Trans Fatty Acids Promote Atherosclerosis and Sudden Cardiac Death in Experimental Models

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Epidemiological data indicates that there is a strong association between intake of *Trans* fatty acids (TFAs) and sudden cardiac death. Increased dietary TFA intake is associated with elevated LDL and reduced HDL levels, which predispose to the development of atherosclerosis. To date, few laboratory studies on TFAs have been conducted and therefore, there is an apparent lack of knowledge about the mechanisms by which TFAs exert harmful effects on the cardiovascular system. This investigation studied the effects of TFAs on atherosclerosis in both *in vivo* and *in vitro* systems. In vivo studies: Male rats were subjected to coronary ligation to induce myocardial infarction and were randomly assigned to diets high in omega-3 fatty acids (n-3 FAs) or TFA. A diet high in TFAs was associated with a lower 6-month survival rate due to sudden cardiac death (50% TFA group, vs. 80% n-3 FA group). Animals on TFA diets also exhibited variable degrees of atherosclerotic lesions in aortas whereas animals on n-3 diets did not exhibit these lesions. In vitro Studies: Our *in vitro* study determined the effects of incorporated C18:2 TFAs on human arterial endothelial cell (HAEC) functions. Trans18:2 fatty acids were incorporated to a greater extent (2 fold) in the phospholipid fraction of endothelial cells than that of cis-18:2, whereas these fatty acids enriched to a similar extent in triglyceride fractions. Flow cytometric analysis indicated that treatment with C18:2 TFAs significantly increased the expression of endothelial adhesion molecules, including intracellular adhesion molecule-1 (CD54) and vitronectin receptor (CD51/CD61). TFA incorporation increased HAEC adhesion to fibronectin-coated plates by approximately 40%. Neutrophil adhesion to HAEC monolayers were proportional to CD54 expression. Furthermore, we examined the role of TFAs on HAEC angiogenesis, a process that involves cell migration and differentiation. Chemotactic migration of TFA-treated HAECs toward sphingosine-1-phosphate (SPP) was significantly increased over 50% compared to controls. Conversely, capillary morphogenesis of TFA-treated HAECs was significantly inhibited in response to SPP, suggesting that 18:2 TFAs suppresses endothelial cell differentiation. In conclusion, both *in vitro* and *in vivo* studies demonstrate that TFAs play a role in the induction of atherosclerosis and endothelial dysfunction. These results may partially explain the detrimental cardiovascular effects of high dietary TFAs.