Letters to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Noninvasive Assessment of Flow-Mediated Vasodilation With 30-MHz Transducer in Pregnant Women

To the Editor:

Cockell and Poston (April 1997)\(^1\) reported that flow-mediated vasodilation is enhanced in pregnant women but reduced in preeclampsia. They assessed the vasodilation using biopsies of small arteries. Therefore, their assessment was not in vivo but in vitro study. We assessed flow-mediated vasodilation in pregnant women noninvasively. Noninvasive assessment of flow-mediated vasodilation in nonpregnant subjects was first reported by Celermajer et al.,\(^2\) who measured the brachial artery with high-resolution ultrasound (7.5-MHz transducer). We previously reported that with a 30-MHz transducer it is possible to detect endothelial dysfunction more accurately by measuring the radial artery.\(^3\)

We examined 60 Japanese women including 20 nonpregnant normotensive healthy women (28.7±5.0 years old), 18 normal pregnant women (31.3±5.0 years old, 35.8±3.1 weeks of pregnancy), and 22 pregnant women with preeclampsia (29.8±3.8 years old, 36.0±3.3 weeks of pregnancy). The diagnosis of preeclampsia was made according to the criteria of the Committee on Terminology of the American College of Obstetricians and Gynecologists.\(^4\) All 60 subjects were nonsmokers.

Images of the radial artery in 60 women were obtained longitudinally with a 30-MHz mechanical linear probe and an SSD-550 system (Aloka, Tokyo, Japan). In each study, we confirmed the clear visualization of the three layers of the vessel wall, including the “m” line (the interface between media and adventitia) in both near and far walls. When the clear visualization of these layers was confirmed, the probe was fixed with a steel flexible arm. Adequate scans were obtained in all cases. A cuff of 140 mm Hg in width placed on the upper arm was inflated to 30 mm Hg above the systolic pressure for 5 minutes. The radial artery diameter was measured before inflation (baseline) and after deflation of the cuff. Imaging of the artery was performed for 6 minutes after cuff deflation. The radial artery diameter was defined as the distance from the near side of the “m” line in the near wall to the near side of the “m” line in the far wall. Measurements were taken within 1 minute before cuff inflation (baseline) and 30, 60, 90, 120, 180, 240, 300, and 360 seconds after cuff deflation at end diastole. Flow-mediated vasodilation was determined by calculating the change in the radial artery diameter (percent increase for the baseline diameters). Student’s \(t\) test was used for statistical analysis, and a value of \(P<.01\) was considered significant.

Baseline radial artery diameters in nonpregnant women, normal pregnant women, and preeclamptic women were 2.26±0.42, 2.41±0.38, and 2.22±0.35 mm, respectively. No significant differences were seen among these groups. Maximum dilation was obtained 1 minute after cuff deflation. The percent increases of radial artery diameter during reactive hyperemia in nonpregnant women, normal pregnant women, and preeclamptic women were 11.8±3.6%, 18.9±3.4%, and 7.9±3.0%, respectively. In normal pregnant women, vasodilation was significantly greater than that in nonpregnant women (\(P<.001\)). Vasodilation in preeclamptic women was significantly less than that in normal pregnant women (\(P<.001\)) or nonpregnant women (\(P<.001\)).

Our results indicate that peripheral vascular endothelial function in pregnant women was improved, but in preeclamptic women endothelial function was impaired. Our conclusions were in accordance with the findings of Cockell and Poston. Using our method, we can assess the endothelial function in pregnant women noninvasively. Because Cockell and Poston used biopsies obtained at cesarean section, their assessment was limited to subjects at or near term, but our method is applicable to subjects even in early pregnancy. Further work is in progress to evaluate the usefulness of our method as a predictor of preeclampsia.

Atsushi Yoshida
Shinji Nakao
Hisaaki Kobayashi
Mitsunao Kobayashi
Department of Perinatal and Maternal Medicine
National Defense Medical College
Saitama, Japan


Response

We read with interest the letter of Yoshida et al describing a study of the reactive hyperemic response in radial arteries of nonpregnant and pregnant women and of patients with preeclampsia. Using ultrasonography, the authors have shown blunted dilatation after cuff inflation on the upper arm in women with preeclampsia when compared with findings in normal pregnant women. These data would appear to confirm our in vitro findings described in Hypertension,\(^5\) in which we showed blunted endothelium-dependent, nitric oxide–mediated dilatation to shear stress in small arteries obtained during caesarean section from women with preeclampsia. However, some degree of caution should be applied when ascribing endothelium dependence to the abnormal dilatory response in the radial arteries, since vasodilation induced by hyperemia of the upper arm will undoubtedly lead to endothelium-independent elements of relaxation unrelated to increased flow per se\(^6\) in the lower arm.

