Troponin I and homocysteine levels in mild and severe preeclampsia

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Summary

Objective: To investigate troponın I and homocysteine in pregnant women with severe and mild preeclampsia. *Methods:* 43 women with mild and 22 women with severe preeclampsia, and 34 healthy pregnant women were included in the study. Homocysteine and troponin levels of the three groups were measured at admission and compared. *Results:* Mean troponin I levels were 0.005 ng/ml, 0.0116 ng/ml and 0.007 ng/ml in healthy pregnant women and mild and severe preeclampsia, respectively. These results were similar among the three groups. Homocysteine levels were similar in the mild and severe preeclampsia groups and significantly higher than in healthy pregnant women. *Conclusions:* Troponin I levels are not significantly increased in either mild and severe preeclampsia. Homocysteine increases in preeclampsia, but the severity of preeclampsia is not correlated with homocysteine levels.

Key words: Troponin I; Homocysteine; Preeclampsia; Pregnancy.

Introduction

It is well known that maternal adaptations of the cardiovascular system are needed in normal pregnancy. If pregnancy is complicated with hypertention and/or proteinuria these adaptation mechanisms may fail and result in myocardial damage [1-3].

Troponin I is a constituent of the troponin complex which regulates the interaction of actin and myosin in striated muscle. Cardiac troponin I contains an immunologically distinct N-terminus amino acid chain not expressed in skeletal isoforms. Cardiac troponin I is released into the circulation in response to myocardial injury and has been shown to be one of the most sensitive and specific markers of myocardial damage both in ischemic and nonischemic conditions [4, 5]. Population studies suggest that the 98th percentile lies at 0.03 ng/ml and that 88% of the normal population have serum cTnI of less than 0.01 ng/ml. In the setting of acute chest pain cardiac troponin I of > 0.1 ng/ml has been shown to have prognostic significance, and values above this level are taken as an indicator of significant myocardial damage [6].

Homocysteine is a sulfur containing essential amino acid derived from demethylation of dietary methionine. Plasma homocysteine levels decrease during pregnancy, probably due to changes in the renal handling of homocysteine or due to the hormonal changes associated with pregnancy [7, 8]. Plasma homocysteine concentrations are closely dependent on vitamin B (folate, vitamins B 6 and B 12, riboflavin) intake [9] and are also affected by variants of the methylenetetrahydrofolate reductase gene, particularly the thermolabile 677 C-T variant which results in reduced activity of the enzyme [10, 11]. Recently, increased homocysteine plasma levels have been reported to occur in women with preeclampsia [12-14]. There is a discrepancy in the literature whether homocysteine levels are related to severity of preeclampsia and if troponin levels increase in all preeclampsia cases or not.

Material and Methods

The study was composed of 99 women attending Sisli Etfal Training and Research Hospital 3rd Obsterics and Gynecology Clinic between June 2008 and December 2008. Three groups were generated; the first group consisted of 34 normotensive pregnant women without any pregnancy complications, the second group consisted of 43 pregnant women with mild preeclampsia and the third group consisted of 22 pregnant women with severe preeclampsia. Blood samples were obtained at admission until delivery from all participants. The diagnosis of preeclampsia was based on standard criteria as outlined in the Technical Bulletin from the American College of Obstetrics and Gynecology on Hypertension in Pregnancy [15]. Women before 24 weeks of gestation and those with known pre-existing cardiac or renal disease were excluded from the study. Informed consents on the study were signed by all participants and approval was obtained from the hospital ethical committee. Serum cardiac troponin I was measured using the Beckman Access II immunoassay (Beckman Coulter, Inc., Fullerton, CA) at the Department of Clinical Biochemistry of our hospital [16]. A lower limit of detection of 0.03 ng/ml is suggested for clinical use. Maternal homocysteine concentrations were measured using high-performance liquid chromatography with electrochemical detection procedures as described previously [17]. The interassay coefficient of variation was 7.2%. All laboratory assays were performed without knowledge of case or control status.

Statistical analysis: Comparisons of the demographic factors, troponin and homocysteine levels of the patients in the different groups were made using analysis of variance (ANOVA). The

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post hoc Tukey test was used to find the differences. Correlation analysis was performed using Pearson's correlation test (r = correlarion coefficent). SPSS version 13.0 was used for calculations; $p < 0.05$ was considered as significant at the 95% confidence level.

Results

Demographic characteristics of the groups are demonstrated in Table 1. Mean ages and parity of the pregnant women were similar among the three groups. Mean gestational weeks at labor were similar in the normotensive control and mild preeclampsia groups and was significantly lower in the severe preeclampsia group ($p < 0.05$).

Table 1. — *Characteristics of the study and control groups*.

