Introduction:
The objective of this study was to evaluate the pharmacokinetics (PK) of levetiracetam (LEV) in critically ill patients with normal and augmented renal clearance (ARC), and determine if the recommended dosage regimen provides concentrations in the therapeutic range (12-46 mg/L)[1].

Methods:
A prospective observational study was conducted in a tertiary hospital. Six blood samples were taken during a dose interval at steady state and LEV was quantified by HPLC. A population PK study was carried out. Statistical analysis was conducted to evaluate the differences in PK between patients with and without ARC. The suitability of drug concentrations was also assessed.

Results:
Seventeen patients were included, 13 with normal creatinine clearance (CrCL) (80-129 mL/min) and 4 with CrCl≥130 mL/min (ARC). Ten patients received 500mg q12h, one 1000mg q12h and two 1500mg q12h. The data were best fitted to a two-compartment model. Figure 1 shows LEV concentrations during the dosing interval. Mean clearance (CL) was 4 L/h and mean volume of distribution of central compartment (V) was 44 L. Interindividual variability was 38 and 61% for CL and V, respectively. No differences were identified between both groups (p>0.05) in PK parameters. No correlation was found between LEV CL and CrCL. Trough levels were below the minimum concentration (C_{min}) 12 mg/L of the therapeutic range in all patients except 1. Furthermore, between 3-5 h 50% of samples were below the C_{min}.

Conclusion:
Administered doses were not able to maintain LEV concentrations in the recommended therapeutic range. Other dosage strategies, such the extension of infusion time with higher doses, could be evaluated in order to obtain a more favourable profile. No correlation between LEV CL and CrCL was found.

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References: