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Pharmacokinetics for Pediatrics, Pregnancy, and Other Special Populations



Pharmacokinetics of Lopinavir in HIV-1 infected children

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Introduction: Lopinavir (LPV) is a protease inhibitor (PI) that can be administered in different pharmaceutical forms liquid or tablets co-administered with another PI, ritonavir used like a booster (LPV/r), leading to less fluctuation LPV levels in blood. Therapeutic drug monitoring of antiretrovirals (ARV) may be useful in HIV infected children because of differences in pharmacokinetics of several ARV drugs between children and adults. Moreover maturation of difference organs involved in absorption and metabolism could be related to changes in pharmacokinetics of ARV drugs during growth in children.

Objectives: Previous works have shown a great interindividual variability in LPV levels in children treated with LPV/r. The aim of this work was to study the LPV levels in HIV-1 infected children treated with different oral formulations of LPV/r and to study different co-variables that could be involved in pharmacokinetics variability of LPV in this population.

Material & Methods: 60 patients treated with LPV/r (Kaletra, Abbott-capsules, tablets or solution) were included. Dose regimen was 12 mg/kg/12 hours for children < 15 kg and 10 mg/kg/12 hours for children ≥ 15 kg. Therapeutic drug monitoring of LPV in blood was performed. Samples were drawn between 1 and 4 hours after the corresponding dose (C1) or previous to the corresponding dose (Cmin). The samples were measured by means of HPLC-UV. Demographic data, dose regimen, sampling times and co-medication were also registered.

Results: 104 LPV plasma levels (57 Cmin and 47 C1) were obtained. The median age was 7.0 years old (range: 4 months-19 years old). A significant interindividual variability in LPV levels was observed (CV Cmin: 160.9%, C1: 127.4%). No statistical significant difference in LPV plasma levels were observed after the administration of liquid or solid formulations. 12 patients showed LPV levels < 1 µg/ml. No relationship was observed between LPV level normalized by dose and age. In children ≤ 2 years old, 6 patients showed LPV levels higher than 1 µg/ml, LPV levels were subtherapeutic (< 1 µg/ml) in 5 patients, although 4 patients showed no compliance or intolerance to the liquid formulation.

Conclusions: The great variability observed in LPV levels, including patients with subtherapeutic levels; suggest that therapeutic drug monitoring of LPV could be advisable in HIV-1 infected children treated with LPV/r in order to optimize ARV treatment

No conflict of interest