Progesterone role in regulation of ABCB1 transporter functional activity

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Abstract

On chinchilla rabbits the progesterone role in regulation of ABCB1 transporter (P-glycoprotein) functional activity was studied. Animals were divided into 3 groups: the first group of animals underwent an ovariectomy (n=6); the second and the third groups also underwent an ovariectomy followed by progesterone [2 mg/rabbit/day per os (n=6) and 15 mg/rabbit/day per os (n=6)] administration since 15^{th} day after the operation for 28 days.

The transporter functional activity was estimated by the pharmacokinetics (C_{max}-maximal concentration and AUC_{0-t} – area under curve) of its marker substrate – fexofenadine determined by HPLC. Fexofenadine was administered intragastrically ones a day (67,5 mg/kg b.w.) before the experiment beginning and on the 14^{th}, 28^{th} and 42^{th} days after the operation.

Ovariectomy led to decrease ABCB1 transporter functional activity (increase C_{max} and AUC_{0-t} of fexofenadine) from the 14^{th} day of the experiment. Progesterone administration at a dose 2 mg/rabbit/day after ovariectomy increased ABCB1 transporter functional activity compared with ovariectomy group, but its activity remained reduced compared with baseline data. Use of progesterone at a dose 15 mg/rabbit/day after ovariectomy increased ABCB1 transporter functional activity as compared with parameters of the ovariectomy group, restoring its activity to the parameters of intact animals.

Conclusion. Ovariectomy leads to decrease ABCB1 transporter functional activity determined by fexofenadine pharmacokinetics; progesterone in physiological doses after ovariectomy stimulates it.