Previous studies have circumvented this problem by applying the cuff to the lower arm, thus evoking an increase in shear stress in the upper arm but precluding any influence of locally acting metabolites.\(^7\) Nonetheless, Yoshida et al have shown clearly that vasodilator responses are significantly increased in pregnant women compared with nonpregnant and are blunted in women with preeclampsia. Together with our observations in resistance-sized arteries in vitro, these data add further strength to the hypothesis that impairment of vasodilatory responses may contribute to elevation of the blood pressure in women with preeclampsia.

Lucilla Poston
Anna Cockell
Fetal Health Research Group
Division of Obstetrics and Gynaecology
St Thomas’ Hospital
London, UK

1200
Is Plasma Ac-SDKP Level a Reliable Marker of Chronic Angiotensin-Converting Enzyme Inhibition in Hypertensive Patients? To the Editor:

In a recent article, Azizi et al suggested that the plasma levels of N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) could be a reliable marker of chronic angiotensin-converting enzyme (ACE) inhibition in hypertensive patients treated by ACE inhibitors (ACEI). We were concerned by their results because some of them contradict others.


Response

We are very pleased that Le Meur et al read in detail our article showing that plasma Ac-SDKP concentration is consistently high when ACE is chronically inhibited and that they have used their own recent results on hematopoietic cells. Both results show the importance of the ACEI-induced increase in endogenous Ac-
SDKP levels in plasma\(^1,3\) and possibly also in tissues, not only in accounting for the hematologic effect of ACEIs (in particular for conditions such as CRF\(^4\)) but also as a new therapeutic strategy to prevent hematologic toxicity of anticancer chemotherapy.\(^5,6\)

The discussion on the absence or presence of a relationship between plasma Ac-SDKP levels and creatinine clearance may not be useful and perhaps may be even misleading. Both studies found (1) lower Ac-SDKP levels in patients with normal renal function than in patients with renal dysfunction and (2) a further increase in plasma Ac-SDKP levels in ACEI-treated patients with CRF. Therefore, the data of Le Meur et al agree with our results more than they contradict them. The presence or absence of a correlation may be due to multiple minor problems: selection of different patients and of different types and doses of ACEIs, aberrant values, inappropriate statistical tests, and above all, low power of both studies.

Our last point of concern is that plasma Ac-SDKP determination did not detect chronic ACE inhibition in some of their patients with CRF, the number of whom was not reported. This is in contradiction to the pharmacokinetics of the exogenous peptide,\(^7\) the metabolism of the peptide (for which no enzymatic pathway other than that involving ACE exists\(^8\)), the pharmacokinetics of all ACEIs that accumulate in plasma and tissues during renal failure,\(^9\) and their own data showing urinary elimination of the peptide.\(^2\) Other than a possible problem in the timing of the blood sampling, which was not reported in the study of Le Meur et al (blood taken after dialysis or more than 24 hours after intake of a low dose of an ACEI in a patient with a mild degree of renal failure), the only other possible explanation is lack of compliance with the ACEI treatment by the patients. This emphasizes that the determination of plasma Ac-SDKP is a very sensitive method for the detection of an ACEI in the body, which can be used by physicians to check their patients' compliance with a simple measurement.\(^1\)

Michel Azizi
Broussais Hospital Clinical Investigation Center
INSERM and Assistance Publique des Hôpitaux de Paris
Paris, France

Eric Ezan
Service de Pharmacologie et d’Immunologie CEA,
Gif-sur-Yvette, France

Noninvasive Assessment of Flow-Mediated Vasodilation With 30-MHz Transducer in Pregnant Women
Atsushi Yoshida, Shinji Nakao, Hisaaki Kobayashi and Mitsunao Kobayashi

Hypertension. 1998;31:1200-1201
doi: 10.1161/01.HYP.31.5.1200

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/31/5/1200

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/