3	11.6	23.3	20.5	6.2	18.7	5.7	7.5