Letter to the Editor

Do Commercially Available Assay Kits for B-Type Natriuretic Peptide Measure Pro-BNP1-108, as Well as BNP1-32?

To the Editor:

We read with great interest the recent article by Heublein et al1 on plasma pro-BNP1-108 measurement with commercially available assay kits and the effect of pro-BNP1-108 on cGMP levels. They demonstrated that Shionogi’s or Biosite’s triage assay kit did not cross-react with pro-BNP1-108 and that pro-BNP1-108 did not increase intracellular cGMP levels in cardiac myocytes or fibroblasts. Kangawa et al1 reported that this assay kit measured BNP3-32, BNP5-32, and BNP1-32, but it did not measure C-terminal deletion forms of B-type natriuretic peptide, such as BNP1-30 and BNP1-28. Namely, this assay kit does not measure B-type natriuretic peptide lacking the ring portion or C-terminal tail. Thus, an N-terminal peptide pro-BNP1-76 lacking the ring portion cannot be recognized by the Shionogi’s immunoradiometric assay kit as shown in this article, whereas pro-BNP1-108 is detected by this kit with slight less affinity (≈70% to 80%) than BNP1-32 (unpublished data). In fact, using Shionogi’s immunoradiometric assay kit, we detected and measured immunoreactivity corresponding with pro-BNP1-108, as well as BNP1-32, after gel filtration of human plasma.2

In the study by Heublein et al,1 moreover, pro-BNP1-108 did not increase intracellular cGMP levels in myocytes or fibroblasts. As for the activity of the natriuretic peptide, the studies of the structure-activity relationship demonstrated that the ring structure and the C-terminal tail are essential for eliciting the biological activity, whereas the N-terminal extension from the ring structure confirmed to be not essential.3,4 Indeed, Kangawa et al5 demonstrated previously that pro-atrial natriuretic peptide induced diuresis, natriuresis, and potassium excretion in the rat, although it was less potent than ANP1-28. BNP1-32 and pro-BNP1-108 act on the same natriuretic peptide receptor-A.

Taken together, available evidence suggests that Shionogi’s immunoradiometric assay kit measures pro-BNP1-108, as well as BNP1-32, and both of them are deduced to have the cGMP elevating activity. We do not know the reason why pro-BNP1-108 was not measured by Shionogi’s immunoradiometric assay kit or why pro-BNP did not increase the intracellular cGMP levels of cardiac myocytes and fibroblasts in the study by Heublein et al.1 It is reasonable to consider that the same reason diminished the antigenicity, as well as the biological activity, of the pro-BNP1-108 used in their experiment, although they did not precisely describe how they confirmed the structure of the recombinant pro-BNP1-108.

We agree with the notion by Heublein et al1 that clarifying the molecular form of BNP in plasma and its physiological action in heart failure are of importance. We believe that a better understanding of the structure, biological activity, and plasma concentrations of endogenously present natriuretic peptides, especially BNP, provides useful information in clinical medicine.

Sources of Funding

This work was supported in part by Scientific Research Grants-in-Aid 14570692 and 18590787 from the Ministry of Education, Culture, Sports, Science and Technology; by the Science Research Promotion Fund from the Promotion and Mutual Aid Corporation for Private Schools of Japan; by the Research Grant for Cardiovascular Diseases 17A-1 and 19C-7 from the Ministry of Health, Labor and Welfare; and by the Seki Minato Prize.

Disclosures

None.

Toshiro Nishikimi
Department of Hypertension and Cardiorenal Medicine
Dokkyo Medical University
Tochigi, Japan

Naoto Minamino
Department of Pharmacology
National Cardiovascular Center, Research Institute
Osaka, Japan

Kazukiyo Horii
Diagnostics Department
Shionogi & Co, Ltd
Osaka, Japan

Hiroaki Matsuoka
Department of Hypertension and Cardiorenal Medicine
Dokkyo Medical University
Tochigi, Japan


(Hypertension. 2007;50:e163.)

© 2007 American Heart Association, Inc.

Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.107.098350

e163
Do Commercially Available Assay Kits for B-Type Natriuretic Peptide Measure Pro-BNP1-108, as Well as BNP1-32?
Toshio Nishikimi, Naoto Minamino, Kazukiyo Horii and Hiroaki Matsuoka

Hypertension. 2007;50:e163; originally published online September 17, 2007; doi: 10.1161/HYPERTENSIONAHA.107.098350

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/50/5/e163

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/