

Cardiovascular News

Novel therapy could improve endothelial function after MI

14 September 2007

MedWire News: Patients with myocardial infarction could benefit from taking supplements of tetrahydrobiopterin (BH4), a cofactor of the enzyme endothelial nitric oxide synthase (eNOS), to restore coronary blood flow and preserve myocardial tissue, researchers suggest.

"Impaired endothelial function is of critical importance in patients with acute coronary syndromes, and restoration of normal endothelial vasodilator function would tend to prevent problems of microvascular occlusion after acute recanalization," the authors comment in the *Proceedings of the National Academy of Sciences*.

Jay Zweier (Ohio State University, Columbus, USA) and colleagues found that BH4 depletion contributes to postischemic eNOS dysfunction, and BH4 treatment partially restores endothelium-dependent coronary flow.

They subjected isolated rat hearts to varying durations of ischemia, measured the alterations in NOS-dependent vasodilation, and correlated the data with assays of eNOS activity and cardiac BH4 concentrations.

Ischemia decreased cardiac BH4 concentrations in a time-dependent manner by 85%, 95%, and 97% after 30, 45, and 60 minutes of ischemia, respectively. Similarly, eNOS activity fell by 58%, 86%, and 92% with increasing periods of ischemia.

Notably, infusion of BH4 enhanced eNOS activity in nonischemic hearts and partially restored activity after ischemia. It also suppressed NOS-derived superoxide production and improved impaired coronary flow during post-ischemic reperfusion.

The researchers speculate: "The loss of BH4 is likely to be the result of oxidative degradation secondary to the formation of oxidants and oxygen free radicals that are enhanced during myocardial ischemia and subsequent reperfusion."

Zweier *et al*/ conclude: "Our results suggest that supplementation of BH4 or manipulation of its metabolism might be an important therapeutic approach to reverse the loss of endothelial vasodilatory and NOS function in the post-ischemic heart as well as in other oxidant-associated cardiovascular diseases."

[Proc Natl Acad Sci 2007; Advance online publication](#)

© Copyright [Current Medicine Group Ltd](#), 2006