NO in Early Pregnancy and Development of Preeclampsia

To the Editor:

We read with interest the article published by Khan et al.\(^1\) Between April 2001 and November 2002 we conducted a prospective study approved by the Bioethics Committee.\(^2,3\) There were included 68 healthy pregnant women, primigravidae, younger than 25 years, and attending the Hospital Gineco Obstettrico Isidro Ayora in Quito, Ecuador. All women were included at 16 weeks of gestation and were evaluated every 4 weeks until week 36, after then every 2 weeks up to delivery. Onset of preeclampsia was defined as a blood pressure >140/90 mm Hg on at least 2 occasions more than 6 hours apart and proteinuria greater than 300 mg/dL. In every control a blood sample was taken and immediately transferred into a vial containing 3.15% sodium citrate (1:9 v/v) and gently mixed by inversion. Samples taken at delivery were obtained before labor activity was present. NO was quantified using a chemiluminescence system (NOA 280, Sievers System) as reported.\(^4\) Preeclampsia was found in 13.3% (n = 9) of all studied women.

Concentrations of NO were different in women with normal pregnancy (\(P = 0.009\)), but not in women who developed preeclampsia. During normal pregnancy, NO concentrations at week 16 (29 SEM 3.6 \(\mu\)mol/L) decreased at week 20 (21.1 SEM 1.7 \(\mu\)mol/L; \(P = 0.04\)) and week 24 (18.7 SEM 1.7 \(\mu\)mol/L; \(P = 0.01\)). However, at week 28, there was a slight increase (23.2 SEM 2 \(\mu\)mol/L), followed by a decline at week 32 (19.3 SEM 1.5 \(\mu\)mol/L, \(P = 0.04\) versus week 16). From then to delivery, there was a progressive increase in NO concentrations at week 36 (22.2 SEM 1.5 \(\mu\)mol/L) and week 38 (28.2 SEM 4.2 \(\mu\)mol/L; \(P = 0.04\) versus week 32). Interestingly, NO concentrations at 38 weeks and at delivery (28.8 SEM 3.7 \(\mu\)mol/L) were no different from those at 16 weeks. However, in women with preeclampsia, NO concentrations at week 16 (13.8 SEM 1.3 \(\mu\)mol/L) were lower than those obtained at week 20 (19.3 SEM 2.5 \(\mu\)mol/L; \(P = 0.06\)). At week 24 there was a decline in NO concentrations (14.6 SEM 2.6); this reached its maximum level at week 28 (23.4 SEM 3.7 \(\mu\)mol/L; \(P = 0.06\) versus week 24 and \(P = 0.02\) versus week 16). From then, NO concentrations decreased at week 32 (17 SEM 1.2 \(\mu\)mol/L) and remained with no change until delivery (19.3 SEM 1.2 at week 36). NO concentrations were higher in normal pregnancy compared with preeclampsia at week 16 (\(P = 0.006\)) and delivery (\(P = 0.04\)). Using a cutoff NO concentration at week 16 of 13.25 \(\mu\)mol/L, the relative risk for future onset of preeclampsia was 13.33 (95% confidence interval 1.82 to 97.82), with a sensitivity of 80% and a specificity of 90%. Also, the test showed a positive predictive value of 66.7% and a negative predictive value of 95%, with a likelihood ratio of 8.4. This constitutes the first followup study of NO in women with normal pregnancy and in those who develop preeclampsia.

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