

Postpartum Mood Changes and Plasma Amino-Acids

Abou-Saleh M. T., Ghubash R., Karim L., Krymski M.. and Ibrahim A.

Abstract:

Plasma amino acids and cortisol were measured in groups of women during pregnancy and postpartum in comparison with normal women. Postpartum women were screened for psychiatric symptoms on the Self-Reporting Questionnaire (SRQ) on day 3 and for depressive symptoms on the Edinburgh Postpartum Depression Scale (EPDS) on day 7 after delivery. There were significant differences between the 3 groups in all measures including phenylalanine/tyrosine, L-tryptophan/ large neutral amino acids /LNAA and tyrosine/LNAA values. Moreover, postpartum women who were classified as cases on the SRQ and EPND had significantly lower levels on few of these measures and there were significant correlations between total SRQ and EPND scores and those measures.

Key words: Postpartum depression, pregnancy, amino acids, cortisol.

Introduction

Mood changes are common in the early postpartum period. At least one in two women experiences maternity blues and one in ten women suffer from depressive illness. We have recently reported the results of a prevalence study in a consecutive series of women from Dubai which showed 18% had depressive illness as determined by their scores on the Edinburgh Postnatal Depression Scale (EPDS) (Abou-Saleh & Ghubash, 1997). This rate is similar to the average prevalence rate of non-psychotic postpartum depression derived from the results of a large number of studies (O'Hara & Swain, 1996). This common occurrence cross-cultures, notwithstanding the contribution of psychosocial factors suggests a biological etiology for these mood changes. The study of these changes in the postpartum context offers a heuristic model for the study of pivotal biological factors in mood states (Campbell, 1992). Studies of plasma amino-acids in relation to postpartum mood changes have exclusively focussed on the investigation of plasma tryptophan as the precursor of brain

serotonin, which is implicated in the pathogenesis of depressive illness. Nott et al (1976) studied plasma tryptophan in postpartum women in relation to mood changes measured daily for the first day after delivery. They found an association between the severity of mood changes and low free tryptophan levels, a result, which was similar to results obtained in a group of depressed non-postpartum women. Handley et al (1977) studied mood changes in relation to free tryptophan levels found lower levels in women who suffered from maternity blues, but only during the season of the year when tryptophan is normally high. However, there was a slower rise of low tryptophan in postpartum which was associated with the occurrence of blues and at six months follow-up with depression (Baker et al, 1984). The same group in their replication study reported the finding that a slow rising total tryptophan predicted the occurrence of blues, particularly a low blood level at day one postpartum (Gard et al, 1986).

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Our study of the prevalence of postpartum psychiatric symptoms offered a context to examine the relationship between mood changes and plasma amino-acids. We hypothesized that depressive symptoms are associated with low plasma tryptophan, phenylalanine tyrosine ratios of tryptophan and tyrosine to competing large neutral amino-acids (LNAA).

Methods

The sample was a consecutive series of women admitted to the new Dubai Hospital in Dubai and the Al Ain Hospital in Al Ain, United Arab Emirates for childbirth. Two comparison groups were studied: pregnant women at the end of third trimester and a series of normal women. The pregnant group was studied when they attended the antenatal clinic at the end of the third trimester and the normal control group were employees of the hospital who were ascertained by interview to be free of psychiatric symptoms. The 2 Hospitals' Ethical Committees approved the study and all subjects participated voluntarily.

The psychological status of women was assessed using the Self-Reporting Questionnaire (SRQ) (Harding et al, 1980). The SRQ was administered by the clinician rather than self-completed since a proportion of women were illiterate. The interview was done on the second or third day from childbirth in view of the hospital policy to discharge these women within three days of childbirth. All women were seen again after seven days from childbirth for the second assessment when the EPDS was completed. The EPDS was also administered by the clinicians for the aforementioned reason. The SRQ and the EPDS have been translated into Arabic by a group of bi-lingual psychiatrists and back-translated to English by another group (El-

Rufaie & Absood, 1994; Ghubash et al, 1997). For the SRQ and the EPDS cut off scores of 5/6 and 11/12 were adopted to identify cases respectively. These cut off scores were determined by the aforementioned validation studies on the local populations.

Plasma Amino-Acids

Blood samples were extracted from postpartum women, the pregnant women, and the normal controls between 9 and 10 am. For postpartum women, this was done at day 7 when the EPDS was administered.

