Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **42** (1): 120-6 (2023)

Received: August 22, 2022
Accepted: September 15, 2022

Pharmacokinetics of Meropenem in Elderly Patients with SevereCommunity-Acquired Pneumonia in the Emergency Intensive Care Unit

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SUMMARY. **This research focused on the pharmacokinetic (PK) properties of meropenem in older patients with severe community-acquired pneumonia (SCAP) to see if the dosing regimen of meropenem (2 h infusion of 1 g every 8 h) was suitable. Eleven patients formed the study cohort. We used high-performance liquid chromatography (HPLC) to detect the concentrations of meropenem in plasma and sputum. By adopting WinNonlin, we measured their PK parameters. The Monte Carlo simulation was performed to calculate the probability of target attainments (PTAs) when drug concentrations were above the minimum inhibitory concentration (%T >MIC) at different minimum inhibitory concentrations (MICs). In blood, mean apparent volume of distribution (Vd) of meropenem was 81.12 ± 20.74 L, and the total body clearance (CL) was 18.37 ± 5.41 L/h. The mean peak concentration (C_{max}) of meropenem in blood and sputum were 12.71 ± 2.15 µg/mL and 6.42 ± 1.36 µg/mL, respectively. The mean area under the curve from zero to 8 h ($AUC_{0-8\,h}$) for blood and sputum was 49.11 ± 9.65 µg/mL and 31.99 ± 5.87 µg/mL, respectively. We used two ways to calculate the mean percent lung penetration: C_{max} (50.51%) and $AUC_{0-8\,h}$ (65.14%). In the case of the 40%T >MIC target, MIC ≤ 4 µg/mL resulted in a PTA > 90% in plasma, but only MIC ≤2 µg/mL resulted in PTA>90% in sputum.Aiming at 40%T > MIC, the standard dosing regimen of meropenem works well against pathogens with MIC ≤ 4 µg/mL.**

RESUMEN. Esta investigación se centró en las propiedades farmacocinéticas (PK) de meropenem en pacientes mayores con neumonía grave adquirida en la comunidad (SCAP) para ver si el régimen de dosificación de meropenem (infusión de 2 h de 1 g cada 8 h) era adecuado. Once pacientes formaron la cohorte del estudio. Utilizamos cromatografía líquida de alta resolución (HPLC) para detectar las concentraciones de meropenem en plasma y esputo. Al adoptar WinNonlin, medimos sus parámetros PK. Se realizó la simulación de Monte Carlo para calcular la probabilidad de alcanzar el objetivo (PTA) cuando las concentraciones del fármaco estaban por encima de la concentración inhibitoria mínima (%T > MIC) a diferentes concentraciones inhibitorias mínimas (MIC). En sangre, volumen de distribución aparente medio (Vd) de meropenem fue de 81,12 ± 20,74 L, y el aclaramiento corporal total (CL) fue de 18,37 ± 5,41 L/h. La concentración máxima media (Cmax) de meropenem en sangre y esputo fue de 12,71 ± 2,15 µg/mL y 6,42 ± 1,36 µg/mL, respectivamente. El área media bajo la curva de cero a 8 h (AUC0-8 h) para sangre y esputo fue de 49,11 ± 9,65 µg/mL y 31,99 ± 5,87 µg/mL, respectivamente. Usamos dos formas de calcular el porcentaje medio de penetración pulmonar: Cmax (50,51 %) y AUC0-8 h (65,14 %). En el caso del objetivo 40%T >MIC, MIC ≤4 µg/mL resultó en un PTA >90% en plasma, pero solo MIC ≤2 µg/mL resultó en PTA>90% en esputo. Con el objetivo de 40%T >MIC, el régimen de dosificación estándar de meropenem funciona bien contra patógenos con MIC ≤ 4 µg/mL.

KEY WORDS: elderly patients, emergency intensive care unit (EICU), meropenem, Monte Carlo simulations, pharmacokinetic/pharmacodynamic (PK/PD) severe community-acquired pneumonia (SCAP).

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ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)