

Hypertension in Pregnancy: The Role of Circulating Endothelial Progenitor Cell Dysfunction

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Received date: March 18, 2017; Accepted date: March 28, 2017; Published date: April 05, 2017

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Abstract

Pregnancy-induced hypertension (PIH) development associates well with considerable abnormalities in the structure and function of vascular endothelium. Lowered number and weak function of circulating endothelial progenitor cells (EPCs) as a marker of worsening endothelial integrity were recognized a promising indicator of PIH-related clinical outcomes. Although there are limiting data regarding predictive usefulness of serial EPC count measurement in pregnant women, it has been postulated that EPC dysfunction could be got better prognostication than other biomarkers including serum inflammatory cytokines, von Willebrand factor, E-selectin in prediction of some severe PIH-related states, i.e., fetoplacental insufficiency and premature parturitions. The sort communication is depicted the role of EPC dysfunction as a promising biomarkers in PIH.

Keywords: Hypertension; Pregnancy; Endothelial progenitor cells; Prognosis; Outcomes

Introduction

Recent clinical studies have shown that both number and function of circulating endothelial progenitor cells (EPCs) decrease progressively in pregnant women with hypertension depending on severity of blood pressure elevation [1-3]. It has been postulated that the phenomenon reflects maladaptation in endothelial reparation and vascular injury and consequently relates to endothelial dysfunction [4]. Moreover, EPC dysfunction could associate with complications of hypertension in pregnancy and relates to implications in pregnancy outcomes including thrombosis, fetoplacental insufficiency, and premature parturitions.

Interestingly, there is a large body of strong evidence regarding influence of cardiovascular (CV) risk factors and or metabolic comorbidities on depletion of EPCs' number and appearance of their dysfunction [5-8]. Additionally, whether weak function and lowered number of EPCs appear in a peripheral blood prior to hypertension in pregnancy is not clear [9]. However, the hypertensive pregnant women exhibited considerable imbalance between increased number of circulating mature endothelial cells and lowered count of EPCs compared to healthy normotensive pregnant women and non-pregnant healthy volunteers [1,3]. In this context, EPCs dysfunction could tailor risk discrimination in pregnancy-induced hypertension (PIH) with poor clinical outcomes.

It is well known that EPCs are involved in the endothelial reparation, angiogenesis, neovascularization and they attenuate of vascular function and contribute in pathogenesis of PIH acting as a main component of endogenous repair system [10]. Recent investigations have revealed that there was an exhaustion of circulating number of EPCs labelled as CD34⁺ or CD133⁺, CD133⁺, endothelial cell markers (CD309, CD31, CD144) was found in patient with CV diseases, while there are several controversies regarding the role of

different immune phenotypes of EPCs in tissue reparation [11]. Nevertheless, there is no pretty accurate evidence regarding comparison of discriminative values of several immune phenotypes of EPCs in PIH.

However, there are at least two immune phenotypes of EPCs labelled as early outgrowth EPCs and late outgrowth EPCs and isolated from similar source having similar markers expressing on their surfaces, i.e., CD144, CD309, CD45 [12,13]. Late outgrowths EPCs may shape endothelial colony cells and they produce more nitric oxide and better attenuate capillary structure than early EPC [12]. In contrast to late EPC, early EPCs are able to syntheses and secretion of broad spectrum of pro-angiogenic and angiopoetic cytokines including vascular endothelial growth factor (VEGF) and interleukin (IL)-6 [13]. Finally, we do not exactly know whether both immune phenotypes of EPCs distinguishing their ability to shaping endothelial cell colony in culture. Additionally, there are no a large number of clinical studies opened a clear explanation what immune phenotypes of circulating EPCs play the most prominent role in endothelial regeneration and consequently could be a better biomarker of PIH-related outcomes. However, there is strong evidence regarding close relation between deficiency of circulating CD34⁺ VEGFR⁺ EPCs and elevated plasma von Willebrand factor, soluble E-selectin, tissue factor of coagulation, and some inflammatory cytokines, i.e., interleukin [IL]-2 and IL-6, in hypertensive state [1,3,14,15]. Because biomarkers of endothelial damage/dysfunction mentioned above were found a predictive indicator for hypertension, there is an assumption that the CD34⁺ VEGFR⁺ EPCs could be a biomarker of PIH development and PIH-related outcomes [16,17]. The innate mechanism that correctly describes an established phenomenon is not fully clear, while some theoretical explanations could be reported in a context of hyper coagulation and worsening endothelial reparation [17]. However, this suggestion requires more investigations to clearly explain the predictive role of several immune phenotypes of EPCs in PIH.

In conclusion, the tight association between EPC dysfunction and recently established biomarkers of unfavourable clinical outcomes in

PIH requires confirmation in the large clinical trials. It is suggested that lowered number and weak function of circulating EPCs could be pretty accurate biomarker of PIH development and onset of PIH-related complications.

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