	Mild PE	Severe PE	Control	*p*
No.	43	22	34	–
Maternal age (yrs)	28.1 ± 5.6	26.5 ± 5.2	27.7 ± 6.5	NS
Parity	1.3 ± 1.6	0.6 ± 0.8	1.0 ± 1.5	NS
GA (days)	266.04 ± 16.5	235.00 ± 20.7	272.87 ± 21.2	< 0.05
Proteinuria (mg/l)	944.5 ± 98.2	8786.8 ± 2306.9	41.3 ± 13.2	< 0.001
Birthweight (g)	3114.2 ± 96.5	2020.8 ± 304	3330.7 ±76.8	< 0.05
Apgar score	7.6 ± 0.4	6.0 ± 1.3	8.7 ± 0.2	< 0.05

PE: preeclampsia; GA: gestational age.

Mean troponin I levels were similar among the three groups. Homocysteine levels were similar in the mild and severe preeclampsia groups and significantly higher than the control group ($p < 0.05$) (Table 2).

Table 2. — *Mean troponin I and homocysteine levels of the groups*.

	Troponin I (ng/ml)	Homocysteine (μmol/l)
Healthy pregnant women (control)	0.0050 ± 0.008	6.31 ± 2.33
Mild preeclampsia	0.0116 ± 0.043	8.43 ± 5.20
Severe preeclampsia	0.0070 ± 0.015	9.32 ± 4.45
Significance (*p*)	NS	< 0.001

No correlation was found between homocysteine and gestational age (r = 0.17), between troponin I levels and gestational age (r = 0.15), or between homocysteine and troponin I levels (r = 0.34).

Discussion and Conclusion

There are a limited number of studies concerning troponin I levels in preeclampsia in the literature. Several authors have reported that troponin I levels rise in both mild and severe preeclampsia [18-20]. One study even reported that it increases more in the severe form of preeclampsia [20]. However recently Joyal *et al*. reported that preeclampsia was not associated with a rise in troponin I levels [21]. This discrepancy may be due to small study groups which consist of patients with illnesses known to increase troponin I. There are many cardiac and non-cardiac reasons that can increase troponin I levels reported in the literature. All cardiac interventions and any cardiac disease causing myocardial damage may lead to increased troponin I. Among the non-cardiac reasons, end-stage diseases, chemotherapy, renal failure, septic shock, and ultra-endurance exercises are well known [22].

We designed our study with larger groups defining preeclampsia as mild and severe forms to make this confusing data in previous studies more clear. Our results are in accord with Joyal *et al*. Further we can say that severity of preeclampsia was not related to troponin I levels. Nonetheless although statistically not significant, there was a tendency for a rise in troponin I in mild preeclampsia compared to healthy controls ($p = 0.066$), but interestingly, troponin I in severe preeclampsia was very similar with healthy controls. These findings support the theory of Joyal *et al*. that an elevated troponin level can not be solely attributed to inflammatory events of preeclampsia because it is not correlated with the amount of proteinuria and nor blood pressure levels. There were no cardiac or non-cardiac reasons known to elevate troponin I in the groups in our study. Why then did some of the patients have increased troponin levels – especially the mild preeclampsia group? This could be because some of the patients may be more prone to myocardial injury when they are exposed to high blood pressure or more prone to other inflammatory proccesses seen in preeclampsia.

It has been clearly defined by many studies that elevated homocysteine levels are associated with preeclampsia [13, 14, 23]. Some studies even blamed homocysteine as a causative agent for preeclampsia and the severity of preeclampsia was associated with the levels of homocysteine [24]. According to our study, homocysteine levels increased in preeclampsia, but severity of disease was not related with homocysteine serum levels.

The pathophysiology of hyperhomocysteinemia in vascular disease is still under investigation. Preeclampsia produces diffuse endothelial dysfunction as evidenced by increased levels of fibronectin, thrombomodulin, endothelin and thromboxanes; there is impaired vasodilatation [25].

Endothelial dysfunction, which is thought to play a role in the pathophysiology of hyperhomocysteinemia, can be mediated by oxidative stress. This dysfunctional endothelium may explain the poor cardiovascular outcomes after years. Is this endothelial damage also responsible for alterations of troponin levels? We thought the oxidative stress and dysfunctional endothelium may be the same etiological factor increasing homocysteine and troponin levels in severe preeclamptic women in accord with some studies [18, 20].

Thus we wanted to know if there was any correlation with troponin levels and homocysteine levels in different groups. However we could not find any correlation between homocysteine and troponin I levels (r = 0.34). Therefore we wanted to find out if this result would also be reflected in troponin levels and would they correlate? The relationship between homocysteine and coronary artery disease/cerebrovascular disease is well known. The risk of coronary artery disease is seen across a range of homocysteine levels. Some studies reported that there is

a positive association between homocysteine and ischemic heart disease; for an increase of 5 μmol/l in homocysteine, the rate of ischemic heart disease risk increased by 84% [10, 26]. Our not finding any correlation between troponin I and homocysteine levels may be related with not finding any relation according to severity of the disease. We could not find any other study that compared these two levels so further studies are needed.

Lastly, our study was not designed to explain the etiological role of hyperhomocysteine, so we can not comment as to whether hyperhomocysteine is a causative agent or not. Whether endothelial damage is the cause or a result of preeclampsia is also unknown.

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