IgM ANTIBODY PRODUCTION FOR TROPHOBLAST ANTIGEN IN PREECLAMPSIA

Tatsuo YAMAMOTO, Sachiko YOSHIMURA, Yumi GESHI, Yukifumi SASAMORI, Shoichi OKINAGA, Takuro KOBAYASHI

Department of Obstetrics and Gynecology, Teikyo University School of Medicine, Tokyo 173, JAPAN

INTRODUCTION

In preeclampsia many hypothetical etiology are proposed. Immunological alterations has been reported by some investigators. Immune response against placental antigen has been studied. The antibody production for placental antigen has been reported since 1952.1 In order to investigate the alteration of humoral immune response in preeclampsia, Immunoglobulin M(IgM) binding for placental villous antigen was studied.

MATERIALS AND METHOD

Serum samples were taken from 20 preeclampsia, 23 normal pregnant and 5 non pregnant women. Fresh placentas were taken from normal pregnant and preeclamptic women. The paired samples of serum and placenta were taken from 4 normal pregnant and 6 preeclamptic women. Placental villous surface membrane (PVM) as placental antigen was isolated by using Smith method.2 Total IgM concentration was measured by single radial immunodiffusion. The binding of IgM in sera for PVM was evaluated by ELISA. 50 μl of PVM fraction (50 μg/ml) were coated on the well of 96 well microplate with bicarbonate buffer for overnight. 50 μl of diluted serum samples (x32) were incubated with the wells for 1 hour. After washing, horseradish peroxidase conjugated anti-human IgM rabbit antibody was incubated with the well for 1 hour. After washing, ortho-phenylenediamine was reacted for 30 min. Reaction was discontinued with H2SO4. Optical density (OD) was measured at 492 nm. IgM bindings were evaluated by formula as follows.
IgM Binding 1 = Serum sample OD - BSA OD. In cases which paired samples were tested, they were calculated as follows.

\[
\text{IgM Binding 2} = \frac{\text{Serum sample OD - BSA OD}}{\text{BSA OD}} \times 100
\]

RESULT
1. Total serum IgM concentration in preeclampsia and normal pregnancy.
   Total serum IgM concentrations in preeclampsia and normal pregnancy were 152 ± 69 and 158 ± 114 mg/dl respectively. No statistical difference was found in both groups.
2. The binding of IgM in sera taken from preclampsia and normal pregnancy for PVM (Table 1).
   The binding of IgM in pregnancy was higher than that of non-pregnant women. The binding of IgM in preeclampsia was significantly lower than that of pregnant women. IgM binding of maternal sera for PVM, which were taken from serum sampling mother, showed very low levels in three of six cases of preeclampsia (Table 2).

DISCUSSION
Almost reports for immunoglobulin production in preeclampsia were the findings as pathogenic antibody. Investigators have thought that immunoglobulin binds to placental antigen and that it may work pathogenic. Kaku reported the precipitaion substance in human sera for placental polysacharide.\(^1\) Hulka showed increased immunoglobulin binding for syncytiotrophoblast.\(^3\) Kitzmiller demonstrated the binding of immunoglobulin and complement in decidual vessels.\(^4\) Davies studied the binding capacity of immunoglobulin for PVM. This binding is not allospecific. The IgG binding is high in early stage of pregnancy and goes down gradually toward term. The IgM binding is same as IgG binding but the change is not clear than that of IgG.\(^5\) However Kajino demonstrated that IgM antibody bindings for trophoblast increase significantly in third trimester.\(^6\) In this study we demonstrated decreased binding of IgM for PVM. It is not depend on total serum IgM levels. Moreover we could find that IgM binding of maternal sera
for PVM, which are taken from serum sampling mather, shows very low levels in preeclampsia. Lower production of IgM antibody for PVM in preeclampsia has never been reported. In normal pregnancy, IgM antibody for PVM is produced much more than that in non-pregnant women. This phenomenon relates to blocking antibody production in pregnancy. The decrease of blocking antibody may play a role of the development of preeclampsia. The decreased blocking antibody production has been reported in unexplained habitual abortion. Using immunoblot technique, we are analysing the qualitative difference of IgM between normal pregnancy and preeclampsia. By preliminary experiment, loss of IgM production for 80 kd substance and abnormal production for 75 kd substance were detected in preeclampsia. Recently it has been reported that the expression of HLA-G messenger RNA in trophoblast decreases in preeclampsia. If HLA-G antigen may play a role of antigen presentation in normal pregnancy, decreased antigen presentation may make abnormal pregnancy outcome. We need to study the significance of decreased levels of IgM for PVM in future.

REFERENCE
7. Colbern G T et al. p362, 39th Annual meeting of SGI.
Immunoglobulin M antibody response for PVM (Placental villous membrane) by unrelated and related women

<table>
<thead>
<tr>
<th>PVM</th>
<th>Serum sample (unrelated)</th>
<th>related PVM mother</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>non-preg.</td>
<td>pregnant</td>
</tr>
<tr>
<td>K</td>
<td>16.3±10.8</td>
<td>30.1±15.8 a</td>
</tr>
<tr>
<td>K</td>
<td>54.7±7.4 c</td>
<td>38.2±15.7 d</td>
</tr>
</tbody>
</table>

a-b p<0.05, c-d p<0.01

Table 1

Maternal IgM antibody response for fetal PVM (Placental villous membrane)

<table>
<thead>
<tr>
<th></th>
<th>normal pregnant</th>
<th>Preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR</td>
<td>19</td>
<td>KI 55 *</td>
</tr>
<tr>
<td>SY</td>
<td>32</td>
<td>EN 4 **</td>
</tr>
<tr>
<td>KU</td>
<td>13</td>
<td>KA 17</td>
</tr>
<tr>
<td>OY</td>
<td>28</td>
<td>SA 0 **</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NA 41 *</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NK 5 **</td>
</tr>
</tbody>
</table>

Table 2