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Ecosinoids and blood vessel structure

We should, perhaps, pay more attention to the influence that ecosinoids have on blood vessel behavior and structure, as substances such as nonsteroidal antiinflammatory drugs (NSAIDs) and the so called selective cyclooxygenase 2 inhibitors are extensively employed by the population at large.

In this issue of *Vascular Health and Risk Management*, Claridge and colleagues (2005) have reported a significant association of aortic wall stiffness with the use of NSAIDs. This interesting finding highlights the importance of the physiological and pathophysiological effects of ecosinoids on blood vessel behavior and function, as well as structure. The role of matrix metalloproteinase and plasminogen activator-plasmin systems have been the subject of considerable investigation, and it is now accepted that the remodeling of blood vessels is very much dependent upon degradation of the extracellular matrix (Bobik and Tkachuk 2003). The prostanoid that is thought to be involved in inducing the expression of metalloproteinase and plaminogen activator is prostaglandin (PG) E_2 (Khan et al 2004). Thus, the tendency for increased stiffness of blood vessels as a consequence of NSAID use could possibly result from a reduction in the levels of PG E_2, perhaps in the vasculature.

Based on experiments employing isolated rat aortic rings, indomethacin treatment in vitro produces a reduction in blood vessel compliances (Chin-Dusting et al 1988). Moreover, in animals fed a supplement of fish oil, aortic compliance ex vivo appears to be significantly reduced (Chin-Dusting et al 1988). In experimental animals, a diet high in fish oil results in the lowering of some naturally occurring ecosinoids (Hornstra et al 1981). Accordingly, it is possible that the reduction in biological activities of certain prostanoids may manifest as a significant reduction in aortic compliance ex vivo as observed in rats fed a high fish oil diet. This is not to suggest that the use of fish oil will result in a decrease in vascular compliance in vivo, as this issue remains controversial. However, whether, a similar mechanism is at play when aortic stiffness is increased clinically following the use of NSAIDs remains to be established. Certainly, the impact of NSAID use on blood vessel compliance needs a closer and in-depth investigation in humans. While it would be interesting to further pursue the notion of whether NSAIDs may also affect blood vessel stiffness in animals, it would also be of great interest to delineate the molecular nature of this event in experimental animals. Ultimately, the remodeling of blood vessels leading to altered compliance will result in changes to hemodynamics, which may have a significant impact on cardiac function. It is recognized that an increase in vascular stiffening can significantly impact ventricular-arterial coupling that could eventually compromise ventricular function (Kass 2002).

In a broader context, this is an interesting observation raising the issue as to whether the use of NSAIDs is likely to increase adverse cardiovascular events and at the same time beneficially retard aneurysm growth. Recently, there has been much debate regarding cardiovascular risk (stroke and myocardial infarction, fatal and non-fatal) associated with the use of selective cyclooxygenase 2 inhibitors (Tabrizchi 2005). However, more recently, it has also been suggested that the use of naproxen, a non-selective inhibitor of the enzyme cyclooxygenase, also may pose an elevated

cardiovascular risk (Boyles 2004). The evidence for the latter suggestion is still quite limited and the increase in the incidence of cardiovascular events may only be in patients who have strong risk factors for heart attack and stroke (Boyles 2004). Nonetheless, a pertinent question worthwhile considering is that the cardiovascular *risk/benefit* associated with the inhibition of cyclooxygenase may not be restricted to events such as thrombosis and vasoconstriction, but may now have to be extended to alteration in morphometry of the blood vessels.

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