Antioxidants and Endothelial Dysfunction in Young and Elderly People: Is Flow-Mediated Dilation Useful to Assess Acute Effects?

To the Editor:

Wray et al reported that acute consumption of antioxidants by healthy subjects had diametrically different effects: flow-mediated dilation increased in elderly people but decreased in young people. The opposite effects are difficult to interpret and reconcile with the measured biomarkers of oxidative stress and NO synthesis/bioavailability. Although not representative, an example for the strong limitation of acute changes is the enhancing effect of certain diuretics on the renal excretion of the NO metabolites nitrite and nitrate, which renders NO synthesis measurement impossible.

A crucially important issue with the use of the flow-mediated dilation approach is that antioxidants may directly interact with the arachidonic acid/cyclooxygenase and L-arginine/NO synthase pathways, without primarily acting as antioxidants. N-Acetylcysteine and its metabolites may increase NO synthesis/bioavailability but inhibit cyclooxygenase activity (Figure). Ascorbic acid may inhibit cyclooxygenase activity, whereas its effect on NO synthesis may be double edged (Figure). Finally, antioxidants may severely compromise the analytic outcome by interacting both with biomarkers and reagents being used in their analysis.

At a therapeutic dose, the vasodilator and antioxidant nebivolol decreased oxidative stress in healthy young volunteers. This observation indicates that basal oxidative stress can be reduced even in healthy young subjects and contradicts the findings by Wray et al, which show even increases in oxidative stress and decreases in flow-mediated dilation in young people.

In conclusion, the informational value of flow-mediated dilation concerning acute effects of antioxidants on endothelial function is rather low. Plethysmography and accurate assays for nitrite and oxidative stress biomarkers are more reliable to measure reactive hyperemia and endothelial function in clinical studies.

Disclosures

None.

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