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Low atazanavir concentrations in cerebrospinal fluid.

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OBJECTIVE: Protease inhibitors may not penetrate into the central nervous system in therapeutic concentrations, which may allow ongoing HIV replication and injury. The objective of this study was to determine atazanavir penetration into cerebrospinal fluid (CSF).

DESIGN: Single random plasma or paired plasma and CSF samples were drawn from participants enrolled in a multicenter, observational cohort study and taking atazanavir with or without ritonavir between October 2003 and October 2005.

METHODS: Plasma samples were assayed by high performance liquid chromatography and immunoassay; lower limit of detection was 45 ng/ml. CSF samples were assayed by immunoassay (ARK ATV-test); lower limit of detection was 5 ng/ml.

RESULTS: One hundred and seventeen participants (43 +/- 7.7 years, 79% men, 81 +/- 15 kg) had plasma or plasma and CSF paired samples drawn a median (interquartile range) of 10 (5-17) h postdose. Median (interquartile range) plasma atazanavir concentrations with or without ritonavir were 1278 (525-2265) and 523 (283-1344) ng/ml. The median (interquartile range) CSF concentrations with or without ritonavir were 10.3 (<5-21.1) and 7.9 (6.6-22) ng/ml. Nineteen of 79 (24%) CSF samples were less than 5 ng/ml. CSF concentrations were less than 1% of plasma concentrations and near the atazanavir wild-type IC₅₀ of 1-11 ng/ml.

CONCLUSION: Atazanavir CSF concentrations are highly variable and 100-fold lower than plasma concentrations, even with ritonavir boosting. CSF concentrations of atazanavir do not consistently exceed the wild-type IC₅₀ of atazanavir and may not protect against HIV replication in the CSF.

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