ELEMENTAL VARIATIONS IN PREECLAMPSIA

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ABSTRACT

Objective: There are alterations in elemental metabolism due to physiological and pathological processes in pregnancy. In this study, the physiological distribution of elements between the mother and the fetus is investigated along with the variations in the elemental status of the maternal-fetal-placental unit in pregnancies complicated with preeclamptic toxemia.

Methods: Cu, Zn, Fe, Mg and Ca levels in placental tissue, maternal and fetal plasma and fetal red blood cells in the healthy individuals (n=9) and preeclamptics (n=10) are determined by inductively coupled plasma atomic emission spectrometry.

Results: Within the control group, significant differences between maternal and fetal plasma have been detected with respect to Cu ($p<0.001$) and Fe($p<0.05$) levels. Comparing the preeclamptics with the controls, the most marked variation is observed in Zn status with significantly decreased concentrations in maternal and fetal plasma ($p<0.05$) and fetal red blood cells ($p<0.01$). Significant variations are also determined for Cu in fetal red blood cells ($p<0.05$), Ca in placental tissue ($p<0.01$) and fetal plasma ($p<0.05$).

Conclusion: This study points out the disturbances in the elemental status of the maternal-fetal-placental unit in preeclampsia.

Key Words: Pregnancy, Preeclampsia, Placenta, Trace elements, Ca, Mg

INTRODUCTION

The distribution of major and trace elements between the mother and the fetus and also the alterations in the elemental status due to physiological and pathological processes in pregnancy have recently gained interest (1-4). The elemental status of the mother with preeclamptic toxemia has been investigated by various authors (5-7). To our knowledge, there is no study on preeclamptic toxemia which evaluates the elemental status of the fetus and the placenta along with the mother in order to understand how preeclampsia interacts with the elemental metabolism.

The objective of this study is to determine the distribution of essential trace elements Cu, Zn, Fe along with Ca and Mg in the maternal, fetal, placental unit in order to evaluate the variations in preeclampsia.

MATERIALS AND METHODS

This stduy was carried out by the Department of Obstetrics and Gyneocology, Department of Biochemistry and Clinical Biochemistry and Clinical Research Laboratory of Ege University, School of Medicine between September 1994-June 1995. Approval was obtained from the Ethical Committee of Ege University, School of Medicine. All the patients involved in the study were informed about the content of the study and written consent was obtained.

The control group consisted of 9 full term babies and their mothers with no maternal or perinatal

complications. For the diagnosis of preeclamptic toxemia, (n=10) the patient should have blood pressure 140/90 mm Hg or an increase above baseline of 30 mm Hg in systolic pressure or 15 mm Hg in diastolic pressure. Generalized edema and/or proteinuria were used as additional diagnostic criteria. Mothers with diabetes, chronic urinary tract infection, liver diseases, chorioammionitis, chronic hypertension with superimposed toxemia and smokers were excluded. The control group and the preeclamptic group did not differ significantly with respect to maternal age (28±3.4 vs. 31.1±5.7) or the birthweight (3214±513 g vs 3175±620 g). The babies had an Apgar score of > 7 at 1 min. and 10 at 5 min. after delivery and did not manifest symptoms of disease or signs of malformation.

Blood was drawn from the umbilical cord vein immediately after delivery and from the mothers within an hour of delivery into acid rinsed (soaked in 10% HNO_3 for 12 hours) polypropylene test tubes containing lithium heparinate. Following centrifugation (10 min, 1500 g) plasma samples were stored at -20°C until analysis. For the determination of the elemental content, plasma samples were diluted 1:10 with 0.1 N HCl. Pretreatment for red blood cells (RBC) was performed according to Marunghui and Mahler (8,9).

