

Letter to the Editor

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Changes in Endothelial Function Precede the Clinical Disease in Women in Whom Preeclampsia Develops

To the Editor:

With much interest we read the article published by Khan et al¹ in the November 2005 issue of *Hypertension* on microvascular reactivity during normal and preeclamptic pregnancies. They showed that microvascular responses to iontophoretically applied acetylcholine and sodium nitroprusside are enhanced in women who will develop preeclampsia before the clinical symptoms of the syndrome appear. The authors found, however, no differences in the microvascular responses 6 weeks postpartum and stated that there was no study that had compared these responses shortly after pregnancy.

We recently published our study in which we measured microvascular reactivity using iontophoresis and laser Doppler flowmetry between 3 to 11 months postpartum in 25 women who had a serious early onset (<34 weeks of gestation) of preeclampsia and 23 women with a normal pregnancy.² In contrast to Khan et al, we found increased responses to acetylcholine in the recently preeclamptic group, whereas the response to sodium nitroprusside showed no difference with the normal pregnancy group. Blood pressure, maternal age, and family history of premature cardiovascular diseases could not explain the increased responses to acetylcholine.

There are some differences between both studies; the first one concerns the interval time between delivery and measurement. We chose to perform our microvascular measurements between 3 and 11 months postpartum, when the effects of pregnancy have likely disappeared. Second, Khan and coworkers measured microvascular reactivity on the forearm, a relatively low flow area, whereas we performed our studies on the fingers, a relatively high flow area. We investigated whether the location of the measurement could have influenced our data by measuring on the finger as on the forearm in some participants and found the same trend of reactivity for both locations. Another difference with the imaging setup of Khan et al was that they measured the mean of the two highest flux values in an area, which may have led to preference of skin locations with AV-shunts. Furthermore, the wave length we used, 780 nm, was less sensitive to influences of blood oxygenation than the 633 nm of Khan et al.

In summary, iontophoresis of acetylcholine and sodium nitroprusside to evaluate local vasodilator responses via endothelium-dependent and endothelium-independent pathways indicates that preeclampsia is associated with an enhanced endothelium dependent vasodilatation, during and months after the preeclamptic pregnancy. These findings support the hypothesis of an underlying (micro)angiopathy in preeclampsia.

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Response: Endothelial Function and Preeclampsia

We appreciate Blaauw et al for their careful consideration of our recent article and would like to make the following comments. Blaauw et al claim we stated that there was no study that had compared microvascular responses shortly after pregnancy. However, the statement we made was in fact that “no study had examined vascular responses *sequentially* at different gestations before the clinical syndrome of preeclampsia develops and after delivery.”¹

Blaauw et al are correct that methodological differences between their study² and ours might be the reasons for the different findings. We found no significant differences in microvascular responses between normal and preeclamptic women 6 weeks postpartum, at a time when blood pressure had returned to normal in preeclamptic women. Blaauw et al showed enhanced microvascular responses to acetylcholine (ACh) at 3 to 11 months postpartum and state that they chose a postpartum time point when the effects of pregnancy have likely disappeared. However, they also report in their article that women with a preeclamptic pregnancy had higher systolic and diastolic blood pressures at this time point. Thus, it is difficult to say with confidence that hemodynamic parameters had returned to normal in their particular sample of preeclamptic patients, and this might be the reason for their enhanced ACh responses.

We chose the forearm skin as the site for our measurements. Blaauw et al are correct that this is a relatively low flow area. However, perfusion through the forearm skin is also much more stable than in the finger. Accordingly, the forearm skin is the preferred site over the finger for such studies and the

one that is most widely used.^{3,4} Blauuw et al themselves demonstrate the highly variable nature of finger perfusion by showing a variation in baseline perfusion of as much as 74% in control subjects. We do not agree that our measurements might have led to preference of skin locations with arterio-venous shunts as it is well recognized that the forearm is completely devoid of such vessels. Indeed, this is the main reason why forearm skin is a low flow area. Additionally, our measurements were made over a much larger area of forearm skin using a laser Doppler imager. This overcomes the problems of spatial variability of skin perfusion and thus provides a more accurate measure than single point measurements.

In conclusion, we agree with Blauuw et al that preeclampsia is associated with enhanced skin microvascular responses. However, we suggest that these changes are at a level further down from the endothelium, and that these changes revert to normal in the short-term postpartum when hemodynamic changes have also normalized. Finally, we concur completely that laser Doppler flowmetry and iontophoresis of ACh and sodium nitroprusside are useful tools for the investigation of microvascular function in preeclampsia, but any comparisons between studies using different modes of measurement (imaging versus single point) and different measurement sites (finger versus forearm) must be made with caution and with a good understanding of the underlying factors that regulate blood flow in different vascular beds.

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