EFFECT OF TOCOTRIENOL ON PLAQUE STABILITY IN EARLY AND ESTABLISHED ATHEROSCLEROSIS

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ABSTRACT 1

TOCOTRIENOL-TOCOPHEROL MIXED FRACTION SUPPLEMENTATION PREVENTS LESION PROGRESSION IN EARLY AND ESTABLISHED ATHEROSCLEROSIS

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Background: Inflammation plays a key role in plaque stability and the pathogenesis of atherosclerosis. Palm-derived tocotrienol-tocopherol mixed-fraction (TTMF) is a potent antioxidant with anti-inflammatory effects. The effect of TTMF on the development of early and established atherosclerosis remains unclear.

Objective: To determine the anti-inflammatory effects of TTMF in rabbits with early and established atherosclerotic lesions.

Materials and methods: 60 New Zealand white rabbits were randomized into three major groups which further divided into two groups each with supplementation: (i) TTMF (15mg/kg) or (ii) placebo. Group A were given intervention of TTMF for 2 month followed by high cholesterol diet for either 2 weeks or 2 month with TTMF while group B were induced with high cholesterol diet for either 2 weeks or 2 month before stopped the high cholesterol diet and intervened with TTMF. Group C were given both TTMF and high cholesterol diet concurrently. Blood samples at the intervention interval were analyzed for serum lipid and soluble CRP. At the end of the study, the aortas were evaluated for atherosclerotic lesion using Sudan IV stain and immunohistochemistry staining. Quantitative analysis of the lesion staining was performed using image analysis software.

Results: There were significantly reduced atherosclerotic lesions in early (Mean ± SEM; TTMF vs. placebo:7.92 ±2.9 vs. 16.6 ± 1.6 %; $p<0.05$) and established atherosclerosis (Mean ± SEM; TTMF vs. placebo : 8.45 ± 2.03 vs. 29.47 ± 4.83%; $p<0.05$) in Group A. Expressions of E-selectin were also significantly reduced in established atherosclerosis in Group A (Mean ± SEM; TTMF vs. placebo: 6.70 ± 1.43 vs. 21.18 ± 2.81 %;$p<0.05$) and in early atherosclerosis (Mean ± SEM; TTMF vs. placebo : 0.87 ± 0.23 vs. 5.82 ± 2.05 % ; $p<0.05$) of B1 group. Group C showed no differences in both early and established atherosclerosis with TTMF. However, TTMF gives neutral effects on blood biomarkers of all three groups.

Conclusion: TTMF effectively prevents atherosclerotic lesions and inflammatory marker in early and established atherosclerosis. Further studies should emphasis on the tocotrienol isomers for the therapeutic potential of atherosclerosis.