ACUTE, BUT NOT CHRONIC, SMOKING PARADOXICALLY PROTECTS THE ENDOTHELIUM FROM ISCHEMIA AND REPERFUSION

Background: Cigarette smoking is a well-accepted risk factor for myocardial infarction, stroke, and mortality. Paradoxically, however, several large epidemiological studies reported that, among patients who experience a myocardial infarction, those who smoke have lower mortality and morbidity. We set out to investigate whether the oxidative stress associated with acute, short-term exposure to cigarette smoking could induce a paradoxical protection similar to the phenomenon known as ischemic preconditioning.

Methods and Results: Radial artery endothelium-dependent flow-mediated dilation (FMD) was measured in 10 healthy non-smoker subjects (7 males, 25-28 years old) before and after local ischemia/reperfusion (15 minutes ischemia followed by 15´ reperfusion). Subjects underwent, in randomized order, two protocols: in the first, they smoked two cigarettes 15´ after receiving 2 grams of intravenous vitamin C. In the second, they smoked two cigarettes 15´ after receiving an intravenous placebo. A separate group of 10 light smokers (7 males, age 24-28 years, 3-10 cigarettes/day) underwent the same protocol after a 24-hour non-smoking interval. There were no differences among groups in resting arterial diameter, blood pressure, heart rate, blood flow before each measurement (P>0.5 for all). After smoking+normal saline, FMD was not impaired by ischemia (P=0.3). In contrast, in those who smoked two cigarettes and received 2gr. i.v. vitamin C, this paradoxical protective effect of smoking was lost, and FMD after ischemia/reperfusion was significantly blunted as compared to the baseline FMD (P=0.008). Smoking did not induce any preconditioning-like effect in those who smoked 2-4 cigarettes per day for a week, and ischemia/reperfusion was associated with a significant blunting in FMD (P=0.005).

Discussion: Beyond their role in the pathophysiology of atherosclerosis and endothelial dysfunction, reactive oxygen species are also important agents of cellular signal transduction. In certain situations, short oxidative bursts might paradoxically be associated with protective phenomena. Importantly, this protection appears to be lost in the setting of chronic (light) smoking.