Frequency of macroprolactinaemia in pregnant women

ANNA KOSTRZAK, BLAŻEJ MĘCZEKALSKI

Abstract

Prolactin (PRL) is a 198 polypeptide hormone involved in many biological functions in women. The main role of PRL is primarily associated with lactation and breast development. There are 3 isoforms of PRL: the little (23 kDa), the big (50-60 kDa) and the big-big also named macroprolactin (> 100 kDa). Macroprolactin was described for the first time nearly 30 years ago but the structure of the complex is still unclear. Macroprolactin is reported a large complex consisted of monomeric PRL and mainly immunoglobulin G. The aim of the study was to estimate frequency of macroprolactinaemia in normal pregnant women in the third trimester. Clinical study included 300 healthy pregnant women between 24th and the 28th weeks of gestation. Serum PRL concentration was measured using ELISA method. Prolactin recovery was estimated with the use of polyethylene glycol (PEG) precipitation. We demonstrated that 3% of 300 pregnant women in the third trimester of pregnancy presented macroprolactinaemia. In conclusion, macroprolactinaemia occurs also in healthy pregnant women but in very low percent.

Key words: prolactin (PRL), macroprolactinaemia, prolactin recovery (polyethylene glycol precipitation), pregnancy

Introduction

The prolactin (PRL) is a single chain 198 amino acids long protein lactational hormone secreted by anterior lobe of pituitary gland [1].

PRL is secreted in a pulsatile fashion and tightly controlled by dopamine which is released from tuberoinfundibular (TIDA) neurons of hypothalamus [2].

In the pregnancy serum PRL concentration rises progressively from 8 weeks of gestation reaching maximum values at 40 weeks of pregnancy [3]. The values at the first trimester rises to 70 ng/ml, at the second trimester to 150 ng/ml and nearly the delivery up to 300 ng/ml [4]. After delivery in lactating women PRL serum concentration ranges to 100 to 200 ng/ml but in nonlactating women declines to normal ranges within 1 month [5].

Hyperprolactinaemia in non-pregnant women can be caused by number of pathological conditions and associated with different clinical problems such as: menstrual irregularity, anouvulation and infertility [6, 7].

The pituitary gland increases in size from the first few weeks of pregnancy. Enlargement of the lactotrophs cells is accompanied by increase of PRL in the serum blood [8]. High serum estrogen concentration during pregnancy seems to induce the activity of lactotrophs cells also.

PRL circulates in several isoforms in serum blood [9]. The major is a little PRL (monomeric) with the molecular weight of 23 kDa, which contains up to 85% of the total PRL in the serum blood [10]. Other forms are as follows: big PRL with a molecular weight of 50 kDa accounts for approximately 10-15% and big-big PRL with a molecular weight of more than 100 kDa [11].

Big-big PRL was for the first time described in 1981 and called macroprolactin nearly 3 years later [12].

Although the problem of macroprolactinaemia was reported more than 30 years ago the molecular structure of macroprolactin is not completely understood [13]. Nowadays macroprolactin is reported as a macromolecular complex of 23 kDa monomeric prolactin and an immunoglobulin G (IgG). The structure of macroprolactin is heterogenous and the molecular weight ranges even up to 500 kDa.

The prevalence of macroprolactinaemia is difficult to estimate and varies from 18-42% in non-pregnant women with hyperprolactinaemia [13]. The frequency of macroprolactinaemia is reported in around 3-5% of pregnant women.

Materials and methods

The study group included 300 women from the 24th until the 28th weeks of the gestation who attended the Department of Gynecological Endocrinology or Gynecological Endocrinology Outpatients Clinic, Poznan University of Medical Sciences in Poznan, Poland from January 2008 until April 2010.
Table 1. Clinical characteristics of the study group

<table>
<thead>
<tr>
<th>Number of pregnant women</th>
<th>300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pregnant women with macroprolactinaemia</td>
<td>10</td>
</tr>
<tr>
<td>Number of pregnant women without macroprolactinaemia</td>
<td>290</td>
</tr>
<tr>
<td>Mean age of pregnant women (years)</td>
<td>30 ± 3.8</td>
</tr>
<tr>
<td>Weeks of gestation</td>
<td>24.6 ± 1</td>
</tr>
<tr>
<td>Highest serum PRL concentration (ng/ml)</td>
<td>395.1</td>
</tr>
<tr>
<td>Lowest serum PRL concentration (ng/ml)</td>
<td>47.05</td>
</tr>
<tr>
<td>Mean serum PRL concentration (ng/ml)</td>
<td>148.3 ± 59.5</td>
</tr>
<tr>
<td>Mean PRL recovery (%)</td>
<td>74.5 ± 9.8</td>
</tr>
<tr>
<td>Highest PRL recovery (%)</td>
<td>94.9</td>
</tr>
<tr>
<td>Lowest PRL recovery (%)</td>
<td>41.1</td>
</tr>
</tbody>
</table>

