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Influence of simvastatin at high dose and nifedipine on hemodynamic parameters in rabbits

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Abstract:
Recent findings *in vitro* have shown that statins could reduce cardiomyocyte viability. The correlation between statin cardiotoxicity, assessed *in vitro*, and cardiac efficiency, investigated *in vivo* has not been estimated so far.
The aim of the present experiment was to establish the impact of high-dose simvastatin on the hemodynamic parameters, especially on myocardium efficiency, after continuous infusion of dopamine. Moreover, hemodynamic interaction between simvastatin and nifedipine, metabolized by the same izoenzyme CYP3A4 was examined. The experiments were performed on twenty seven New Zealand white rabbits. The animals were divided into four groups receiving: 0.2% methylcellulose (MC) (control group), nifedipine, simvastatin or simvastatin + nifedipine, for 14 days (*po*). The following hemodynamic parameters were estimated: cardiac output index (COI), heart rate (HR), systolic blood pressure (SBP), mean blood pressure (MBP), diastolic blood pressure (DBP) and total peripheral resistance index (TPRI). The registration of hemodynamic parameters was performed by Doppler method (Hugo Sachs Electronic Haemodyn). Dopamine did not cause a statistically significant increase in COI in rabbits receiving simvastatin alone or concomitantly with nifedipine. Nifedipine significantly lowered COI, BP and HR in rabbits if given simultaneously with simvastatin.
In conclusion, administration of nifedipine may elicit detrimental impact on statin therapy, resulting in the worsening of cardiac performance. This may suggest another mechanism of drug-drug interaction than the one based on CYP3A4 inhibition.

Key words:
simvastatin, nifedipine, hemodynamic parameters, rabbits