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COMBINATION OF OMEGA-3 FATTY ACID AND MENAQUINONE-7 PREVENTS PROGRESSION OF AORTIC CALCIFICATION IN ADENINE AND LOW PROTEIN DIET INDUCED RAT MODEL

Young ki SON¹, Hyo in RHYOU¹, Hyuck jae CHOI¹, Hyo jin JEONG², Su mi LEE¹, Seong eun KIM¹, *Won suk AN¹

¹Department of Internal Medicine, Dong-A University, Korea, South, ²Department of Internal Medicine, Dong-Eui Medical Center, Korea, South

Objectives : Vascular calcification is common and progressing in chronic kidney disease and dialysis patients. Diet with high-dose menaquinone-7 (MK-7) (100 ug/g diet) inhibited the development of cardiovascular calcification in 5/6 nephrectomy rat combined with high phosphate diet. Eicosapentaenoic acid (1g/kg/day), one of omega-3 fatty acid (FA), attenuates arterial medial calcification induced by warfarin. We evaluated whether the effect of omega-3 FA and MK-7 on aortic calcification in adenine and low protein diet induced vascular calcification rat model.

Methods : Male Sprague Dawley rats were fed the diets containing 0.75% adenine and 2.5% protein for 3 weeks. After 3 weeks, 4 rats were sacrificed for calcification evaluation of thoracic aorta. Thirty two rats were randomly divided into four groups, which were treated and fed the diets containing 2.5% protein for 4 weeks: adenine control (0.9% saline), adenine control treated with omega-3 FA (300 mg/kg/day by gastric gavage), adenine control treated with MK-7 (50 ug/kg/day by gastric gavage), adenine control treated with omega-3 FA and MK-7. Serum creatinine, blood urea nitrogen (BUN), calcium and phosphate were measured. Normal control rats were fed the diets containing 2.5% protein for 7 weeks. For quantitative assessment of aortic calcification, von Kossa stain of aorta was done and calcium contents were measured with calcium colorimetric kit.

Results : Serum creatinine of adenine control group treated with omega-3 FA and MK-7 was lower than adenine control group without treatment. Serum calcium and BUN levels were not significantly different between adenine control group with treatment and without treatment. All treated groups and group without treatment were exposed to higher serum phosphate level without difference. Two rats among 4 rats showed aortic calcification at 3 weeks. After 4 weeks, aortic calcification was progressed in adenine control group without treatment on von Kossa stain and calcium contents analysis of aorta. Aortic calcification on von Kossa stain and calcium contents was the least progressed

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in adenine control group treated with combination of omega-3 FA and MK-7 compared to omega-3 FA or MK-7 single therapy.

Conclusions : Combined treatment with omega-3 FA and MK-7 definitely prevents progression of aortic calcification compared to rat without treatment in adenine and low protein diet induced vascular calcification rat model.

Keywords : Omega-3 fatty acid; Menaquinone-7; Vascular calcification; Chronic kidney disease