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+ 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.5

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 in part explained by enhanced venoconstriction 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.

Is Creatine Kinase the Intrinsic Factor of Smooth Muscle Enhancing Vascular Contractility in Subjects of African Ancestry?
Fares A. Karamat, Joseph F. Clark and Lizzy M. Brewster

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

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

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/