Resveratrol Improved Flow-Mediated Outward Arterial Remodeling in Ovariectomized Rats with Hypertrophic Effect at High Dose

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Résumé en anglais	OBJECTIVES: Chronic increases in blood flow in resistance arteries induce outward remodeling associated with increased wall thickness and endothelium-mediated dilatation. This remodeling is essential for collateral arteries growth following occlusion of a large artery. As estrogens have a major role in this remodeling, we hypothesized that resveratrol, described as possessing phytoestrogen properties, could improve remodeling in ovariectomized rats. METHODS: Blood flow was increased in vivo in mesenteric arteries after ligation of adjacent arteries in 3-month old ovariectomized rats treated with resveratrol (5 or 37.5 mg/kg per day: RESV5 or RESV37.5) or vehicle. After 2 weeks arterial structure and function were measured in vitro in high flow (HF) and normal flow (NF) arteries isolated from each rat. RESULTS: Arterial diameter was greater in HF than in NF arteries in ovariectomized rats treated with RESV5 or RESV37.5, not in vehicle-treated rats. In mice lacking estrogen receptor alpha diameter was equivalent in HF and NF arteries whereas in mice treated with RESV5 diameter was greater in HF than in NF vessels. A compensatory increase in wall thickness and a greater phenylephrine-mediated contraction were observed in HF arteries. This was more pronounced in HF arteries from RESV37.5-treated rats. ERK1/2 phosphorylation, involved in hypertrophy and contraction, were higher in RESV37.5-treated rats than in RESV5- and vehicle-treated rats. Endothelium-dependent relaxation was greater in HF than in NF arteries in RESV5-treated rats only. In HF arteries from RESV37.5-treated rats relaxation was increased by superoxide reduction and markers of oxidative stress (p67phox, GP91phox) were higher than in the 2 other groups. CONCLUSION: Resveratrol improved flow-mediated outward remodeling in ovariectomized rats thus providing a potential therapeutic tool in menopause-associated ischemic disorders. This effect seems independent of the estrogen receptor alpha. Nevertheless, caution should be taken with high doses inducing excessive contractility and hypertrophy in association with oxidative stress in HF arteries.
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