Diabetes: Chapter 10. Resveratrol and Oxidative Stress in Diabetes Mellitus

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Oxidative stress plays a key role in the pathogenesis of diabetes mellitus, contributing not only to the development, but also to the progression of diabetes and its related complications. Both immunosuppressive and antioxidant effects of resveratrol in attenuating the increased oxidative stress due to responses of β-cells to leukocyte activation have been implicated in the prevention of type 1 diabetes mellitus. Resveratrol affords advantageous effects by decreasing the oxidative injury and the recruitment of the nutritive precapillary arterioles in the context of disease states associated with insulin resistance, such as metabolic syndrome, pre-diabetes, and type 2 diabetes mellitus. The antioxidant properties of resveratrol could result from its direct effects by acting as a free radical scavenger, as well as its ability to indirectly activate antioxidant enzymes, and other mechanisms. These indirect effects could be conferred either via increased expression/activation/translocation of sirtuin 1, nuclear factor erythroid 2-related factor 2, superoxide dismutase, catalase, heme oxygenase-1, and glyoxalase or the suppression of inducible nitric oxide synthase and p47phox translocation/expression with the resultant inhibition of nicotinamide adenine dinucleotide (phosphate) oxidase. In addition to reducing oxidative stress, resveratrol could also improve the carbohydrate metabolism by promoting similar beneficial metabolic processes to those found in caloric restriction via the activation of sirtuin 1, as well as by increasing the level of glucagon-like peptide 1, by exerting an estrogen-like effect, or by stimulating the peroxisome proliferator-activated receptor-γ activity. In our preliminary human study we examined the effects of resveratrol in type 2 diabetic patients. In agreement with animal studies, we found that resveratrol treatment markedly decreased the insulin resistance and blood glucose levels, whereas we could not detect increases in insulin secretion. We also found that the onset of the postprandial glucose peak was manifested after a longer lag time in the postprandial period with resveratrol treatment, while there were no changes in amylin, glucagon-like peptide 1, and gastric inhibitory polypeptide levels; hormones that prolong gastric emptying. Additionally, we found decreased urinary excretion rates of ortho-tyrosine with resveratrol treatment, indicating a lowered degree of the hydroxyl free radical production in these patients. These findings support the notion that resveratrol decreases oxidative stress through its broad direct and indirect antioxidant effects, and this could be a promising approach for the prevention and treatment of diabetes mellitus. Further studies are undoubtedly warranted to better comprehend the effects of resveratrol in humans, since there is very limited data from human observations.

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