

POSTER PRESENTATION

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0730. Plasma endocan levels are associated with endothelial dysfunction during experimental human endotoxemia

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Introduction

The endothelium plays a central role in pathophysiology of sepsis. Systemic inflammation results in endothelial dysfunction, contributing to the development of shock and multiple organ dysfunction. However, an easy to obtain, early, and clinically applicable marker of endothelial dysfunction is currently not available. Such a marker could guide early and targeted therapy such as selective iNOS inhibition. Endocan is a soluble proteoglycan secreted by endothelial cells in response to pro-inflammatory cytokines, bacterial endotoxins, and angiogenic factors, and enhances microvascular permeability. Plasma endocan levels are increased in septic patients, and have been shown to correlate with sepsis severity and mortality. However, the direct relationship between endocan and endothelial function has not yet been investigated in humans *in vivo*.

Objectives

To investigate the kinetics of plasma endocan levels during human endotoxemia and to examine their relation with inflammation-induced endothelial dysfunction.

Methods

Seventeen healthy male volunteers were subjected to experimental endotoxemia (infusion of 2 ng/kg *E. Coli* lipopolysaccharide [LPS]). Plasma levels of inflammatory cytokines (TNF- α , IL-6, IL-10, and IL-1RA), endocan, ICAM, and VCAM were measured at T = 0, 0.5, 1, 1.5, 2, 4, 6 and 8 hrs after LPS infusion. Both before and 4 hrs after LPS administration, endothelial function was

assessed by determination of the vasodilatory response of forearm blood vessels to the incremental intra-arterial infusion of endothelium-dependent (acetylcholine) or endothelium-independent (nitroglycerine/nitroprusside) vasodilators using venous occlusion plethysmography. Furthermore, correlations between the increases in plasma endocan, ICAM, and VCAM levels, and the endotoxemia-induced changes in vasodilatory responses were explored.

Results

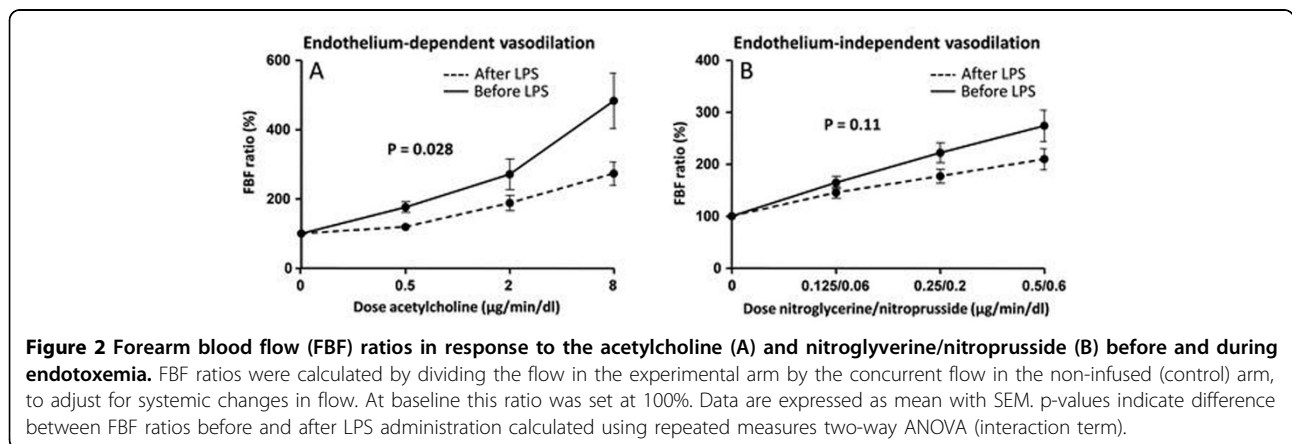
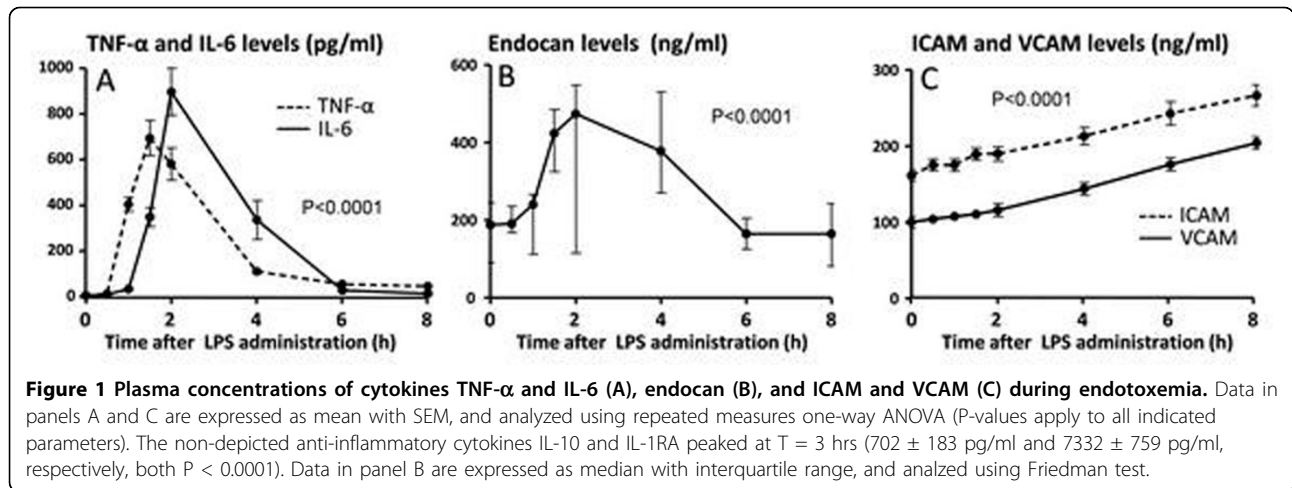
Plasma levels of all measured cytokines, endocan, ICAM, and VCAM concentrations significantly increased after LPS administration (Figure 1). LPS administration resulted in a significantly blunted response of forearm vasculature to acetylcholine (P = 0.028, Figure 2A), whereas the response to nitroglycerine/nitroprusside was not significantly affected (P = 0.11, Figure 2B). Furthermore, there was a significant correlation between the increase in plasma endocan levels and the attenuation of vasodilatory responses to acetylcholine (Pearson's $r = -0.49$, P = 0.049). No correlation existed between plasma levels of ICAM or VCAM and the attenuation of the acetylcholine-induced vasodilatory response.

Conclusions

Endocan levels are related to endothelial dysfunction during systemic inflammation in humans *in vivo*. Therefore, it may prove to be a suitable marker for the early identification of endothelial dysfunction and could guide targeted therapy.

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