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Abnormal Menstrual Cycle in Second Year Medical Students at Siriraj Hospital

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ABSTRACT

Objective To determine the effect of psychological stress on the menstrual cycle in second year medical students.

Design Before and after study.

Setting Department of Physiology, Faculty of Medicine Siriraj Hospital.

Subjects Forty-nine volunteers (18 - 21 years old) from second year medical students were studied. Two blood samples were collected from each student, one during the assumed non-stressed (ANS) period and the other during the assumed stressed (AS) period.

Main outcome measures Characteristic of menstrual cycle was recorded. Serum cortisol, prolactin, gonadotropins and progesterone were measured using radioimmunoassay.

Results Abnormal cycles were found in 2 characteristics : (1) irregular cycle comprised 22% of all subjects ; (2) low serum progesterone in the assumed luteal phase, implying anovulation or luteal defect, comprised 62% and 70% of subjects during the ANS and the AS periods respectively. There was no significant difference in the incidence of abnormal cycle between the two periods. No correlation between serum levels of progesterone and cortisol, prolactin or LH : FSH ratio could be demonstrated.

Conclusion Over 60% of second year medical students at Siriraj Hospital had abnormal menstrual cycles. We could not demonstrate the correlation between this high incidence and the level of stress hormone, i.e. cortisol.

Key words : abnormal menstrual cycle, medical students, psychological stress

Medical school is a stressful environment in which various stressors have been identified.[1] Female medical students are reported to have higher level of stress than male colleagues.[2] Mental stress, which can affect academic performance and health of medical students,[2] produces numerous alterations in psychoneuroendocrine responses which consequently affect reproductive function.[3] Abnormal female reproductive function is usually expressed as an abnormal menstrual cycle, for example abnormal luteal phase, anovulation (with or without cycle irregularity) or amenorrhoea.[4]

Due to the curriculum of the Faculty of Medicine Siriraj Hospital, during the second year which is the first of two preclinical years, medical students have to attend three major subjects, i.e. Anatomy, Physiology and Biochemistry, and also other minor subjects. Since these subjects are entirely different from those of first premedical year, the students have to adjust themselves so much, hence, induce them some level of stress.

This study aims to determine : (1) the incidence of abnormal menstrual cycle in second year medical students whom are assumed to have high level of stress and (2) the correlation between serum levels of progesterone in the assumed luteal phase and some other hormones that are affected by stress and have putative effects on reproductive functions.

Materials and Methods

Subjects were second year medical students attending Physiology class at the Faculty of Medicine Siriraj Hospital, Mahidol University.

Forty-nine female volunteers, aged 18 - 21 years, were asked to answer the questionnaire enquiring about their health status and menstrual history. All subjects were healthy and within an acceptable range of body mass index (16.03 - 25.80 kg/m^2).

Two blood samples were collected from each volunteer. The first sample was taken during the assumed non-stress (ANS) period at the beginning of the second semester when they commenced their Physiology class. The second sample was taken during the assumed stress (AS) period within a few days before the Physiology examination.

Ten millilitres of blood were drawn between 8.00-9.00 a.m. from each subject and collected in a non-heparinized glass tube. Serum was separated and frozen at -20 °C until hormonal assay was performed. Serum cortisol, prolactin, progesterone and gonadotropins, i.e. luteinizing hormone and follicle stimulating hormone (LH and FSH) were measured using radioimmunoassay techniques (WHO protocol).[5]

Day of menstrual period, especially the assumed luteal phase, was estimated from last menstrual period (LMP) on 2 assumptions. One is that a woman who has a cyclic, spontaneous and predictable menstruation is strong evidence for recurrent ovulation[4] and the other is that adequate luteal phase lasts at least 11 days (range 11 - 17 days).[6]

Abnormal menstrual cycle was defined as an irregular cycle or a regular cycle with low serum progesterone in the assumed luteal phase (less than 9.8 nmol/L) within the day between 4 and 11 days before menstruation.[7-9]

The results were tabulated as mean ± SD and percent. Paired t-test and Chi-square test were used to compare values in the ANS with those in the AS period. Linear regression analysis was used to determine the correlation between serum progesterone and other hormones. Statistical significance was accepted at P value of less than 0.05.

Results

From 49 subjects, 11 students (22%) had an irregular menstrual cycle while another 38 students had a regular cycle of every 28.32 ± 3.25 days (range 21 - 35 days).

Among 38 students who reported a regular cycle, 21 students in the ANS and 10 students in the AS period were expected to be in the luteal phase : 62% of the former and 70% of the latter had serum progesterone levels in the assumed luteal phase less than 9.8 nmol/L (Table 1). No significant difference in the incidence of students having low luteal progesterone levels between the ANS and the AS periods was found (P = 0.725).

There was no significant difference between serum cortisol levels during the ANS period (788 ± 216 nmol/L) and the AS period (800 ± 228 nmol/L) (P = 0.240) The data on hormone profile in both periods were grouped together when linear regression between serum progesterone and other hormones were analysed. No correlation between serum levels of progesterone and cortisol, prolactin or LH:FSH ratio could be demonstrated (Fig. 1).

