ANTIOXIDATION EFFECT OF SIMVASTATIN IN RABBIT HIPPOCAMPUS: ROLE OF SUPEROXIDE DISMUTASE, GLUTATHIONE PEROXIDASE, MALONDIALDEHYDE AND HAEM OXYGENASE-1

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Objectives
Hypercholesterolemia contributes to coronary artery disease progression but little is known about its effect on hippocampus. The pleiotropic effects of HMG-CoA inhibitors...
Abstracts

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(statins), which include anti-inflammation, antioxidation and immunomodulation. It has been reported that statins exert direct anti-inflammation effects dependent of vascular adhesion molecule and chemokine expression of aortae, but its effects of hippocampus are not yet fully understood. The present study was designed to elucidate the role of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), malondialdehyde (MDA) and haem oxygenase-1 (HO-1) in the antioxidation effect of Simvastatin.

Methods The study was carried out on adult male Japanese white (JW) rabbits weighing approximately 2.0 kg. The animals were randomised into three groups of eight animals each: one control group and other two groups which were maintained on high-cholesterol diet (HCD) for 6 months. After 2 months on this diet, the animals were divided into two groups: non-treated group and simvastatin group. The animals were euthanised with an overdose of sodium pentobarbital. The hippocampus were excised, placed in ice-cold sterile saline, and cleaned of connective tissue. Blood was taken through cardiac puncture and plasma was used for biochemical assay of lipid peroxides. Levels of SOD, GSH-Px and MDA were measured by use of Enzyme-linked immunosorbent assay (ELISA) kits. HO-1 mRNA in hippocampus were analysed by using Real Time Quantitative PCR methods and expression of HO-1 protein, plasma malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) were also measured.

Results Hypercholesterolaemia decreased SOD (6.43±1.29 vs 10.10±1.08 μg/ml control) and GSH-Px (36.95±5.53 vs 48.85±8.59 U/L control group) and increased cytotoxic MDA (16.69±1.42 vs 9.17±2.44 mg/ml control group) in hippocampus, and it has same trend in plasma SOD, GSH-Px and MDA. HO-1 mRNA expression of non-treated group decreased respectively (about 4.9-fold vs control group), but increased (about 5.5-fold vs non-treated group) after treatment with Simvastatin. SOD and GSH-Px were as well as increased significantly than the non-treated group (p<0.01 or p<0.05) after treatment with Simvastatin. Simvastatin partially restored the HO-1, SOD and GSH-Px, decreased MDA levels.

Conclusions Atherosclerosis induced an oxidative damage in hippocampus. Simvastatin showed antioxidation effects mediated by HO-1, restoring the SOD and GSH-Px levels and reducing cytotoxic MDA levels.