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Evaluation of the functional role of P-glycoprotein in brain uptake of tramadol in rat.

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Background and Aims: Efflux transporters at the blood-brain barrier (BBB) limit the brain tissue exposure to a variety of drugs and xenobiotics. P-glycoprotein is one of the most important efflux transporters which is located throughout the body. Tramadol Hydrochloride is a widely-used centrally acting analgesic drug, which has some features of being a P-gp substrate. The present study evaluates the possible functional involvement of P-gp in brain penetration of Tramadol Hydrochloride.
Methods: The functional role of P-gp in brain distribution of tramadol was assessed by using a single-passage pharmacokinetic approach. Plasma and brain samples were collected at 1, 5, 10, and 30 min following dose of 10 mg/kg of tramadol in both control and Pgp-inhibited groups. Each group contain six male Sprague-Dawley rats weighing between 250 and 300 gram. Verapamil hydrochloride was used as a P-gp inhibitor.
Results: The brain uptake clearances of tramadol in Pgp-inhibited and control rats were 3.50±0.60 and 3.14±1.02 mlmin-1kg-1, respectively. The brain extraction ratios of tramadol in Pgp-inhibited and control rats were 6.06±0.73 and 5.43±1.22, respectively. The data of Pgp-inhibited and control animals, showed no significant differences and indicated active brain uptake.
Conclusions: The results of the present study indicate that tramadol isn't the P-gp substrate and concurrent use of P-gp modulator may not affect its brain uptake.

Keywords: P-glycoprotein; Blood brain barrier; Tramadol; Tissue uptake