C-Reactive Protein and Nitric Oxide Production in Ischemic Stroke

To the Editor:

We read with great interest the article by Dr Shantikumar and colleagues1 dealing with the relationship between the inflammatory biomarker (C-reactive protein [CRP]) and long-term mortality after acute ischemic stroke. The results of their study demonstrated that CRP was higher in subjects who died compared with survivors, and that CRP remained predictive for mortality after adjusting for conventional clinical and demographic risk factors (age, stroke subtype, previous stroke/transient ischemic attack, and atrial fibrillation). However, CRP was no longer independently predictive of mortality after additionally adjusting for β-thromboglobulin (a marker for platelet activation) or von Willebrand factor (a marker for endothelial dysfunction). The authors propose that CRP might be upregulated, at least in part, as a consequence of endothelial dysfunction and platelet activation.

Evidence indicates that nitric oxide (NO) may actively participate in neuroprotection in cerebral ischemia. In a study we presented previously, a relationship between membrane fluidity (a reciprocal value of membrane microviscosity) of erythrocytes and NO was investigated by means of an electron paramagnetic resonance method.2 The decreased membrane fluidity of erythrocytes might cause a disturbance in the blood rheological behavior and the microcirculation, which could contribute, at least in part, to the pathophysiology of circulatory disorders. We demonstrated that NO increased the membrane fluidity of erythrocytes and improved the rigidity of cell membranes in humans.2 In the separate series of the study, we showed that the lower membrane fluidity of erythrocytes was associated with decreased levels of plasma NO-metabolites and increased levels of asymmetrical dimethylarginine (an endogenous inhibitor of NO synthase).3 One hypothesis is that NO would be a defense against vascular complications in circulatory disorders.

Recently, it has been shown that CRP could reduce NO-bioavailability, which would induce endothelial and cardiovascular dysfunctions. Venugopal et al4 observed that CRP directly decreased endothelium-type of NO synthase expression in human aortic endothelial cells in vitro.4 In a clinical study, it was demonstrated that increased levels of high-sensitivity CRP were associated with reduced endothelium-mediated dilatation of arteries.5 In this context, we speculate that insufficient NO-production and reduced NO-bioavailability might partially explain the poor prognosis in subjects with higher CRP levels. Therefore, we would like to know whether plasma or urinary NO metabolite levels might be linked to the CRP levels in the study of Dr Shantikumar and colleagues. Further studies should be necessary to assess more precisely the functional interactions between CRP and NO, and their contribution to the pathophysiology of ischemic stroke.

Disclosures

None.

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Stroke. 2009;40:e471; originally published online April 30, 2009;
doi: 10.1161/STRK.109.551150
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/40/6/e471

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