Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol10Issue3abst020P.pdf

P534

Adverse Cardiac Responses to Alpha-Lipoic Acid in a Rat Diabetic Model: Possible Mechanisms?

NM AL-Rasheed, NM AL-Rasheed, HA Attia, IH Hassan, HN AL-Ajmi, MA AL-Amin, RA Mohamad.
King Saud University, Pharmacology and Toxicology, P.O.Box:22452,Riyadh:11495, Saudi Arabia

Background:

Alpha-lipoic acid (ALA) is widely used to improve diabetic complications, but its adverse cardiovascular effects are recently recognized. This study was designed to investigate whether ALA supplement may induce oxidative protein modifications which may contribute to cardiac toxicity in both diabetic and non-diabetic rats.

Methods:

Adult male Wistar rats (150-200 g) were divided into four groups of ten rats each (n=10). Diabetes was induced by intraperitoneal injection of streptozotocin (55mg kg^{-1}, dissolved in cold citrate buffer adjusted to pH 4.5). Diabetic and/or non-diabetic animals were treated by ALA (100mg kg^{-1}, p.o) for four consecutive weeks. Cardiovascular biomarkers, lipid profiles, oxidative stress markers and protein oxidation parameters were measured. A one-way analysis of variance followed by the Newman-Keul's comparisons test was carried out. Data are expressed as mean ± SEM. Differences were considered significant at a P value <0.05.

Results:

After 4 weeks, non diabetic rats treated with ALA showed cardiovascular toxicity reflected by significant elevation of troponin-I [808.75±76.2 Vs 111±8.4 pg/ml (P<0.001)], creatine kinase (CK) [971.45±19.2 Vs 188.1±27.2 U/L (P<0.001)], aspartate aminotransferase (AST) [178.09± 3.4 Vs 77.988±3.45 U/L (P< 0.05)], as well as lipid profile (P< 0.05) as compared to normal control. There was highly significant increase in advanced oxidation protein product (AOPP) [268±39.7 Vs 56.4 ±11.1 nmol/gm (P<0.001)] in addition to reduced total thiol (T-SH) (P<0.001), non-protein thiol (NP-SH) (P<0.01) and catalase (P<0.001) as compared with normal control. In addition, vascular endothelial growth factor (VEGF) levels significantly reduced as compared to normal control [162.22 ±40.2 Vs 248.8 ± 37.7mg/dl (P<0.05)]. No significant changes were observed in ALA-treated diabetic rats compared to control diabetic concerning cardiac biomarkers, lipid profile or protein oxidation markers.

Conclusion:

Data suggest that the potential pro-oxidant effects of ALA on oxidative protein damage in diabetic and/or non-diabetic heart tissue may induce cardiotoxicity.

Keywords: Alpha-lipoic acid; protein oxidation; advanced oxidation protein products; lipid peroxidation.