Amino acids were measured: phenylalanine, leucine, isoleucine, threonine, tryptophan, tyrosine and valine. The ratio of phenylalanine/tyrosine (P/T), L-tryptophan/large neutral amino-acids (LNAA) and tyrosine/LNAA were calculated. LNAA were phenylalanine, valine, leucine and isoleucine.

0.8 ml of venous blood was collected in a lithium heparinised bottle and centrifuged immediately for five minutes at 2000 rpm. The plasma was deproteinised by adding 20ul of 50% sulphosalicylic acid, and centrifuged at 10,000 rpm for 10 minutes at -4° C. The supernatant stored at -20°C until analysis. The supernatant was diluted 1:1 with Li-Beckman buffer and analysis was carried out for individual free amino acid according to Spackman et al., (Spackman et al, 1958) ion exchange chromatography techniques on Beckman 6300 automatic amino acid analyser by Beckman method: a three Li-buffer system used with a cation exchange resin column 10 x 0.4 (I.D) cms at around 1200 psi and at 20 ml/hr. buffer flow. The method is based on the post column derivatisation by ninhydrin coloring reagent at 135° C; derivatised amino acids were detected at

570 nm, while proline and hydroxyproline at 440 nm.

Statistical Methods

One-way ANOVA was carried out to compare the results of the plasma amino-acids and cortisol between the three groups of postpartum women, the pregnant group and the normal controls. Subjects who were cases and non-cases on the SRQ and the EPDS were compared using student t- tests and Pearson product-moment correlations were calculated between the total SRQ, EPDS scores and plasma amino-acid. Significant differences were considered at the 5% level. Using SPSS for Windows carried out all statistical analyses.

Results

Comparisons between the three groups showed significant differences between groups in the levels of amino-acids (Table 1). The pregnant group invariably had lower plasma levels of plasma amino acids than the normal control group. The postpartum group had significantly greater levels of phenylalanine/tyrosine ratio than normal controls but had significantly lower levels of tryptophan/LNAA and than normal controls. Comparisons in plasma amino acids between postpartum women who were SRQ cases (20%) and non cases (80%) with cases having significantly lower levels of phenylalanine, tyrosine and tryptophan than non cases. Comparisons between postpartum women who were classified cases (8%) and non-cases (92%) on the EPND revealed no significant differences. There were significant

correlation's between the total EPND score and levels of tryptophan, phenylalanine/tyrosine(P/T) ratio and tyrosine/LNAA ratio, correlations which were all negative except for the P/T which was a positive correlation. There were significant negative correlation's between total SRQ score and phenylalanine, tryptophan, tyrosine, and tyrosine/LNAA ratio except for phenylalanine/tyrosine ratio which was a significant positive correlation. There were no significant correlations between age and the levels of amino acids. However, there was a significant negative correlation between age and cortisol levels ($p < 0.001$). Comparisons between the three groups of plasma cortisol concentrations showed that both the pregnant and postpartum groups had significantly higher concentrations of cortisol than normal controls. There were no differences between women who were SRQ and EPND cases and non cases in their plasma cortisol concentrations. In the postpartum group, there were significant correlations between plasma cortisol and levels of phenylalanine/tyrosine ratio (+) and tyrosine/LNAA ratio (-) and all other correlations were not statistically significant. Within the pregnant group, there were no significant correlations between cortisol and the levels of plasma amino-acids.

In the 3 groups combined there were significant negative correlations between cortisol and phenylalanine, tryptophan, tyrosine, tyrosine/LNAA except with P/T which was a positive correlation.

Table 1:

Comparisons Between Groups Of Postpartum, Pregnant And Normal Controls
(ANOVA: Results Expressed As Mean $\pm$ SD) Groups

	Normal Control	Postpartum	Pregnant
	N=38	N=70	N=23
Age (yrs)	36.2 $\pm$ 9.0	30.8 $\pm$ 6.2	27.8 $\pm$ 6.8
Phenylalanine(bc)	68.73 $\pm$ 16.37	65.18 $\pm$ 16.17	0.81 $\pm$ 8.40
Tryptophan (abc)	48.38 $\pm$ 10.78	40.77 $\pm$ 12.48	25.20 $\pm$ 4.15
Tyrosine (bc)	82.37 $\pm$ 25.72	72.28 $\pm$ 29.89	29.64 $\pm$ 5.94
Cortisol** (abc)	11.79 $\pm$ 6.02	23.96 $\pm$ 8.26	36.56 $\pm$ 8.73
Phe/Tyr (bc)	0.87 $\pm$ 0.19	0.99 $\pm$ 0.32	1.17 $\pm$ 0.39
Trp/LNAA ©	0.11 $\pm$ 0.02	0.09 $\pm$ 0.02	0.12 $\pm$ 0.03
Tyr/LNAA (bc)	0.15 $\pm$ 0.03	0.15 $\pm$ 0.03	0.13 $\pm$ 0.03

