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Evaluation of Some Prominent Biochemical Agents in Menstrual Phases of Women

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Abstract: *Menstrual cycle is the key to open the shutdowned monthly reproductive cycles in a woman's reproductive age. Of course, it is multifactorial in nature, while the reproductive hormones are found as the prime agents in menstrual cycle events. The functional role of sex hormones and some other biochemical substances are noticed as phase specific in these monthly cycles. The fluctuation of these biochemical agents are found to be associated with crucial roles in menstrual cycles of women.*
Keywords: *estradiol, follicle stimulating hormone, luteinizing hormone, progesterone, prolactin, serotonin.*

I. Introduction

Menstruation is an integral part of the female reproductive period, an indication of fertility which is geared up when a girl reaches sexual maturity during puberty. This integral prime biological signal in the reproductive period serves as a biomarker that a woman has not become pregnant. Endocrine, ovarian and endometrial co-ordination favours a successful normal menstrual cycle.

This monthly mega event in the reproductive age of women is associated with a complex interplay of hormones (1). The endocrine system controlled menstrual cycle consists of three phases (viz.) follicular phase, ovulatory phase and luteal phase (2).

The menstrual phase specific occurrence of estrogen (3), FSH (4), LH (5), progesterone (4), testosterone (6), prolactin (7), TSH (8) lead (9) and serotonin (10) are reported in the earlier studies. However, large scale studies on the phase specific prevalence of sex hormones on human menstrual cycle is very scarce. Some prominent biomarkers assay in menstruating women reveals their phase specific roles in reproductively active women.

The present study aims at 1) to recognize the menstrual phase specific occurrence of some of the vital reproductive hormones and 2) to confirm whether menstrual cycle act as a pavement to the exit of poisonous substances like lead in menstruating women.

II. Materials and methods

Study area and subjects

The study has been carried out in Nagercoil, the district headquarters of Kanyakumari the Southernmost part of the Indian sub-continent (11). The study subjects are 17-22yr old college girls with different socio-economic backgrounds. Informed consent is obtained from the study groups before the collection of blood samples. Priority has been given to human values during the course of the study and Ethics Committee's recommendations are strictly followed.

Blood samples are collected from the respondents on the 2^{nd}, 7^{th}, 14^{th}, and 25^{th}, days of the menstrual cycle. A total of 96 subjects (36 preteen and 60 teen menarche respondents with normal menstrual cycles) are used for the present study and 10 ml venous blood is collected from each girl by a well trained lab technician, and serum samples are separated and used for various biochemical studies.

Standard methods are used for the estimation of serum LH (12), FSH (13), testosterone (13), progesterone (14), prolactin (13), estradiol (15), TSH (16), lead (17) and serotonin (18). Statistical analysis are made with SPSS statistical package (version 11) (19).

III. Results

The reproductive hormones in serum such as LH, FSH, testosterone, progesterone, prolactin and estradiol are shown in table.1. A narrow level of decrease of LH is seen in the luteal phase, while it is high in the preovulatory and very high in the ovulatory phase when compared with the menstrual phase. The decrease is 8.1% in preteens and 17.4% in teens in the luteal phase, while an increase of 217.6% in the preteens and 222.9% in teensin the preovulatory phase, but an increase of 2325% in the preteens' and 2178% in the teens' ovulatory phase.

An enhanced level of serum FSH is observed in preovulatory, ovulatory and luteal phases of the study subjects. The increase is 1.97mlu/ml in preovulatory, 19.27mlu/ml in ovulatory and 4.21mlu/ml in the luteal

phase of the preteen menarche girls and 2mlu/ml in preovulatory, 18.92mlu/ml in ovulatory and 3.17mlu/ml in luteal phase of the teens with respect to their menstrual phase.

Table.1. reveals the reproductive hormones in serum of the selected pre-teen and teen menarche subjects.

(n = 96 subjects; pre - teen: 9 subjects in each phase; teen : 15 subjects in each phase)
(Values are ± SD)

Hormones/ period (Yrs)	Menstrual cycle phases (days)			
	a. Menstrual (2^{nd})	b. Preovulatory (7^{th})	c. Ovulatory (14^{th})	d. Luteal (25^{th})
1. LH				
a. Pre - teen (10 - 12)	2.73±0.37	8.67±0.6	66.2±2.31	2.51±0.52^{NS}
b. Teen (13 -17)	2.93±0.34	9.46±1.19	66.76±1.39	2.42±0.42
2. FSH				
a. Pre - teen	2.17±0.21	4.14±0.33	21.44±0.73	6.38±0.38
b. Teen	2.41±0.35	4.41±0.32	21.33±0.9	6.12±0.45
3. Testosterone				
a. Pre - teen	0.33±0.03	0.91±0.01	0.4±0.01	0.22±0.02
b. Teen	0.32±0.02	0.91±0.01	0.41±0.01	0.22±0.02
4. Progesterone				
a. Pre - teen	0.64±0.05	1.2±0.07	21.33±0.87	0.54±0.05
b. Teen	0.64±0.04	1.25±0.09	21.47±0.64	0.54±0.05
5. Prolactin				
a. Pre-teen	4.08±0.11	5.04±0.09	8.4±0.14	7.09±0.11
b. Teen	4.07±0.08	5.05±0.11	8.38±0.17	7.15±0.09
6. Estradiol				
a. Pre - teen	22.09±1.98	116.67±11.01	330.53±20.24	59.24±7.04^{NS}
b. Teen	25.47±1.62	116.01±4.75	341.44±13.63	62.18±6.39^{NS}
7. TSH				
a. Pre - teen	4.74±0.07	ND	5.47±0.11	1.26±0.05
b. Teen	4.75±0.07	ND	5.52±0.12	1.26±0.05

