BLOOD LEVELS OF SEROTONIN AND TRYPTOPHAN AND THEIR RELATIONSHIP WITH MOOD CHANGES DURING PREGNANCY AND POSTPARTUM PERIOD

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Abstract: The mood changes during pregnancy and postpartum period was recorded in 104 women belonging to various ethnic groups. The study was conducted in a hospital after institutional approval for the consented females. The information were recorded by interview of the study subject using a validated questionnaire. The analysis of questionnaire showed that 23.08% (24) women were clinically depressed during pregnancy and, 22.61% (23) women after childbirth. However, these 23 women included 8 women who were already depressed prenatally. On exclusion of these 8 cases, the postnatal depression was observed in 14.4%. Thirty (29.76%) women experienced a brief period of “pathological” happiness (joy of motherhood) after childbirth. The levels of serotonin and tryptophan were determined in two groups of subjects identified as who experienced depression during pregnancy and after childbirth. The blood samples (during pregnancy and postpartum period) were analysed for serotonin and tryptophan quantification using a validated HPLC method. The tryptophan level in prenatal depression and postpartum depression was found to be 12.7 ±2.5 and 11.9 ±2.4 ng/ml, respectively and that of the serotonin was 7.4 ±1.8 and 7.7 ±1.7 ng/ml, respectively in the above groups. It was concluded that the blood level of tryptophan and serotonin can guide us in the prevention and control of depression.

Key Words: Pregnancy, serotonin, tryptophan and depression

Introduction

Women are vulnerable to mood changes during pregnancy and postpartum period. A significant majority of women are reported to commonly suffer from psychiatric morbidity in the form of anxiety and depression, both during pregnancy and after childbirth (Watson and Elliot, 1984). About 10-15% of recently delivered women are afflicted with non-psychotic depression commonly known as postpartum depression (Lee, et al., 2001). It is also established now that the risk for affective disorders in women is higher during the prenatal period.
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compared to at other times (Ross, et al., 2004). Mood swings of sadness and elation are common during pregnancy especially at around 6-10 weeks of pregnancy and then again in the third trimester as the body begins to prepare for labour and delivery and in the first five days following child birth (Glover, et. al., 1994). To the detriment of both women and their infants, these psychiatric disorders generally remain under-diagnosed even in the developed countries. The general awareness level of this disorder is very low as there is evidence that in spite of multiple contacts with health providers women with postpartum depression often remain unrecognized and untreated. Serotonin has been implicated in the pathophysiology of depression and bipolar disorders (mania and depression occurring in the same patient at different times) (Quendo and Mann, 2000). Depletion of tryptophan lowers the mood of patients (Stewart, et al., 2002).

A proper understanding of biochemical basis of serotonin and related mood disorders occurring in procreation is likely to contribute towards better management and possibly effective prevention of these disorders. In Malaysia, to our knowledge no study has so far been conducted to detect blood tryptophan and serotonin levels in pregnancy and child birth-related depression and excessive happiness. Excessive happiness in the first week after childbirth is paradoxically a risk factor for subsequent depression in the same woman.

Again this relatively unknown but interesting and important risk factor has not so far been studied in Malaysia. The main purpose of the study was detection of women at risk for depression during pregnancy and after child birth by studying mood variations (excessive happiness and excessive sadness) and to explore the possibility of correlation between the serotonin and tryptophan blood levels and depression during pregnancy and both depression and excessive happiness after child birth.

Material and Methods

Study Protocol

This study was approved by the relevant ethical committee of IIUM Kulliyyah Ethics Committee. An informed consent was secured from all individuals to be included in this study. The sample size was computed to be about 300 women, (100 women from each three main ethnic groups). However we could only enlist 104 women in the stipulated time period of the study.

Use of Questionnaire

The study was conducted through a questionnaire and patients consent form, the patients were informed before collecting data and the consent forms were signed by the patients. The questionnaire was used for collecting the data consisted of various questions.

Ethnic Distribution of the Subjects

The ethnic distribution consisted of four groups i.e. Malay 78% (82), Chinese 17% (18), Indians 2.8% (3) and others 0.9% (1)

Assessment of Depression

Depression was assessed by observation at two stages, during 3rd trimester and during 2nd week after child birth until the end of postpartum period i.e. up to the 6th week after child birth. Excessive happiness was assessed in the
first week after delivery. Excessive sadness (clinical depression) was assessed by using the Malay translated and validated version of Edinburgh postnatal depression scale (Azidah, et. al., 2004). Excessive happiness was detected by employing Glover’s “High Scale” (Glover, 1994).

