Lipid peroxidation in preeclamptic and eclamptic pregnancies

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Abstract

Preeclampsia and eclampsia remain one of the most serious complications of pregnancy, and the pathophysiology of the diseases is not fully understood. To investigate lipid peroxidation status in preeclamptic and eclamptic pregnancies, we measured the serum malondialdehyde (MDA) level, a product of lipid peroxide, in pregnant women with or without preeclampsia or eclampsia. Serum MDA levels were raised in women with preeclamptic (4.5 ± 0.6 μmol/L) (P < 0.005) or eclamptic (4.9 ± 0.8 μmol/L) (P < 0.005) pregnancies compared with uncomplicated pregnancy (3.3 ± 0.7 μmol/L). An increased MDA level was also present in uncomplicated pregnancy compared to non-pregnant women (2.6 ± 0.4 μmol/L) (P < 0.05). Serum MDA levels were significantly decreased at the third day post-delivery in either uncomplicated pregnancy (P < 0.05), preeclamptic pregnancy (P < 0.005) or eclamptic pregnancy (P < 0.005). A positive correlation was seen between MDA level and both systolic and diastolic blood pressure in preeclamptic and eclamptic pregnancies. These results provide further evidence that excessive lipid peroxidation may contribute to the pathophysiology and pathogenesis of preeclamptic and eclamptic pregnancies.

Keywords: Malondialdehyde; Lipid peroxidation; Preeclampsia; Eclampsia

1. Introduction

Preeclampsia and eclampsia remain serious complications of pregnancy that affect both mother and child [1,2]. Although they were both described over 100 years ago, their pathophysiology is not fully understood. Uncontrolled preeclampsia can lead in certain cases to eclampsia. Eclampsia is the occurrence of convulsions in association with the signs and symptoms of preeclampsia and may occur before, during or shortly after delivery and it is characterised by the occurrence of major epileptiform convulsions in patients with serious consequences for both mother and fetus [2,3]. Both preeclampsia and eclampsia are the leading cause of maternal death and perinatal morbidity, even in countries with modern obstetric services.

An impairment of vascular endothelial cell function, causing vasoactivity, may play role in the pathophysiology of preeclampsia or eclampsia [2,4], and this vascular endothelial cell dysfunction may be caused by lipid peroxidation [5]. Lipid peroxidation is an oxidative process that normally occurs at low levels in all cells and tissues [6,7]. In a disease state such as preeclampsia, an uncontrolled lipid peroxidation may occur and impair normal endothelial cell function. A number of studies have reported that blood levels of lipid peroxidation products are elevated in women with preeclampsia [8–10]. However, little is known about lipid peroxidation in eclampsia, a more severe condition in pregnancy.

The aim of this study was to evaluate lipid peroxidation status in preeclamptic and eclamptic pregnancies by measuring serum malondialdehyde (MDA) levels, an end product of lipid peroxide, in women with or without preeclampsia and eclampsia.

2. Materials and methods

2.1. Subjects

Thirty pregnant women (10 with an uncomplicated pregnancy, 10 with a preeclamptic pregnancy and 10 with an eclamptic pregnancy) and 10 non-pregnant
Table 1
Subjects data (X ± S.D.)

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnancy</th>
<th>Uncomplicated pregnancy</th>
<th>Preeclamptic pregnancy</th>
<th>Eclamptic pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>27.4 ± 3.8</td>
<td>27.8 ± 3.5</td>
<td>26.5 ± 4.0</td>
<td>27.1 ± 3.4</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>111 ± 15</td>
<td>115 ± 18</td>
<td>151 ± 10</td>
<td>172 ± 22</td>
</tr>
<tr>
<td>Diastolic</td>
<td>74 ± 6</td>
<td>76 ± 7</td>
<td>105 ± 8</td>
<td>110 ± 8</td>
</tr>
<tr>
<td>Urine protein (g/24 h)</td>
<td>0.18 ± 0.09</td>
<td>0.15 ± 0.08</td>
<td>2.2 ± 1.0</td>
<td>2.5 ± 1.2</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>40.2 ± 2.2</td>
<td></td>
<td>38.6 ± 2.8</td>
<td>38.2 ± 3.0</td>
</tr>
</tbody>
</table>

