Kano H, Hayashi T, Sumi D, Matusi-Hirai H, Tsunekawa T, Endo H, Iguchi A. *Estriol retards and stabilizes atherosclerosis through an NO-mediated system.*
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Estriol (E3) has little effect on the female genitals. E3 is used in hormone replacement therapy, particularly in Europe and Japan, since it obviates the need for progestin administration. However, the effect of E3 on atherosclerosis has not been elucidated. In this study, we evaluated the effect of E3 on the progression of atherosclerosis in a rabbit model. Thirty-six rabbits total were used. Twenty-eight were bilaterally oophorectomized, and 8 were not. The rabbits were divided into 5 groups and treated for 12 weeks as follows. Gp I (n = 8) was fed a high cholesterol diet (HCD; standard diet plus 0.5% cholesterol); Gp II (n = 8) was fed a HCD with E3 (0.3 mg/kg/day); Gp III (n = 8) was fed a HCD with 17beta estradiol (E2) (0.1 mg/kg/day); Gp IV (n = 8), the non oophorectomized group, was fed a HCD; and Gp NC was oophorectomized (n = 4), and fed a regular diet. E3 treatment increased the plasma E2 and E3 levels in Gp II. The plasma lipid levels were not altered by the E2 or E3 treatment. A HCD diminished the acetylcholine-induced NO mediated relaxation in the thoracic aorta. The E2 treatment (Gp III) and E3 treatment (Gp II) restored the aortic basal NO release and the aortic cyclic GMP levels, particularly effectively in the E3 group. E3 treatment also decreased the atherosclerotic area, and its effect was comparable with E2 (surface involvement: 41.2 +/- 5.1% in Gp I; 10.1 +/- 2.7% in Gp II; and 6.5 +/- 1.3% in Gp III). All four hyperlipidemic groups showed an increase of eNOS mRNA in the aortae, and this was especially pronounced in Gps II and III. The level of peroxynitrite, as determined by immunohistochemical nitrotyrosine staining, was lower in Gps II and III than in Gp I. E3 strongly activates NO-mediated systems, and could play a role in retarding the progression of atherosclerosis and in stabilizing atheroma.