**Blood Samples for Measurement of Serotonin and Tryptophan**

Blood samples (10 mL) for measurement of serotonin and tryptophan were taken at the time of two psychological assessments (first blood sample after 12 hours of fasting during last trimester and second blood sample within 40 days after child birth). 10 mL of blood was collected into silicone glass tube containing 100 µL of 10% sodium EDTA and centrifuged at 3000 rpm for 15 minutes at room temperature. Without shaking the tube, approximately half of the volume of the intermediate part of the serum (avoiding the small platelets in the upper part) was transferred with a polyethylene pipette to a micro centrifuge tube and kept at -70 °C.

**HPLC Analysis**

For the determination of the serotonin and tryptophan, a validated reverse phase liquid chromatography (RP-HPLC) was used (Luis, et al., 2000). Preparation of the standards was made according to the procedure described by Chin (1992).

**Chemical and Reagents**

HPLC grade water was used. Acetonitrile was HPLC grade from Fisher. Unless and otherwise mentioned all reagents were of analytical grade. Phosphoric acid, citric acid, ascorbic acid and Di hydrogen sodium phosphate were from Merck. Perchloric acid was from Fisher. L Cysteine hydrochloride was of biomedical grade from BDH, UK. EDTA disodium salt analytical grade was from Merck. Serotonin and tryptophan were from Sigma Aldrich USA. All standards were prepared following the method described by Chin (1992). 0.1 mg/mL stock standard solutions were prepared for each standard.

**Chromatographic Conditions**

The aqueous and acetonitrile ratio was 97: 3 (v/v). The mixture was filtered through a 0.45 µm filter prior to the use. Agilent 1100 HPLC system was used for the study. Data acquisition was performed with the Agilent Chemstation processor. The analytical column employed was a Waters (Nova Pak) C18. Fluorescence detection wavelength was set at Excitation 270 nm and Emission 310 nm. Sample of 10µL was injected by the programme controlled auto injector. Chromatographic separation was performed at ambient temperature and flow rate was maintained at 1.0 mL/min.

**Results and Discussion**

The Fig.1 shows the mood fluctuation in women under study. The analysis of the questionnaire received from the subjects enlisted for this study indicated that 23.08% (24) women were clinically depressed during pregnancy, 22.61% (23) women were clinically depressed after childbirth. Of these, 23 women found depressed after childbirth, eight were already depressed prenatally. If excluded these 8 cases, then the postnatal depression was 14.4%. The women who experienced a brief period of “pathological” happiness (joy of motherhood) after childbirth were 29.76% (30).
The levels of serotonin and tryptophan were determined in two groups of subjects identified experiencing depression during pregnancy and after child birth. Chromatographic analysis was performed on 39 subjects, of which 24 had experienced prenatal depression and 15 had a postpartum depression. The mean result of the serotonin and tryptophan for these two groups of subjects are given in Table 1.

The incidence of depression after child birth in the subjects under study was 22.61% which is slightly higher than that of reported rates in Asian Chinese women (0-18%) (Dominic, et al., 2001). The current high rate of prenatal depression might be due to the screening of the subjects conducted by the ward staff nurses rather than properly trained medical graduates. Another less often reported finding in the current study was the depression during pregnancy slightly more common than the postpartum depression [Prenatal 23.08%; Postnatal 22.61% (14.4 after excluding women depressed at both stages prenatally and postnatally)].

Maternal depression during pregnancy can impact adversely on the intrauterine development of children. The same depression in pregnancy may continue after

Table 1. Serotonin and tryptophan levels in subjects experienced depression during pregnancy and postpartum period

<table>
<thead>
<tr>
<th>Endogenous substances</th>
<th>Blood levels (ng/mL in subjects with Depression as Mean ± SD, N= 24)</th>
<th>Postpartum Depression as Mean ± SD, N= 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td>12.7 (±2.5)</td>
<td>11.9 (±2.4)</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>7.4 (±1.8)</td>
<td>7.7 (±1.7)</td>
</tr>
</tbody>
</table>
Blood Level of Serotonin and Tryptophan, and Their Relationship with Mood……

child birth as postpartum depression in a significant number of cases. In our sample subjects, for example 8 women were prenatally depressed and perhaps their depression continued in postnatal period. With regular screening during pregnancy, these women could have detected early and their psychiatric morbidity could have been shortened with timely intervention.

Our sample subjects’ blood serotonin level (pre natal 12.7 ± 2.5; post natal 11.9 ± 2.4) are comparable with the findings of some recent studies such as (10.8) (Almedia-Montes, et al., 2000). We also observed that postpartum serotonin levels were slightly lower than that of prenatal levels in our study. Therefore, postpartum depression may be more severe with infanticide risk, hence warrants more intensive preventive and therapeutic intervention.

Conclusions

A systematic prospective study of blood levels of tryptophan and serotonin in general population and in would be mothers may provide us with an early and useful clue to future depressive illness in people at risk for depression. Timely institution of preventive measures may significantly reduce psychiatric suffering in the people at risk.

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