Is Creatine Kinase the Intrinsic Factor of Smooth Muscle Enhancing Vascular Contractility in Subjects of African Ancestry?

To the Editor:

In a recent article, Adefurin et al presented interesting results on ethnic differences in venous smooth muscle contractility in response to α-receptor agonists. Healthy subjects of African ancestry showed greater vasoconstriction to phenylephrine than subjects of European ancestry, with a geometric mean ED50 that was 45% lower in the African group, 172 versus 310 ng/min. Notably, the effect was more pronounced in men than in women. The authors concluded that their study did not shed light on the mechanism of this enhanced α1-adrenoreceptor–mediated vascular sensitivity, and called for further studies to address the pathways involved in this response. During the past 10 years, we have collected mounting evidence that vascular smooth muscle contractility of subjects of African ancestry is intrinsically enhanced, related to greater activity of the ATP-regenerating enzyme creatine kinase (CK). The enzyme rapidly regenerates ATP near ATPases involved in smooth muscle contractility, including Ca2+-dependent and Ca2+-independent pathways, including myosin ATPase and myosin ATPase. α1-Adrenergic stimuli are reported to lead to enhanced vasoconstriction through Ca2+-dependent and Ca2+-independent pathways, including myosin light chain phosphorylation.

Greater activity of CK, as a possible final common pathway of vasoconstrictive responses, is thought to lead to enhanced agonist-mediated vasoconstriction. Importantly, contractility of human vessels ex vivo was found to be highly CK dependent, and CK inhibition led to a dose-dependent block of vasoconstriction on norepinephrine stimulation. The ethnic difference in CK activity is less pronounced in women, and this may explain the smaller differences in women found by Adefurin et al. Thus, consistent with the observations of Adefurin et al, we propose that their data could be interpreted in part explained by enhanced vasoconstriction in people of African ancestry as being attributable to greater CK activity in smooth muscle. Further studies should assess the effect of a CK blocker on the enhanced α1-adrenergic agonist–mediated response in vivo.

Disclosures

L.M.B. is an inventor on NL patent WO/2012/138226 (filed).

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Hypertension. 2013;62:e7; originally published online July 22, 2013;
doi: 10.1161/HYPERTENSIONAHA.113.01853

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/62/3/e7

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