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Effect of simvastatin on nitric oxide synthases (eNOS, iNOS) and arginine and its derivatives (ADMA, SDMA) in ischemia/reperfusion injury in rat liver

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Abstract:
Hydroxymethylglutaryl-CoA reductase inhibitors play a role in nitric oxide synthesis. In this study, the impact of simvastatin (SV) on the levels of nitric oxide synthases, and arginine (Arg) and its derivatives was evaluated in rat liver under ischemia-reperfusion (I/R) conditions. Rats received SV (25 mg/kg) (groups S and S-IR) or saline solution (groups C and C-IR) intragastrically for 21 days. The livers of groups C and S were homogenized after treatment while those of groups C-IR and S-IR underwent ischemia and reperfusion before homogenization. Endothelial (eNOS) and inducible (iNOS) nitric oxide synthase concentrations were determined in the homogenates. Alanine and asparagine aminotransferase (ALT, AST, respectively), arginine (Arg), and asymmetric (ADMA) and symmetric (SDMA) methylarginine levels were determined in the blood before I/R and during reperfusion. I/R injury produced significant increases in aminotransferase, ADMA, eNOS, and iNOS, but decreases in Arg and Arg/ADMA levels. Arg concentration increased significantly after warm ischemia in the S-IR group, but decreased significantly during the first 30 minutes of reperfusion in both the S-IR and C-IR groups. eNOS concentration was significantly higher in group S than in group C. Both I/R and SV exerted no influence on SDMA concentration. SV exerted a protective action by increasing eNOS levels under normal conditions and Arg levels after ischemia and by preventing a significant increase in iNOS concentration after I/R. SV had no effect on ADMA concentration under normal and pathological conditions.

Key words:
simvastatin, liver, rat, ischemia/reperfusion, nitric oxide synthetase