Placental tissue samples obtained from the mid-disk region were perfused with 0.9% cold saline solution within two hours, membranes and vessels being excluded. Tissue samples were then weighed and wet digested in 15 ml of HNO_3 : $HClO_4$: H_2 SO_4 mixture (3:1:1) (v:v). Elemental analysis was performed by ICP-AES (Jobin Yvon JY 24). The wavelengths were 213.768 nm for Zn, 324.754 nm for Cu, 238.204 nm for Fe, 280.270 nm for Mg and 393.366 nm for Ca.

RESULTS

Data for the control group and the preeclampsia group including the concentration of Cu, Zn, Fe, Mg and Ca in placenta, maternal and fetal plasma and fetal RBC are presented in Tables I, II and III respectively. In the control group, maternal and fetal plasma levels of Cu and Fe show significant differences ($p<0.001$ and $p<0.05$). Fetal plasma Cu levels are 13.4% of maternal plasma Cu. Fetal plasma Fe levels are significantly higher than that of maternal plasma. In the preeclampsia group the only element which shows a significant difference between maternal and fetal plasma is Cu ($p<0.001$). The difference observed in Fe levels is not statistically significant.

Comparing the preeclamptics to the healthy controls reveals that Zn levels in maternal ($p<0.05$) and fetal plasma ($p<0.05$) as well as in fetal RBC ($p<0.01$) are significantly lower. In fetal RBC Cu levels are also significantly decreased ($p<0.05$). An increased concentration of placental Ca in preeclamptic group is accompanied by a decrease in fetal plasma Ca, both being statistically significant ($p<0.01$, $p<0.05$ respectively).

Table I : Placental tissue concentrations of Cu, Zn, Fe, Mg, and Ca in preeclampsia (n=10) and control (n=9) groups

	PREECLAMPSIA		CONTROL	
	Mean ± SEM	**Range**	**Mean ± SEM**	**Range**
Cu (nmol/g)	7.08 ± 1.11	4.17 - 13.32	5.38 ± 0.59	2.58 - 8.25
Zn (µmol/g)	0.16 ± 0.02	0.11 - 0.28	0.18 ± 0.03	0.08 - 0.37
Fe (µmol/g)	1.07 ± 0.13	0.51 - 1.37	1.24 ± 0.12	0.79 - 1.92
Mg (µmol/g)	1.63 ± 0.27	1.11 - 3.49	1.65 ± 0.19	0.88 - 3.02
Ca (µmol/g)	6.29 ± 0.61*	4.37 - 8.48	3.11 ± 0.44	1.09 - 4.31

* $p<0.01$

Table II : Maternal and fetal plasma Cu, Zn, Fe, Mg, and Ca levels in preeclampsia (n=10) and control (n=9) groups.

	PREECLAMPSIA		CONTROL	
Maternal Plasma	**Mean ± SEM**	**Range**	**Mean ± SEM**	**Range**
Cu (µmol/L)	32.59 ± 4.94	20.0 - 50.55	35.59 ± 2.20	24.09 - 46.45
Zn (µmol/L)	9.17 ± 0.76*	6.88 - 11.01	17.28 ± 2.75	9.78 - 36.08
Fe (µmol/L)	24.91 ± 5.36	14.16 - 44.98	32.97 ± 6.99	12.54 - 73.48
Mg (mmol/L)	0.59 ± 0.09	0.43 - 0.98	0.66 ± 0.02	0.58 - 0.83
Ca (mmol/L)	2.22 ± 0.09	2.01 - 2.47	2.62 ± 0.08	2.26 - 3.04
Fetal Plasma	**Mean ± SEM**	**Range**	**Mean ±SEM**	**Range**
Cu (µmol/L)	5.48 ± 1.46[a]	1.41 - 11.34	4.76 ± 0.28[a]	3.46 - 5.98
Zn (µmol/L)	11.16 ± 1.07*	7.34 - 15.59	14.98 ± 1.64	8.7 - 22.78
Fe (µmol/L)	35.48 ± 7.88	12.54 - 66.30	48.56 ± 8.1[b]	25.98 - 80.42
Mg (mmol/L)	0.57 ± 0.09	0.28 - 1.02	0.67 ± 0.04	0.39 - 0.79
Ca (mmol/L)	1.87 ± 0.16*	1.38 - 2.51	2.45 ± 0.15	1.73 - 2.93

*$p<0.05$, (Comparison between preeclampsia and control groups).

