Vascular insulin resistance of a rat model of polycystic ovary syndrome: Effects of parallel vitamin D3 treatment

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Aim: Our aim was to clarify the effects of dihydrotestosterone (DHT)-induced polycystic ovary syndrome (PCOS) on insulin-dependent vasodilatation of thoracic aorta and resistance arteries. We also aimed to investigate the possible modulatory role of vitamin D3 (vit D) in an animal model.

Design: In this controlled experimental animal study, thirty female Wistar rats were divided into groups at age of 21-28 days. Twenty of them were subjected to dihydrotestosterone (DHT) treatment (83 µg/day); ten of them also received parallel vit D treatment (120 ng/100 g/week). Oral glucose tolerance tests with insulin level measurements were performed. Gracilis arterioles were tested for their contractility as well as their nitric-oxide (NO)-dependent and insulin-induced dilation using pressure arteriography. Thoracic aorta segments were also isolated. Insulin-dependent vasodilation of the aorta rings in normal Krebs-Ringer solution was compared to the response of rings treated with NO-synthase (by nitro-L-arginine methyl ester) or cyclooxygenase (by indomethacin) blockade.

Results: DHT treatment increased the passive diameter of resistance arterioles, lowered norepinephrine-induced contraction, reduced acetylcholine-induced and insulin-induced dilation. VitD treatment restored insulin relaxation and norepinephrine-induced contractility; in contrast, it failed to alter NO-dependent relaxation of arterioles. Insulin-dependent vasorelaxation of thoracic aorta segments was impaired in DHT-treated groups independent of vit D treatment. Impaired NO-relaxation and enhanced prostanoid contraction of the aorta rings were observed.

Conclusion: Vit D treatment prevented systemic insulin resistance. In DHT-treated rats, in addition to metabolically proven insulin resistance, decreased insulin-induced vasorelaxation was observed and was improved by vit D treatment without affecting NO-dependent relaxation. The reduction in insulin-induced dilation of arterioles is an important as yet undescribed pathway of vascular damage in PCOS and might explain the clinical effectiveness of vit D treatment. DHT treatment also caused deterioration of insulin-induced vasodilation on aorta rings. Vit D did not influence vascular insulin resistance of the aorta. Controlling insulin resistance with vit D alone did not resolve the endothelial dysfunction of the aorta caused by the hyperandrogenic state.

Biography
Levente Sara, MD, JD, has completed PhD and postdoctoral studies from Semmelweis University Budapest in 2012. His thesis was the "Alterations of Arteriolar Reactivity in a Rat Polycystic Ovary Syndrome Model". He is Ob&Gyn specialist and assistant professor of the Semmelweis University. His research field is the cardiovascular alterations, pharmacological reactivity of arteries and veins in PCOS.