Discussion

There are several methods for evaluation of female reproductive functions. In this study, serum

Table 1. Serum progesterone in the assumed luteal phase of the students during the assumed non-stressed (ANS) and the assumed stressed (AS) periods

Serum progesterone (nmol/L)		Number of students (%)	
		ANS	AS
low	(< 9.8)	13 (62)	7 (70)
normal	(≥ 9.8)	8 (38)	3 (30)
total		21 (100)	10 (100)

p = 0.725 (Chi-square test)

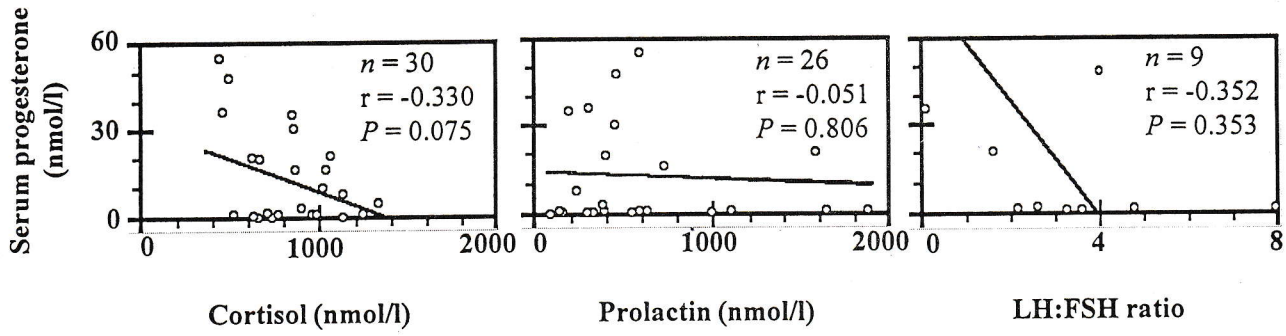

Fig. 1. Correlation between serum progesterone in the assumed luteal phase and cortisol, prolactin and LH : FSH ratio.

progesterone in the assumed luteal phase was used because it is difficult to interpret other parameters or hormones in a cross-sectional study like this.

In this study, 22% of subjects had an irregular menstrual cycle which implied abnormality in reproductive function.[4] Furthermore, over 60% of students who reported previously regular cycles had abnormal low serum progesterone in the assumed luteal phase and therefore should be considered as having abnormal cycles, either anovulation or luteal defect. There were evidences that cyclic bleeding found in an anovulatory cycle was clinically indistinguishable from normal ovulatory menstruation[10] but this proposition is still debated.[4]

The incidence of luteal defect and/or anovulation in the general population varies with the groups studied and the diagnostic measures.[10-12] Our results indicated that this incidence in second year medical students was high. An abnormal cycle in these girls may be associated with chronic stress that concurrently induced persistently high serum cortisol. The instability of the hypothalamic-pituitary-gonadal axis, the function of which still does not reach maximum in this late adolescent age group,[11] was another possibility. However, a girl at this age should have ovulatory cycle in 60-80% of menstrual cycles.[13]

Stress produces considerable alteration in psychoneuroendocrine responses which in turn affect reproductive function.[3,14] The increased corticotropin-releasing hormone (CRH) associated with increased activity of central opioid peptide and serotoninergic pathway can interrupt reproductive function[15] via disturbance of gonadotropin releasing hormone (GnRH) pulsation[14,16] which in turn affects LH secretion. In addition, concurrently elevated CRH and opioid peptide cause changes in both cortisol and prolactin levels which also affect reproductive function. Other than these hormones and peptides, central neuroregulation of the secretion of multiple pituitary hormones, for example thyroid stimulating hormone, are also disturbed.[17] They also have effects on reproductive function.

In the present study, there was a tendency to have lower serum progesterone levels with higher serum cortisol levels. However, no significant correlation between serum progesterone levels and cortisol or prolactin levels was observed.

The LH : FSH ratio is considered abnormal if it is higher than 3 except at the time of ovulation. An abnormal LH:FSH ratio is usually found in the condition with chronic anovulation.[6] Nevertheless, this study could not confirm any correlation between low serum progesterone and a high LH : FSH ratio.

From this study the correlation between an abnormal menstrual cycle and psychological stress could not be proven since the incidence of students showing abnormal menstrual cycle during the ANS and the AS periods were not significantly different. This may be because of equality in the levels of stress between these two periods, as indicated by comparable serum cortisol levels in both periods.[18] High cortisol levels in the ANS period may arise from stressors other than examination. Persistently high cortisol level in the AS period may refer to an inability of subjects to cope with stress[19,20] or their inability to increase cortisol level in response to additional stress.

In conclusion, this result suggested a high incidence of abnormal menstrual cycles in second year medical students at Siriraj Hospital. Although no correlation between low serum progesterone and other hormones responding to stress could be demonstrated, we were unable to discount the

possibility that anovulatory cycle in these students may be associated with high cortisol, prolactin or abnormal LH : FSH secretion. Since second year medical students at Siriraj Hospital seemed to fall under a prolonged or chronic stress (as suggested by persistently high cortisol level), other groups of students who have fluctuated level of stress might be a better subject to study.

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