RESEARCH ABSTRACT FORM

TITLE: The Effects of Pro-oxidants on the progression of Prediabetes in SHROB rats.

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Obesity, high blood pressure, insulin resistance, and associated factors are collectively known as metabolic syndrome or prediabetes. An estimated 50 million Americans have metabolic syndrome increasing their risk for heart disease and stoke. Oxidative stress in the body produces free radicals, and is hypothesized to trigger diabetes. The body uses enzymes such as superoxide dismutase to detoxify free radicals such as superoxide. Using the obese spontaneously hypertensive rat (SHROB/Kol) as a prediabetic model, oxidative stress was induced through injections of an oxidizing agent, hydroquinone, and a glutathione depleting agent, L-buthionine sulphoximine (both 50mg/kg ip). Hepatic superoxide dismutase activity was increased in SHROB rats relative to lean SHR controls, suggesting an adaptive response to oxidative stress. Compared to control lean SHR rats, testing of kidney, liver, and plasma showed the SHROB rats reaching approximately 3-fold higher peroxide levels. Pro-oxidant injections led to transient increases in oxidative stress over twenty-four hours measured by plasma peroxides indicative of oxidative damage. Antioxidant anti-hypertensive therapy using captopril was also administered. The captopril successfully lowered peroxide levels two-fold in SHROB rats. Blood glucose data gathered at each injection linked oxidative stress to diabetes onset and possible reduction of insulin levels. The treatments had no effect upon food intake or body weight. Currently, a second and more extensive trial is underway to further investigate the targets of oxidative attack, the enzymes and mechanisms involved, and a correlation between blood pressure and oxidative stress.