Healthy women were studied. Preeclampsia was defined as the onset of hypertension (blood pressure > 140/90 mmHg or a rise of at least 30/15 mmHg) and proteinuria (> 0.3 g/day) during the latter half of the pregnancy [11]. Of the 10 eclamptic pregnancies, 6 were antepartum cases, 2 intrapartum and 2 postpartum occurring 4 and 6 h after delivery, respectively. All the eclamptic women had pre-existing pregnancy-induced hypertension. Antepartum eclampsia was defined as generalised convulsions starting before the start of labour in a pregnant woman with hypertension or proteinuria. Intrapartum eclampsia included convulsion starting after the onset of labour in a pregnant woman with hypertension or proteinuria. Postpartum eclampsia was defined as convulsions appearing within 7 days after delivery of the fetus and the placenta in a patient with hypertension or proteinuria during pregnancy, labour or the post-delivery period [12]. Ten healthy antenatal women and 10 non-pregnant women served as controls. The characteristics of the subjects studied were summarised in Table 1.

2.2. Serum

Pre-delivery samples were collected at the time of the hospital presentation. Post-delivery samples were collected within 24 h of delivery and at the third day after delivery, respectively. Serum was isolated by centrifugation and stored at -70°C until MDA assay.

2.3. Reagent's

All chemicals were obtained from Sigma Chemical Co. (Shanghai, China). Thiobarbituric acid (TBA) reagent was a mixture of equal volumes of 0.67% TBA aqueous solution and acetic acid. Standards of 1,1,3,3-tetramethoxypropane were diluted to 5 μmol/L with double-distilled water and stored at 4°C.

2.4. MDA assay

MDA, the end product of lipid peroxide, reacts with TBA to produce a fluorescence product, which is measured by fluorimetry. Thus, serum MDA levels were measured as an index of lipid peroxidation according to the TBA fluorescence method described by Yagi using a fluorescence spectrophotometer (Hitachi 850). The wavelengths of excitation and emission were 515 nm and 553 nm, respectively [13].

2.5. Statistics

Statistical analysis was performed using Student t-test and linear regression analysis. Data were expressed as mean ± standard deviation (X ± S.D.) and results were expressed as MDA μmol/L.

3. Results

Serum MDA levels before delivery were significantly greater in women with preeclamptic or eclamptic pregnancies than in women with uncomplicated pregnancy (Table 2). An increased MDA level was also present in women with uncomplicated pregnancy when compared with non-pregnant women (Table 2). Although no differences were found between pre-delivery and within 24 h of post-delivery MDA levels in the three pregnant groups, serum MDA levels were significantly decreased at the third day of post-delivery in women with either uncomplicated pregnancy or preeclamptic pregnancy or eclamptic pregnancy (Table 3). A positive correlation was seen between MDA level and both systolic blood pressure and diastolic blood pressure.

Table 2
Pre-delivery serum MDA levels in different study groups (X ± SD)

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>MDA (μmol/L)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-pregnancy</td>
<td>10</td>
<td>2.6 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td>10</td>
<td>3.3 ± 0.7</td>
<td>&lt;0.03*</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>10</td>
<td>4.5 ± 0.6</td>
<td>&lt;0.005*</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>10</td>
<td>4.9 ± 0.8</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*Of the 10 eclamptic pregnancies, 6 were antepartum cases, 2 intrapartum and 2 postpartum occurring 4 and 6 h after delivery, respectively. †Compared to non-pregnancy. ‡Compared to normal pregnancy.
Table 3
Comparison of serum MDA levels of pre- and post-delivery in the three pregnant groups (X ± S.D.)

