

6<sup>th</sup> Global Diabetes

# Summit and Medicare Expo

November 02-04, 2015 Dubai, UAE

## Role of $\alpha$ -lipoic acid as cardioprotective therapy in type 1 diabetes

**Osama El Razaky**  
Tanta University, Egypt

**Background:** The development of Diabetic cardiomyopathy(DCM) is multifactorial and mellitus several pathophysiologic mechanisms have been proposed to explain structural and functional changes associated with DCM.  $\alpha$ -Lipoic acid (ALA) a powerful antioxidant may has a protective role in diabetic cardiac dysfunction.

**Aim of the work:** This study aimed to assess the potential role of oxidative stress, inflammatory cytokines, apoptosis and fibrosis in diabetic cardiac insult. It also investigated the possible protective role of  $\alpha$ -lipoic acid on diabetic left ventricular (LV) dysfunction in type 1 diabetic children and adolescents.

**Subjects and methods:** 30 patients were randomized to receive insulin treatment (n = 15) or insulin plus  $\alpha$ -lipoic acid 300 mg twice daily (n = 15). Age and sex matched healthy control children and adolescents (n = 15) were also included. Patients were evaluated with conventional 2-dimensional echocardiographic examination (2D), pulsed tissue Doppler (PTD), and 2-dimensional longitudinal strain echocardiography (2DS) before and after therapy. Plasma level of glutathione, malondialdehyde (MDA), nitric oxide, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), Fas Ligand (Fas-L), matrix metalloproteinase-2 (MMP-2) and troponin-I were determined before and after treatment.

**Results:** Diabetic patients had significant lower level of glutathione and significant higher levels of malondialdehyde (MDA), nitric oxide, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), Fas Ligand (Fas-L), matrix metalloproteinase-2 (MMP-2) and troponin-I than control subjects. Increased expression of transforming growth factor- $\beta$  (TGF- $\beta$ ) mRNA in peripheral blood mononuclear cells was also observed in diabetic patients.  $\alpha$ -lipoic acid significantly increased glutathione level and significantly decreased MDA, nitric oxide, TNF- $\alpha$ , Fas L, MMP-2 ,troponin I levels and TGF- $\beta$  gene expression levels. Moreover,  $\alpha$ -lipoic acid significantly increased mitral e/a ratio, ventricular global peak systolic strain in diabetic patients. There were significant negative correlation between Global peak systolic strain (G) and glutathione and significant positive correlations between G and MDA , NO , TNF- $\alpha$  , and Fas-L . In addition, a significant positive correlation between e/a ratio and glutathione (r = 0.515) and significant negative correlations between e/a and MDA , NO , TNF- $\alpha$  , and Fas-L were also observed

**Conclusion:** These data suggest that oxidative stress, inflammatory cytokines such as TNF- $\alpha$ , apoptosis and fibrosis play a role in the development of diabetic cardiac dysfunction and that  $\alpha$ -lipoic acid may have a beneficial role in the management of type 1 diabetic patients as a cardioprotective therapy and prevention of development of diabetic cardiomyopathy.

[usama.toulba@med.tanta.edu.eg](mailto:usama.toulba@med.tanta.edu.eg)

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