Short Communication

The activity of cytochrome P450 CYP2B in rat liver during neuroleptic treatment

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Abstract:
The aim of the present study was to investigate the influence of classic and atypical neuroleptics on the activity of rat CYP2B measured as a rate of 16β-hydroxylation of testosterone. The reaction was studied in control liver microsomes in the presence of neuroleptics, as well as in microsomes of rats treated intraperitoneally for one day or two weeks (twice a day) with pharmacological doses (mg/kg) of the drugs: promazine, levomepromazine, thiorthidizine and penazine, 10 each; chlorpromazine 3; haloperidol 0.3; risperidone 0.1; sertindole 0.05, in the absence of the neuroleptics in vitro. Some of the neuroleptics added in vitro to control liver microsomes decreased the activity of CYP2B. The obtained Kᵢ values indicated that thiorthidizine was the most potent inhibitor of the studied reaction (Kᵢ = 26 μM). The inhibitory effects of chlorpromazine, penazine and sertindole were moderate (Kᵢ = 45-75 μM), while promazine, haloperidol, levomepromazine and risperidone were rather weak inhibitors of CYP2B activity (Kᵢ = 125-225 μM, respectively). After a one-day (i.e. 24 h) exposure of rats to the investigated neuroleptics, the decreased CYP2B activity was observed after haloperidol, risperidone and sertindole. All the investigated neuroleptics did not produce any significant effect on CYP2B activity when administered in vivo for two weeks. Considering relatively high pharmacological/therapeutic doses and liver concentrations of phenothiazines, it seems that the direct inhibitory effect of those neuroleptics with Kᵢ values below 100 μM found in vitro (thioridazine, chlorpromazine, penazine), as well as indirect effects produced by one-day treatment with haloperidol, risperidone or sertindole may be of some physiological, pharmacological or toxicological importance in vivo.

Key words:
phenothiazines, haloperidol, risperidone, sertindole, CYP2B, testosterone 16β-hydroxylation, liver microsomes, rat, in vitro study, one-day treatment, chronic treatment