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EXPERIMENTAL STUDY

Effects of atorvastatin on heart mitochondrial function and coenzyme Q content in the experiment

Kucharska J[1], Ulicna O[1], Gvozdjakova A[1], Vancova O[1], Waczulikova I[3], Bozek P[4], Bada V[2]

Pharmacobiochemical Laboratory of Third Department of Internal Medicine, Faculty of Medicine, Comenius University, Bratislava, Slovakia. **jarmila.kucharska@fmed.uniba.sk**

Abstract: We focused on determination of whether atorvastatin: 1) reduces CoQ content, 2) impairs mitochondrial function and 3) induces dose-dependent changes. Although the high dose of atorvastatin exerted a beneficial effect on the lipid peroxidation in plasma, coenzyme Q content was reduced and heart mitochondrial function was impaired. Physicians should be aware when prescribing statins mainly in higher doses to the patients with co-existing proved or supposed CoQ_{10} deficiency resulting from age-related decline, and metabolic or mitochondrial diseases *(Ref. 3)*. Full Text in free PDF *www.bmj.sk.*
Key words: atorvastatin, heart mitochondrial function, coenzyme Q.

Statins are effective lipid lowering agents which are beneficial in prevention of coronary artery disease. They reduce cholesterol biosynthesis by inhibiting the enzyme HMG-CoA reductase. This results in a diminished synthesis of other mevalonate pathway downstream products, namely coenzyme Q (CoQ). Since CoQ is an essential part of mitochondrial respiratory chain responsible for ATP production, its inhibited biosynthesis may be involved in some adverse effects of statins. Decreased levels of CoQ_{10} in plasma were found in patients treated with statins (1, 2). It is assumed that CoQ_{10} deficiency might be detrimental to the long term prognosis of chronic heart failure (3). However, there is only scarce documentation on mitochondrial function and CoQ content with regard to the used dose of statins.

Aim of study

We focused on determination of whether atorvastatin: 1) reduces CoQ content, 2) impairs mitochondrial function and 3) induces dose-dependent changes.

[1]Pharmacobiochemical Laboratory of Third Department of Internal Medicine and [2] Third Department of Internal Medicine, Faculty of Medicine and [3]Division of Biomedical Physics, Faculty of Mathematics, Physics and Informatics, Comenius University, Bratislava, Slovakia, and [4]St. Michael Hospital, Department of Clinical Biochemistry and Haematology, Bratislava, Slovakia

Address for correspondence: J. Kucharska, PharmD, PhD, Pharmacobiochemical Laboratory of Third Department of Internal Medicine, Faculty of Medicine, Comenius University, Sasinkova 4, 811 08 Bratislava, Slovakia.
Phone/Fax: +421.2.59357242

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Material and methods

Hypercholesterolemia was evoked by feeding the Wistar rats for 8 weeks with a high cholesterol (4 %) and saturated fat (10 %) added to the standard diet. Atorvastatin was administered orally by a gastric tube either at a low dose (LD – 10 mg/kg/day) or at a high dose (HD – 80 mg/kg/day) to both control (C) and hypercholesterolemic rats (CH) for 4 weeks. Each group consisted of 10 animals. The experiment was carried out according to the guidelines for the care and use of laboratory animals. Heart mitochondria were isolated by differential centrifugation, functional parameters of mitochondria were examined on the basis of oxygen consumption with Clark oxygen electrode with an Oxygraph. CoQ_9 and CoQ_{10} concentrations were determined by HPLC, lipid peroxidation (TBARS) spectrophotometrically, total cholesterol (tChol) on analyzer Hitachi. Statistical evaluation was performed with a StatsDirect 2.7.7. software.

Results

Atorvastatin at HD decreased plasma concentration of CoQ_9 and CoQ_9/tChol ratio in both, C and CH rats. TBARS formation decreased to the control values in CH rats given HD of atorvastatin. Both doses decreased mitochondrial respiration, rate of ATP production, and concentrations of CoQ_9 and CoQ_{10} in CH rats. HD of atorvastatin decreased mitochondrial function and CoQ content also in the healthy animals.

Conclusions

Although the high dose of atorvastatin exerted a beneficial effect on the lipid peroxidation in plasma, coenzyme Q content was reduced and heart mitochondrial function was impaired. Physicians should be aware when prescribing statins mainly in

higher doses to the patients with co-existing proved or supposed CoQ_{10} deficiency resulting from age-related decline, and metabolic or mitochondrial diseases.

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