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Microvascular Injury by High Sodium Intake in Normotensive Patients. Role of Nitric Oxide and Oxidative Stress

Ramick MG, Brian MS, Matthews EL, Patik JC, Seals DR, Lennon SL, et al. Apocynin and Tempol ameliorate dietary sodium-induced declines in cutaneous microvascular function in salt-resistant humans. **Am J Physiol Heart Circ Physiol.** 2019;317:H97-H103. <http://doi.org/c8wq>

Excessive sodium intake is strongly associated with cardiovascular diseases, such as hypertension, and lower synthesis of vascular nitric oxide. Reduced bioavailability of nitric oxide plays a key role in predicting the development of cardiovascular diseases, as well as in the physiopathology of many of these disorders. The deficit of nitric oxide leads to lower vasodilation, proliferation of smooth muscle cells, platelet aggregation and inflammatory response in atherosclerotic plaques.

Although the loss of endothelial function due to salt consumption has been known for many years, it was always assumed that it was caused by the associated hypertension. Recently, experimental findings and some patient studies have shown that greater salt intake is able to impair the vascular endothelium independently of increased blood pressure.

Ramick et al. studied the role of sodium-induced oxidative stress on the cutaneous microvascular function of normotensive patients during increased salt intake. In the first stage, a group of adult, healthy patients were subjected to an increasingly salt-rich diet and their blood pressure was assessed during 24 hours to identify salt-sensitive individuals. Salt sensitivity

was defined as the presence of blood pressure changes ≥ 5 mmHg. As the hypothesis of the study was that changes in vascular function are independent of the increase in blood pressure, all the subsequent studies were performed on 29 normotensive, salt-resistant subjects. Patients received two consecutive 7-day periods of a controlled low-sodium (2 mmol/day) or high-sodium (300 mmol/day) diet. At the end of each period, the patients were instrumented with four microdialysis fibers inserted in the forearm skin, and each was perfused with one of the following solutions: Ringer solution (control group), ascorbic acid, apocynin (NADPH oxidase inhibitor) or tempol (which eliminates superoxide anion). Next, the patients received locally increasing temperatures on the skin region of fiber insertion, while blood flow was assessed with laser Doppler. With this technique, the authors observed a reduction of nitric-oxide-dependent microvascular blood flow in the patients receiving a rich-sodium diet. This impairment was restored by the administration of apocynin, but not of tempol. Finally, measurements in endothelial cells demonstrated increased nitrotyrosine expression after elevated salt consumption, suggesting a response to increased oxidative stress.

Overall, these authors' findings suggest that a high-sodium diet has deleterious effects on microvascular function through greater production of NADPH oxidase-dependent free radicals. In addition, this vascular involvement is independent of the increase in blood pressure and can be restored if the production of superoxide is reduced. These conclusions support the notion of the benefit of a reduced salt intake, not only in hypertensive patients, but also, in the normotensive and apparently healthy population.