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Effects of the environment (air pollution and antioxidant diet) on hypertension - the role of reactive oxygen species

Oxidative stress has been implicated as a causal factor in hypertension.^{1,2} Increased production, or decreased scavenging, of oxidants such as superoxide anion can give rise to hypertension by superoxide interacting with nitric oxide, forming peroxynitrite,^{2,3} which results in reduced nitric oxide availability.

Peroxyntirite is a strong oxidant that promotes inflammation by activating nuclear transcription factors such as NF- κ B.^{2,3} Environmental factors may be responsible for the persistence of elevated blood pressure levels in hypertensive subjects. In recent studies, fine particulate matter <2.5 μ m (PM_{2.5}) has been shown to have vasoconstrictor effects which could be responsible for potentiation of systemic hypertension.⁴ This brief article summarizes recent experimental findings regarding the effects of conditions associated with oxygen free radical production and scavenging on blood pressure.

Air pollution and hypertension: animal experiments. Sun et al⁴ investigated the effects of short-term exposure to PM_{2.5} in an angiotensin II (AII) infusion animal model. In this study, Sprague-Dawley rats were exposed to PM_{2.5} or filtered air for 10 weeks. At week 9, minipumps containing AII were implanted and the responses to the infusion of AII studied over a week. After AII infusion, mean arterial pressure was significantly higher in the group of animals receiving PM_{2.5} and AII, compared with animals receiving filtered air and AII. Superoxide radical production was increased in the aorta of rats receiving PM_{2.5}-AII compared to that in animals receiving filtered air. Superoxide production was inhibited by apocynin and L-NAME, and this was associated with upregulation of NAD(P)H oxidase subunits p22^{phox} and p47^{phox} and depletion of tetrahydrobiopterin. Exposure to PM_{2.5} also resulted in aortic vasoconstriction to phenylephrine, with exaggerated relaxation to the Rho-kinase (ROCK) inhibitor Y-27632 and increase in ROCK-1 mRNA levels in the PM_{2.5}_AII group.⁴

In the same set of experiments,⁴ tissue was exposed to ultrafine particles and PM_{2.5}—in vitro—which increased ROS production. Pretreatment of the specimens with the N-acetylcysteine (an antioxidant) and the Rho kinase inhibitors Fasudil and Y-27632 prevented oxidative stress by ultrafine particles. These results suggest that PM_{2.5} and UFP exert their deleterious effects through the production of superoxide radical. Sun et al therefore concluded that short-term air pollution can lead to hypertension through superoxide-mediated upregulation of the Rho/ROCK pathway.⁴

Diet, oxidative stress, and hypertension. Induction of phase 2 proteins promotes oxidant scavenging; hence it was proposed that intake of dietary phase 2 protein inducers would improve hypertension in the spontaneously hypertensive stroke-prone rat.⁵ For 14 weeks, Wu et al⁵ fed rats 200 mg/day of dried broccoli sprouts that contained glucoraphanin, which is metabolized into the phase 2 protein-inducer sulforaphane (Group A), sprouts in which most of the glucoraphanin was destroyed (Group B), or no sprouts (Group C). Whilst no significant differences were seen at follow-up between rats in groups B and C, animals in Group A had significantly decreased oxidative stress in cardiovascular and kidney tissues. Decreased oxidative stress improved endothelium-dependent relaxation of the aorta and significantly lowered blood pressure. Dietary antioxidant interventions also resulted in reduced inflammation. Indeed, tissue from animals in groups B and C had increased numbers of activated macrophages compared with animals in group A. The results of this experimental study⁵ suggest that a diet containing phase 2 protein inducers can reduce hypertensive responses.

Implications for management of hypertension in man.

Oxidative stress is a major player in the development of endothelial activation and dysfunction in humans, particularly in the setting of systemic hypertension.¹⁻³ The renin-angiotensin-system plays a modulatory role in this process. A II can activate NF- κ B, and this proinflammatory response is attenuated by the administration of ACE inhibitors.^{6,7} This could explain at least in part the beneficial effects of ACE inhibitors in clinical trials such as the Heart Outcomes Prevention Evaluation (HOPE) study,⁸ the EUROPEAN trial on Reduction Of cardiac events with Perindopril in stable coronary Artery disease (EUROPA),⁹ and PERTINENT,¹⁰ a substudy of EUROPA. In the latter, perindopril—an ACEI with high tissue ACE affinity—showed a protective effect of endothelial function via anti-inflammatory mechanisms.

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