<table>
<thead>
<tr>
<th>Groups</th>
<th>MDA (μmol/L)</th>
<th>P values b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-delivery</td>
<td>3.3 ± 0.7</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Within 24 h after delivery</td>
<td>3.0 ± 0.7</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>At the 3rd day after delivery</td>
<td>2.4 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-delivery</td>
<td>4.5 ± 0.6</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Within 24 h after delivery</td>
<td>4.2 ± 0.8</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>At the 3rd day after delivery</td>
<td>2.7 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>Eclampsia a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-delivery</td>
<td>4.9 ± 0.8</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Within 24 h after delivery</td>
<td>4.6 ± 1.0</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>At the 3rd day after delivery</td>
<td>2.9 ± 0.6</td>
<td></td>
</tr>
</tbody>
</table>

aOf the 10 eclamptic pregnancies, 6 were antepartum cases, 2 intrapartum and 2 postpartum occurring 4 and 6 h after delivery, respectively. bCompared to pre-delivery.

pressure in preeclamptic and eclamptic pregnancies (Table 4). However, there was no significant correlation between MDA level and the number of seizures in women with eclampsia (r = 0.350; P > 0.05)

4. Discussion

The study has shown that significantly increased serum MDA levels are present in pregnancy, and all further increased in preeclamptic and eclamptic pregnancies. This provides further evidence that inappropriate or excessive lipid peroxidation may play an important role in the pathophysiology of preeclamptic and eclamptic pregnancies. Previous studies have demonstrated an increase in lipid peroxidation products and a decrease in antioxidant superoxide dismutase activity in normal pregnancy [9,14,15]. Our data revealed similar results in normal pregnancy. This may be a normal oxidative stress due to the pregnancy [9]. The effects of higher serum MDA, a product of lipid peroxide, on mother and baby in normal pregnancy remain obscure. Raised serum MDA levels persist for 24 h of post delivery. The present data show no difference in the levels of serum MDA between eclampsia and preeclampsia.

Table 4
Correlation between serum MDA and systolic or diastolic blood pressure

<table>
<thead>
<tr>
<th>MDA</th>
<th>Preeclampsia (n = 10)</th>
<th>Eclampsia (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure</td>
<td>r = 0.635</td>
<td>r = 0.687</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.025</td>
<td>P &lt; 0.025</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>r = 0.610</td>
<td>r = 0.706</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.025</td>
</tr>
</tbody>
</table>

Damage from free radicals has been implicated in many pathologic conditions. Free radical-mediated cytotoxicity is thought to be mainly secondary to lipid peroxidation of the cell membrane and lipid peroxide may be a marker of free radical-mediated cell or tissue injury [6,13]. Lipid peroxide, an unstable but highly reactive and very damaging compound, arising as a consequence of tissue damage can propagate further lipid peroxidation locally and at sites distal to areas of initial damage [5,9]. Hence, extensive lipid peroxidation and elevated serum lipid peroxide products during preeclamptic and eclamptic pregnancies will cause vascular endothelial cell damage, which subsequently leads to vascular endothelial cell dysfunction. Signs of endothelial cell dysfunction in preeclampsia and eclampsia include endothelial cell damage, decreased blood levels of prostacyclin, platelet aggregation, and increased blood levels of fibronectin. Impaired function of the vascular endothelium may contribute both to vasospasm and the general increase in sensitivity to vasopressors occurring in preeclampsia and convulsions due to brain edema occurring in eclampsia [5,7].

In conclusion, a significant elevated serum MDA levels were found in pregnant women, especially preeclamptic and eclamptic pregnancies, which may contribute to pathophysiology and pathogenesis of preeclampsia and eclampsia. Some antioxidant systems, such as the superoxide dismutase and the lysate thiol, have been demonstrated to be reduced in red blood cells in preeclampsia [14]. Hence, the present investigation still suggests that the supplements of antioxidants or free radical scavengers may benefit pregnant women at risk of developing preeclampsia and eclampsia.

Acknowledgement

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References


