DOXEPIN INHIBITS CYP2D6 ACTIVITY IN VIVO

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Objective. Doxepin is a tricyclic antidepressant formulated as a mixture of E-(trans) and Z-(cis) stereoisomers. Cytochrome P450 2D6 (CYP2D6) catalyzes the hydroxylation of E-doxepin and E-N-desmethyldoxepin stereospecifically. There is evidence that tricyclic antidepressants might inhibit CYP2D6 activity but there is no data about the influence of doxepin on CYP2D6.

Materials and methods. Eleven patients diagnosed with depression according to ICD-10 criteria were included in the study. After wash-out period, before doxepin treatment, sparteine metabolic ratio (MR1) was assessed. After 2-weeks of doxepin treatment, MR2 was estimated. Sparteine and its metabolites were determined in urine by gas chromatographic method of Eichelbaum et al.

Results. Based on MR1 values, 10 patients were classified as EM (extensive metabolizers) and 1 patient as PM (poor metabolizer). During the study, after doxepin treatment, none of patients has changed phenotype status. However, MR2 values were statistically significantly higher than MR1.

Conclusion. These results show the inhibitory effect of doxepin on CYP2D6 activity and may be of clinical value, especially in polymedicated patients treated with other CYP2D6 substrates or inhibitors.

Key words: doxepin, CYP2D6, inhibition, tricyclic antidepressants

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