Reactive Oxygen Species and Angiotensin II Response in Human Omental Arteries: What About Tachyphylaxis?

To the Editor:

With great interest we read the recent article in Hypertension by Mishra et al.\(^1\) They report an enhanced omental artery constrictor response to angiotensin II in preeclamptic women versus normal pregnant women, which they attribute to reactive oxygen species (ROS) activation of the RhoA kinase pathway. To reach this conclusion, they constructed 2 consecutive concentration-response curves to angiotensin II (0.001–10 μmol/L) in endothelium-intact omental arteries, 1 in the absence and 1 in the presence of either the ROS scavengers superoxide dismutase (SOD) or catalase or the RhoA kinase inhibitor Y-27632. This approach ignores the well-known angiotensin II–induced tachyphylaxis, which normally does not allow the construction of 2 identical angiotensin II concentration-response curves in a row in the same vessel. In fact, tachyphylaxis often already starts to occur at angiotensin II concentrations >1 μmol/L during the construction of the first concentration-response curve. An alternative explanation of the blocking effects of SOD or catalase or Y-27632 might therefore be that angiotensin II was no longer capable of inducing any vasoconstrictor effect, for example, because of rapid internalization of angiotensin II type 1 receptors.\(^2,3\)

Second, the application of SOD and catalase to the vessel chamber assumes that these enzymes are capable of reaching the intracellular sites of ROS production and/or that ROS are secreted to the extracellular space. In earlier studies in human coronary arteries, we were unable to show an effect of the cell-permeable SOD-mimetic Tempol on angiotensin II–induced vasoconstriction.\(^4\) Moreover, endogenous H\(_2\)O\(_2\), if anything, dilated human coronary arteries (possibly reflecting its function as endothelium-derived hyperpolarizing factor), and the addition of xanthine + xanthine oxidase similarly relaxed preconstricted human coronary arteries. Mishra et al\(^1\) have tested the consequences of ROS generation by adding hypoxanthine + xanthine oxidase to endothelium-denuded omental arteries, which, according to the expanded Materials and Methods section, display “clean” responses to angiotensin II not hampered by tachyphylaxis. This approach will generate ROS in the organ bath, and, thus, it is not surprising that the extracellular application of SOD + catalase prevents the consequences of such generation. To fully appreciate the findings, however, the authors should preferably (1) include a second angiotensin II concentration-response curve in the absence of inhibitors, both in intact and endothelium-denuded vessels, to rule out the possibility that blockade in reality represents desensitization, and (2) show that the extracellular application of SOD + catalase truly lowers the levels of superoxide and H\(_2\)O\(_2\) in omental arteries.

Disclosures

None.

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References

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