Interleukin-2 receptor concentrations in pregnant women with a history of recurrent miscarriage

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BACKGROUND: The mechanism by which the maternal immune system tolerates the fetus during pregnancy is unclear. METHODS: This study measured interleukin-2 receptor (IL-2R) concentrations in the serum of non-pregnant women (Group 1); healthy first trimester pregnant women (Group 2); pregnant women with a history of recurrent miscarriage whose pregnancies again failed later in the first trimester (Group 3); and first trimester pregnant women with a history of recurrent miscarriage but whose pregnancies on this occasion went successfully to term (Group 4). An initial sample was obtained from all women in Groups 1, 2, 3 and 4. A further sample was obtained 4 weeks later from women in Groups 1, 2 and 4. RESULTS: The initial sample showed no significant difference in IL-2R concentrations between Groups 1 and 2. Concentrations were significantly higher in Groups 3 (667 ± 244 U/ml; P < 0.003) and 4 (730 ± 360 U/ml; P < 0.05) compared with healthy pregnant women (425 ± 94). When the second sample was obtained concentrations in Group 4 were found to have fallen so that they no longer differed from Group 2. CONCLUSIONS: Our results confirm earlier findings that a successful pregnancy is associated with significantly lower concentrations of IL-2R.

Key words: pregnancy/miscarriage/IL-2R

Introduction

The mechanism by which the maternal immune system tolerates the fetus during pregnancy is unclear. There is evidence to suggest that there is a bi-directional interaction between the maternal immune system and the reproductive system during pregnancy (Kennedy and Jones, 1991). The maternal immune system can therefore enhance or inhibit the development of the fetoplacental unit. Previous studies have suggested that some of the changes which occur during pregnancy result in a suppression of the immune system (Wegmann et al., 1993). However, previous studies also showed that women suffering spontaneous abortion (MacLean et al., 1991) and recurrent miscarriage (Kilpatrick, 1992) had elevated concentrations of interleukin-2 receptors (IL-2R) in their blood. IL-2R are known to be sensitive and quantitative markers of T cell activation and proliferation (Rubin et al., 1985).

The aim of this study was to re-investigate this topic in women with a history of recurrent miscarriage (at least 3 previous miscarriages) some of whom had a successful pregnancy and some of whom did not.

Materials and methods

Patient groups

The following groups were enrolled into the study: Group 1 comprised 30 healthy non-pregnant women; Group 2 comprised 36 healthy pregnant women of 9.4 ± 1.7 weeks gestation; Group 3 comprised 8 pregnant women of 7.4 ± 1.8 weeks gestation who had had at least 3 previous miscarriages—all pregnancies again ended in miscarriage later in the first trimester; and Group 4 comprised 5 pregnant women of 7.9 ± 0.7 weeks gestation with a history of at least 3 previous miscarriages—on this occasion all pregnancies went successfully to term.

Analysis

Blood was obtained from all patients on their first visit to the clinic and again 4 weeks later. Serum was stored at −70°C till assayed. Samples were analysed for IL-2R concentrations using enzyme-linked immunosorbent assay (ELISA) kits purchased from Laboratory Impex (Impex House, Wimborne, Dorset, UK).

Statistics

All results are expressed as the mean ± 1 standard deviation. Data was analysed for statistical significance using a Wilcoxon Rank Sum Test.

Results

The results obtained are given in Table I. Healthy pregnant women with no history of miscarriage showed no significant change in IL-2R concentrations compared with the non-pregnant group. Compared with women in Group 2 concentrations of IL-2R were significantly increased in Groups 3 and 4.
Table I. Interleukin-2 receptor (IL-2R) concentrations in pregnant women with a history of recurrent miscarriage compared with pregnant and non-pregnant healthy controls. Results are given as mean ± 1 SD

<table>
<thead>
<tr>
<th>IL-2R (U/ml)</th>
<th>Sample 1</th>
<th>Sample 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy non-pregnant (Group 1)a</td>
<td>415 ± 74</td>
<td>410 ± 58</td>
</tr>
<tr>
<td>Healthy pregnant (Group 2)b</td>
<td>425 ± 94</td>
<td>477 ± 139</td>
</tr>
<tr>
<td>Recurrent miscarriage (Group 3)</td>
<td>667 ± 244bc</td>
<td></td>
</tr>
<tr>
<td>Recurrent miscarriage ongoing (Group 4)</td>
<td>730 ± 360f</td>
<td>530 ± 219</td>
</tr>
</tbody>
</table>

aData taken from MacLean et al., 1992.
bP < 0.003 versus Group 2.
cP < 0.001 versus Group 1.
dP < 0.05 versus Group 2.
eP < 0.05 versus Group 1.

(690 ± 278 versus 425 ± 94 U/ml; P < 0.001). At the time of the first sample IL-2R concentrations were significantly higher in both groups of pregnant women with a history of miscarriage compared with the group of healthy pregnant women. There were no significant differences in IL-2R concentrations between the women in Group 3 whose pregnancies failed later in the first trimester and those in Group 4 that continued to term. When the women were tested again 4 weeks later values had not changed significantly in Groups 1 and 2. However, women in Group 4 showed a reduction in IL-2R concentrations so that they no longer differed significantly from the group of healthy pregnant women. No data were available from women in Group 3, as all had miscarried by this time.

Discussion

This study has found concentrations of IL-2R to be elevated in pregnant women with a history of recurrent miscarriage. This increase was observed early in the first trimester when all the women had viable pregnancies. Not all the pregnancies continued to term. We have previously found IL-2R concentrations to be increased in women admitted with spontaneous abortion (MacLean et al., 1992). Kilpatrick found significantly increased concentrations of IL-2R in women with a poor obstetric history possessing anticardiolipin antibodies (Kilpatrick, 1992). Increased IL-2R concentrations were also found in women with very bad obstetric histories (at least 5 previous miscarriages) without anticardiolipin antibodies. Unlike the present study concentrations were found to be lower in early pregnancy in those whose pregnancies continued with those that failed. IL-2R concentrations have been found to rise towards the end of a normal pregnancy (Burns et al., 1999). This rise was attributed to a decrease in the concentrations of circulating immunosuppressive markers at this time.

This study was based on a relatively small number of women. However the increased concentrations of IL-2R found in this study in Groups 3 and 4 indicates that there is an activation of the immune system in these women. This activation occurred regardless of whether or not the pregnancy continued. This suggests that in these women there is, at least initially, no depression of immunosuppressive factors. What triggers the fall in IL-2R concentrations after 4 weeks in the group of ongoing pregnancies is not clear. Neither is it clear whether it is the pregnancy itself that causes the activation of the immune system in the recurrent miscarriage patients or whether there is an underlying problem in these women.

References


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