

Plasma concentrations of risperidone in children, adolescents and adults with psychiatric disorders

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Risperidone is a second-generation antipsychotic widely used in children and adolescents with schizophrenia, bipolar disorder, irritability associated with autistic disorder and disrupting behavior disorder. Risperidone is extensively metabolized in the liver by CYP2D6 and, to a lesser extent, CYP3A4 to 9-hydroxyrisperidone, which is approximately equipotent with the parent drug in terms of receptor binding profile. While the pharmacokinetic properties of risperidone have been thoroughly examined in adults, few investigations have involved the pediatric population. Aim of the present study was to evaluate steady-state plasma concentrations of risperidone in children and adolescents and in adults. Risperidone samples sent to a routine therapeutic drug monitoring service over a period of 6 years (January 2007-December 2012) were considered for the study. Samples for which the request forms did not include information about dose and/or time interval between last intake of medication and blood sampling were excluded. Plasma concentrations of risperidone and 9-hydroxyrisperidone were measured by HPLC. The final data set consisted of 514 plasma concentrations values from 258 adult patients (153 males, 105 females, aged 19-84) and 249 plasma concentrations from 123 children/adolescents (88 males, 35 females, aged 3 to 18 years). Mean (95% CI) plasma concentrations of the active moiety of risperidone (sum of concentrations of risperidone + 9-hydroxyrisperidone) normalized per dose were higher in children and adolescents, 13.91 ng/mL per mg/day (95% CI 12.83, 15.07) than in adults, 10.73 ng/mL per mg/day (95% CI 10.12, 11.38) ($p < 0.01$). In both populations, females exhibited significantly higher concentrations of risperidone than males ($p < 0.01$). These findings suggest an age effect for risperidone resulting in higher plasma levels in younger patients. Moreover, in agreement with earlier observations, a gender effect was detected in both adult and pediatric population as total plasma concentrations of risperidone were significantly higher in female than in male patients. Future prospective studies are necessary to clarify whether the prescribed dosage should be different in young and older patients.