In all pregnant women PRL serum levels and polyethylene glycol precipitation (PEG) were measured. Serum samples were taken in fasting stage early in the morning between 7 to 8:30 a.m. Prolactin assay was done as routine analysis on Elecsys 2010 (Roche) with the reference range from 7 to 23.3 ng/ml.

To identify macroprolactinaemia the polyethylene glycol (PEG) method was used. PEG technique is a simple, quick and cheap laboratory method. PEG technique precipitates substances with the molecular mass higher than 100 kDa [8].

PEG recovery (%) is a percentage of the PRL derived in the supernatant and it is considered to be big-big prolactin. The results of the measurement can be as follows: recovery < 60% means significant amount of macroprolactin and recovery > 60% means significant amount of monomeric prolactin in the testing sample.

Results

300 healthy women between the 24-28th weeks of gestation were involved. The mean age of the study group was 30 ± 3.8 years old. Mean week of gestation was 24.6 ± 1.01 week. All serum blood samples were taken to assess the prolactin serum concentrations and were screened for the presence of macroprolactinaemia. The presence of macroprolactinaemia was determined by PEG (polyethylene glycol precipitation) with the result < 60%. In the study group the highest serum PRL concentration was 395.1 ng/ml and the lowest was 47.05 ng/ml.

Macroprolactinaemia was identified in 10 pregnant women, it means in 3% of the subjects. In this group of pregnant women with macroprolactinaemia the lowest prolactin recovery was 41.1% and the highest prolactin recovery was 59.68%.

Discussion

Pregnancy is related to the numerous adaptive processes associated with the brain function [12]. The pituitary gland in pregnant women undergoes enlargement. This process is associated with the increase of serum PRL concentration. The placental estrogen stimulates the lactotrophs of the pituitary gland and promotes synthesis of prolactin. High prolactin levels play a primarily role in the development of the mammary gland and induces changes associated with the pregnancy, lactation and the maternal adaptation after childbirth. The studies about different isoforms of prolactin in pregnant women are limited.

We studied 300 pregnant women in the second and the third trimester of the pregnancy and assessed prolactin concentrations in the serum blood. We also evaluated the variations in the molecular forms of prolactin. Macroprolactin was determined by using polyethylene glycol precipitation method. Presented study reported that 3% of healthy pregnant women demonstrated macroprolactinaemia in the serum blood.

Similar results were reported by Hattori et al. [14]. He examined 105 pregnant women and observed a frequency of macroprolactinaemia in 2.9% of them. However all these women (3 of 105) suffered from hyperprolactinaemia before the pregnancy. Different etiologies of the macroprolactinaemia were also observed and anti PRL antibodies in the serum blood were presented [14].

Pascoe-Lira et al. [15] identified frequency of macroprolactinaemia related to the presence of the autoantibodies against prolactin in pregnant women. The study included of 209 healthy women at the different stages of pregnancy and polyethylene glycol (PEG) method was used. Sera from 8 pregnant women (3.8%) were positive for macroprolactinaemia (PEG > 45%) and in 5 of them the anti-PRL antibodies were found.

Pansini et al. [16] studied multiple molecular forms of prolactin during pregnancy in women. The isomorphic forms of prolactin were studied by gel filtration chromatography. At 33 weeks of gestation little prolactin was accounted for 63.2 ± 7.7% of the total circulating hormone of 5 pregnant women. Pansini et al. [16] noticed also increase in the low molecular weight prolactin...
During the progression of the pregnancy, Fonseca et al. [17] determined variations in the molecular forms of prolactin during pregnancy and lactation. In pregnant women the major form of prolactin was little prolactin with the molecular weight 22 kDa. Also in nursing mothers a little prolactin was a prominent form.

According to these studies we conclude, that macro-prolactinaemia occurs also in healthy pregnant women but in very low percent.

References


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