Issues in the interpretation of serum endothelin levels in preeclampsia

Charles G. Coffey
PO Box 368, Golconda, IL 62938, United States

ABSTRACT

In this paper are discussed reasons to suspect that measurements of serum endothelin levels in women with preeclampsia may not provide accurate estimations of the degree of systemic endothelin receptor activation and reasons to suspect that systemic endothelin receptor saturation studies should provide such estimations more accurately.

Introduction

Not long after the discovery of endothelin [1,2], several studies demonstrated that serum levels of this substance were significantly elevated in women who had preeclampsia [3–6]. Additional further research on endothelin (much of it done without regard to preeclampsia) has demonstrated that interaction of the substance with its receptors in endothelial cells and in hepatocytes is capable of giving rise to many of the aberrancies known to occur in preeclampsia [7], from the classic triad of hypertension, proteinuria, and edema [8,9] to hyperuricemia and hypertriglyceridemia [10]. As such, endothelin has been suspected of playing a significant role in the pathogenesis of preeclampsia [11–18]. In this paper are discussed reasons to suspect that measurements of serum levels of endothelin in women with preeclampsia may be inadequate to assess the extent of maternal systemic endothelin receptor activation.

Hypothesis

Usually when serum levels of a substance are measured, the blood samples are drawn from the antecubital veins. For most substances it can be expected that serum levels of this substance were significantly elevated in women who had preeclampsia [3–6]. Additional further research on endothelin (much of it done without regard to preeclampsia) has demonstrated that interaction of the substance with its receptors in endothelial cells and in hepatocytes is capable of giving rise to many of the aberrancies known to occur in preeclampsia [7], from the classic triad of hypertension, proteinuria, and edema [8,9] to hyperuricemia and hypertriglyceridemia [10]. As such, endothelin has been suspected of playing a significant role in the pathogenesis of preeclampsia [11–18]. In this paper are discussed reasons to suspect that measurements of serum levels of endothelin in women with preeclampsia may be inadequate to assess the extent of maternal systemic endothelin receptor activation.

This would occur as a result of both dilution and attrition.

Dilution would occur as blood from the uterine veins enters larger vessels. Significant points of dilution would be where the uterine veins meet the portal vein, where the hepatic vein meets the inferior vena cava, and where the inferior vena cava meets the right ventricle.

Attrition would occur all along the movement of blood from the uterine veins to the antecubital veins, as endothelin receptors are present throughout the endothelium (and also on hepatocytes). Therefore, it would be expected that serum levels would drop by attrition as the blood progresses from the uterine veins to more distant points in the circulatory system. This attrition would be especially pronounced at the capillary level due to the greater surface area of the endothelium relative to blood volume. The endothelin molecules entering maternal circulation from the uterine veins would have to pass sequentially through three capillary systems (hepatic sinusoidal system, pulmonary alveoli, and the systemic capillary system) before any would reach the antecubital veins [19].

Another issue is that endothelin is different from most other blood borne substances, in that it is a paracrine factor.

Paracrine factors are substances which are released by the source cell to act upon receptors in adjacent cells (as opposed to endocrine factors, which act upon receptors in cells distant from the source cells) and thus would generally travel distances of microns to millimeters - not meters, from their source cells. Given that endothelin receptors are present throughout the circulatory system, that a significant number of endothelin molecules are consistently traveling all on the way from the uterine veins to the antecubital veins despite these dilutional and attritional factors, then it is likely that a near saturation of systemic endothelin receptors has been reached in women with preeclampsia.

Conclusion

Preeclampsia may be characterized as a state of prolonged near
saturation of maternal systemic endothelin receptors, this being the result of what essentially is a continuous intravenous infusion of endothelin via the uterine veins. With most situations of continuous intravenous infusions of bioactive substances, in a matter of a few days a steady state will be reached. Women with preeclampsia may be experiencing such a steady state. Rather than studying only serum levels, systemic receptor saturation studies should provide more direct estimations of the degree of systemic endothelin receptor activation in pregnancies complicated by preeclampsia, as well as in normal pregnancies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References


