Effects of protein kinase C broad spectrum inhibitor Gö 6983 on real-time blood nitric oxide and hydrogen peroxide release in femoral artery/vein ischemia and reperfusion

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Background: Vascular endothelial dysfunction is a key component initiating oxidative stress in ischemia/reperfusion (I/R). Endothelial dysfunction is characterized by an increase in hydrogen peroxide (H$_2$O$_2$) and a decrease in the bioavailability of nitric oxide (NO). Previous studies using protein kinase C (PKC) inhibitor Gö 6983 improved cardiac function in myocardial I/R, decreased leukocyte-endothelial interactions and leukocyte superoxide release and increased endothelial-derived NO release in vitro.

Methods: This study examined the effects of Gö 6983 on real-time H$_2$O$_2$ and NO release in femoral I/R in vivo. NO or H$_2$O$_2$ microsensors (100 µm) were inserted into both femoral veins in the anesthetized rat. One limb is subjected to I/R in which the femoral artery and vein was clamped for 20 min and released for 45 min and the other served as a sham.

Results: H$_2$O$_2$ release significantly increased in the I/R compared to the sham femoral vein in the control group (n=7, P<0.01). NO release showed a trend to decrease in the I/R compared to the sham femoral vein in the control group (n=6). Gö 6983 (7.4 µg/kg) given at the beginning of reperfusion significantly decreased H$_2$O$_2$ (n=7, P<0.05) and increased NO release (n=7, P<0.01) compared to control. Collectively, the data suggest that Gö 6983 attenuates oxidative stress in femoral I/R, which may be due to inhibition of leukocyte/endothelial NADPH oxidase and increasing endothelial-derived NO release.

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