[a]$p<0.001$, [b]$p<0.05$ (Comparison between maternal and fetal plasma).

Table III: Cu, Zn, Fe, Mg, and Ca concentrations in Fetal Red Blood Cells (RBC) in preeclampsia (n=10) and control (n=9) groups.

	PREECLAMPSIA		CONTROL	
	Mean ± SEM	**Range**	**Mean ± SEM**	**Range**
Cu (µmol/L)	4.72 ± 0.50*	3.46 - 6.29	6.77 ± 0.62	2.68 - 9.76
Zn (µmol/L)	22.48 ± 1.57 **	17.43 - 25.99	49.84 ± 5.81	23.24 - 82.56
Fe (µmol/L)	170.61 ± 34.32	114.69 - 283.15	153.94 ± 25.98	72.04 - 315.77
Mg (mmol/L)	0.69 ± 0.06	0.55 - 0.83	0.94 ± 0.16	0.35 - 1.56
Ca (mmol/L)	0.27 ± 0.03	0.20 - 0.34	0.44 ± 0.10	0.12 - 0.94

* $p<0.05$, ** $p<0.01$

DISCUSSION

In this study, the elemental distribution between the mother and the fetus along with the placenta has been investigated in physiological pregnancies. It has been previously reported that Cu in cord blood at term, is about 1/5 of maternal blood (10,11). Contrary to reported high Zn levels in neonate when compared to maternal plasma (12), our neonate plasma Zn levels are found to be slightly lower. In this study, fetal plasma Fe levels are significantly elevated which is consistent with already published data.

It is pointed out that total or ionized levels in fetal plasma exceed maternal plasma levels (13). However, in our series no significant differences could be detected with respect to these elements.

Comparison of the preeclamptics with healthy controls reveals that the most prominent elemental variation is in Zn with significantly decreased concentration in maternal and fetal plasma as well as in fetal RBC. This marked lowering in Zn is in accordance with Lazebnik et. al. who report that plasma Zn is 19% lower in parturients with preeclamptic toxemia (5). Bassiouni also points to low Zn in maternal plus umbilical blood of preeclamptic cases (14). The decreased maternal Zn levels possibly responsible for the concomitant lowering in fetal Zn suggest the potential role of Zn deficiency as an underlying cause of pregnancy induced hypertension (15).

Data related to plasma Cu are contradictory. Both elevated and lowered levels are reported (6,12). As to our findings, with respect to maternal and fetal plasma Cu no significant difference could be detected. The reason for the decreased Cu levels in fetal RBC in our preeclamptic group remains unclear. Fe deficiency has been considered as a factor contributing to preeclampsia (15). In our series supporting this view, maternal and fetal plasma Fe levels are noted to be lower although not statistically significant.

In preeclampsia Mg and Ca are the elements which have been investigated most extensively. In these cases, the alterations in Ca homeostasis are attributed either to disordes in calcium regulating hormones or to changes in kidney function (16, 17). While some authors estimate decreased maternal plasma Ca (4, 6, 18), others indicate that no differences in Ca levels exist between hypertensive and normotensive pregnant women (16). In our preeclamptic group, although maternal plasma Ca levels are not affected, the lowering in fetal plasma Ca and the elevation in placental Ca are still indicative of disturbances in Ca metabolism in preeclampsia.

As to Mg, though not statisticaly significant, a decrease is noted in maternal and fetal RBC as well as placental tissue. There is evidence that Mg deficiency might be an etiological factor in the pathogenesis of preeclampsia, however its exact role still remains to be elucidated.

In conclusion, this study provides some evidence for perturbations in the elemental status of the fetoplacental unit in preeclampsia. In order to elucidate the role of disturbed elemental status in toxemia, studies in larger series should be continued.

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