Modulation of Inflammatory Mediators Involved in Experimentally Induced Heart Failure by Using Omega-3 Fatty Acids

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Summary and Conclusion

Summary:

Heart failure (HF) is a progressive disease that starts as a myocardial injury that leading to a defect in the normal architecture of the left ventricle of heart (Klapholz, 2009). Such ventricular changes appear in the form of hypertrophy, dilatation and fibrosis, are mediated by high neurohormonal activity and high adrenergic tone (Cohn, 1986; Packer, 1992). Many common causes may lead to heart failure such as hypertension, congenital heart disease, idiopathic cardiomyopathy, rheumatic fever, valve disease, coronary artery disease and ischemic heart disease (Killip, 1985; Mendez and Cowie, 2001; Ntusi and Mayosi, 2009).

Recently the important role of inflammatory mediators in HF was established. Accordingly modulation of the activity of these inflammatory mediators is a promising therapeutic target to improve the failed heart & to protect it. It is obvious that targeting the immune elements involved in the pathophysiology of HF is the present way to modulate the activity of the inflammatory mediators produced by these cells. The aim of this study is involving omega-3 fatty acids as an essential part of the dietary regimen of both healthy individuals & those that suffer from HF as a protective & therapeutic tool against this disease induced by using doxorubicin which is an anthracycline anticancer drug used for the treatment of many malignancies. Assessment of electrophysiological examinations, histopathological and biochemical evaluation were done. HF compensatory mediators, proinflammatory cytokines, antioxidant effect and lipid peroxidation were analyzed in this experimental work. Omega-3 fatty acids resulted in control and remarkable decrease in the mortality rate caused by Dox, almost normalized the ECG findings by decreasing the heart rate, controlling the QT interval and R amplitude in the QRS complex wave when compared to Dox group and carvedilol group (as standard group). Omega-3 fatty acids administered to (OMG-P + Dox and OMG-T + Dox groups) also control cardiac hypertrophy and shown significant decrease in HW/BW ratio and angiotensin-II (Ang-II) serum level. In both groups (OMG-P + Dox and OMG-T + Dox) cardiac malondialdehyde (MDA) levels was significantly decreased while there was significant increase in serum Na⁺/K⁺ ATP1A1. Cardiac reduced glutathione (GSH) level was significantly elevated in (OMG-P + Dox and OMG-T + Dox) groups. Interesting significant decrease in lipid profile parameters
(cholesterol, triglycerides, and low-density lipoprotein cholesterol) and significant elevation in high density lipoprotein cholesterol serum level was showed in both groups (OMG-P + Dox and OMG-T + Dox). Dox induced cardiac injury indicated by a significant increase in serum creatine kinase-MB (CK-MB) activity, serum lactate dehydrogenase (LDH) activity and serum alkaline phosphatase level (ALP). Omega-3 fatty acids administration decreased these markers indicating its beneficial effect. Omega-3 fatty acids, when used as protective or treating agent, decrease the inflammatory cytokines tumor necrosis factor-alpha (TNF-α) serum level significantly.

Omega-3 fatty acids used in (OMG-P + Dox and OMG-T + Dox groups) resulted in the improvement of cardiac contraction and membrane integrity and reduce cardiomyopathy in rats injected by Dox through decreasing TNF-α, cardiac MDA, increasing cardiac GSH, and also lowering angiotensin II (Ang-II) level.

Histopathological examination of cardiac sections from rats received omega-3 fatty acids showing that most of cardiac muscle fibers show normal arrangement and structure while few ones are corrugated and swollen. Also a very mild amount of collagen fibers was seen around blood vessels and between muscle fibers.

**Conclusion:**

Healthy life style and healthy food involving omega-3 fatty acids as an essential part of the dietary regimen of both healthy rats & those that suffering from HF as a protective & therapeutic tool against this disease will significantly improve the cardiac function and prevent tissue remodeling. This occurs by lowering the pro-inflammatory cytokine (TNF-α) level, controlling lipid profile, decreasing lipid peroxidation and controlling the oxidative stress parameters and improving kidney and liver functions. Further experimental work on other models should be done to introduce omega-3 fatty acids as a pharmacological treatment or as a protective agent against cardiomyopathies including HF.