Response to letter to the editor

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Editorial

Response to letter to the editor

Dear Dr Venkatappa and colleagues,

Thank you for your interest in our paper entitled 'Healthy and pre-eclamptic pregnancies show differences in Guanylate-Binding Protein-1 plasma levels' [1]. We are happy to clarify your questions and do so below.

With respect to the remark on including all factors that define pre-eclampsia, we would like to mention that the samples that we used in the present study were collected between 10 and 15 years ago, in a time when preeclampsia was defined by new-onset diastolic blood pressure $\geq$ 90 mmHg and proteinuria of $\geq$ 300 mg/24 h (ISSHP guideline). At that time, the use of prophylactic aspirin was not common practice in our hospital and none of the patients from experiment 1 or 2 have been treated with aspirin.

The fact that our samples were collected between 10 and 15 years ago also means that the samples have been used for other purposes. Unfortunately, for the first experiment, only Li-heparin samples were available and for the second experiment only EDTA samples were available. From some women both Li-heparin and EDTA samples were available and we compared GBP-1 concentrations between Li-heparin and EDTA samples. We found that the Li-Heparin GBP-1 concentrations were steadily a factor 2.7 lower than the concentrations in EDTA samples.

With respect to the first moment of sampling in the longitudinal study, which was 12 weeks of gestation: This is due to the fact that in the Netherlands in pregnant women blood samples are routinely taken, for e.g bloodgroup typing and for screening of infections, at the 12 weeks visit.

In the experiment in which placental GBP-1 mRNA and protein expression was measured, we matched the placentas for mode of delivery. The best matching obviously would have been matching for gestational age, however, it is extremely difficult to get control placentas matching for gestational age with early onset preeclampsia. We therefore choose the second best matching, i.e. matching for mode of delivery. There are different reports showing that the mode of delivery influences biological processes such as protein expression and oxidative stress in the placenta [2]. With respect to inflammatory cytokines Hu et al., for instance, found a correlation between cytokine expression and mode of delivery [3]. In a previous study, we have observed that ESM-1 mRNA levels in the placenta showed a tendency to be different in different modes of delivery [4].

In our discussion we hypothesize that the increase in GBP-1 during healthy pregnancies might be due to the generalized pro-inflammatory condition associated with pregnancy, with the most likely source of increased GBP-1 being endothelial cells. We also hypothesized why the GBP-1 concentration were decreased in preeclampsia. We suggest that angiogenic factors, like VEGF and bFGF, could influence the GBP-1 level negatively. Decreased free VEGF may result in endothelial dysfunction and thereby inhibit GBP-1 production [5,6]. Also bFGF, which is increased in preeclampsia [7,8], has been shown to inhibit GBP-1 production [9]. We also analyzed the data of sFlt, sEng, and plgf together with the GBP-1 and found that there is no correlation between these factors in our samples.

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