a significant difference between normal controls and postpartum group

b significant difference between normal controls and pregnant group

c significant difference between postpartum and pregnant group

* All amino acids concentrations in mm/L

** Cortisol concentration in mg/dl

Phe/Tyr : Phenylalanine/Tyrosine ratio

Trp/LNAA : L-Tryptophan/Large Neutral Amino Acids ratio

Tyr/LNAA : Tyrosine/ Large Neutral Amino Acids ratio

Discussion

This study shows a number of interesting relationships between postpartum mood changes and plasma tryptophan, phenylalanine and tyrosine. There was an association between the occurrence of postpartum psychiatric symptoms and low plasma levels of tryptophan, phenylalanine and tyrosine in days 2-3 postpartum, i.e. the occurrence of maternity blues, but there was no similar association between these amino acids and depressive symptoms assessed on day seven postpartum on the EPND when amino acid levels were measured. Numerous significant negative correlations were obtained between quantitative measures of psychiatric morbidity (total SRQ and EPND scores) and these amino-acids including L-tryptophan/LNAA and tyrosine/LNAA.

The correlations between P/T and total SRQ and EPND were positive which is consistent with lower biosynthesis of catecholamines. We have previously introduced the P/T index as a measure of phenylalanine to tyrosine hydroxylation which was shown to be increased in depression and is lowered on recovery (Anderson et al, 1994).

These results confirm the findings of previous investigations in relation to plasma tryptophan levels (Handley et al, 1977; Handley et al, 1980; Baker et al, 1984; Gard et al, 1986). In relation to cortisol concentrations, postpartum women had significantly higher levels than normal controls but there were no significant associations with psychiatric symptoms

including depressive symptoms. However, there was an association between high cortisol levels in the postpartum group and lower values of P/T and tyrosine/LNAA ratios. A recent study reported comparisons between the availability of L-tryptophan, tyrosine and cortisol levels in the early puerperium between postpartum women, women taking oral contraceptives and normal controls (Maes et al, 1992). Plasma cortisol and tyrosine were significantly higher and lower respectively in postpartum women and in women under contraceptive therapy as opposed to normal controls. L-tryptophan was significantly lower in postpartum females while the L-tryptophan/LNAA ratio did not differ between the 3 groups. Postpartum females revealed a significant negative relationship between L-tryptophan and postpartum mood as measured by the Zung Depression and Anxiety Scale and State Anxiety Inventory.

The association between plasma cortisol and L-tryptophan is probably mediated by the induction of cortisol of liver tryptophan pyrrolase causing increased peripheral metabolism.

Okano and Nomura (1992) reported an association between maternity blues and high serum cortisol. Taylor et al (1994) have shown that postpartum women tend to have higher cortisol levels than normal controls but postpartum women with 'highs' of mood, however, had lower cortisol levels than normal controls. Pedersen et al (1993) reported increased plasma cortisol levels in women with postpartum 'blues' and in those who had a previous history of depression. Harris et al (1994), found no association between maternity blues and salivary cortisol concentrations.

In conclusion, our findings support the contribution of pivotal amino acids and their vital ratios to the occurrence of postpartum psychiatric symptoms.

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Address of Correspondence

Abou Saleh M.T.

Prof. & Chairman of Depart. of Psychiatry
& Behavioural Sciences
Faculty of Medicine and Health Sciences
U.A.E. University

التغيرات المزاجية بعد الولادة و علاقتها بالاحماض الامينية في الدم

تم قياس الاحماض الامينية في السائل الدموي و الكورتيزول في مجموعة من النساء في فترة الحمل و فترة ما بعد الولادة مقارنة بنساء غير حوامل. تم البحث عن امراض نفسية في النساء في فترة ما بعد الولادة عن طريق اسئلة ذاتية الاجابة و التقييم. و ايضا تم البحث عن مرض الاكتئاب مستخدمين في ذلك مقياس ادنبرة في فترة ما بعد الولادة. كان هناك فرق واضح ما بين المجاميع في نسبة فتايل اليد- تيرقرين- تريبتوفان و الاحماض الامينية الطبيعية ذات الجزيئات الكبيرة. ايضا النساء في مرحلة ما بعد الولادة الذين ثبت انهم يعانون من اضطرابات نفسية و اكتئاب قد اظهروا نقص واضح في هذه النسب.