(ND – done)
t values: a Vs b; a Vs c; a Vs d (p<0.05 highly significant; p>0.05 not significant $^{(NS)}$)

Table.2. explains some important serum biomarkers in the selected pre-teen and teen menarche subjects.

(n = 96 subjects; pre – teen : 9 subjects in each phase; teen: 15 subjects in each phase)

(Values are ± SD)

Biomarker / period (Yrs)	Menstrual cycle phases (days)			
	a. Menstrual (2^{nd})	b. Preovulatory (7^{th})	c. Ovulatory (14^{th})	d. Luteal (25^{th})
1. Lead				
a. Pre - teen (10 - 12)	6.16±0.1	7.17±0.09	8.18±0.1	8.89±0.05
b. Teen (13 - 17)	6.37±0.06	7.78±0.11	8.28±0.06	9.03±0.16
2. Serotonin				
a. Pre - teen	99.89±3.52	178.89±2.76	274.89±7.1	106.44±3.71
b. Teen	104.93±3.17	181.87±3.07	274.8±6.18	106.4±3.48^{NS}

t values: a Vs b; a Vs c ; a Vs d
P < 0.05 highly significant; P>0.05 Not Significant $^{(NS)}$

An initial level of increase, followed by an abrupt level of increase and a remarkable level of decrease of serum progesterone is noticed in the preovulatory, ovulatory and luteal phase of our respondents when compared to their respective menstrual phase. In preteen menarche subjects it is 0.56ng/ml, 20.69ng/ml and 0.10ng/ml in preovulatory, ovulatory and luteal phase respectively. Similar trend is also noticed in the serum testosterone levels of the subjects. There is a decrease of 33% in luteal phase of the preteens, while it is 31% in teen menarche subjects. In preteens the increase is 176% in the preovulatory phase and 21% in ovulatory phase, but in teens,it is 28% in ovulatory phase and 184% in the preovulatory phase compared to their respective menstrual phase.

An enhanced level of serum prolactin is seen in the preovulatory, ovulatory and luteal phase of preteen and teen menarche cases when compared to their respective menstrual phase. In preteens the increase is 0.96ng/ml in preovulatory, 4.32 ng/ml in ovulatory and 3.08ng/ml in luteal phase with respect to their menstrual phase. But, it is 0.98ng/ml in preovulatory, 4.31 ng/ml in ovulatory and 3.08ng/ml in luteal phase of teens with respect to their menstrual phase.

Elevated level of serum estradiol is found in thepreovulatory, ovulatory and luteal phase of the subjects when compared to their respective menstrual phase. In preteen menarche girls it is 94.58pg/ml, 308.44 pg/ml and 37.15 pg/ml in preovulatory, ovulatory, luteal phase respectively. Likely in teens it is 90.54 pg/ml in preovulatory, 341.44 pg/ml in ovulatory and 36.71 pg/ml in luteal phase. It is quite obvious from the table that an increased level of serum TSH is observed in the ovulatory phase (0.73µlu/ml), while it is decreased (3.48µlu/ml) in the luteal phase of preteen menarche subjects with respect to their menstrual phase. Similar results have been noticed in teen menarche individuals also. An increase of 0.77µlu/ml in ovulatory phase and a decrease of 3.49µlu/ml are detected in luteal phase with respect to their menstrual phase.

A noticeable level of increase of serum lead is found in the preovulatory (16.4%) , ovulatory (32.8%) and luteal phase (44.32%) of preteen menarche subjects than their respective menstrual phase.Likely in teen menarche girls it is 22.14% in preovulatory, 30% in ovulatory and 41.76% in luteal phase with respect to their menstrual phase. In teen menarche girls the serum serotonin level in preovulatory, ovulatory and luteal phase is 73%, 162%, 1.4% respectively when compared with their respective menstrual phase. In preteen menarche subjects there is an increase of 79% in preovulatory, 175% in ovulatory and 6.6% in luteal phase with respect to their menstrual phase (table.2.)

IV. Discussion

Menstruation is an integral, prime biological signal noticed as a biomarker event to confirm gestation in a woman's fertile age. It is the opening ceremony of the reproductive age and an eye opener discerning the reproductive health of women. This cycle event decides the continuation of generations in menstrual animals. The integration of hormonal, neural and endometrial factors designs the factors, fate and type of menstrual cycles.

A normal, natural and monthly menstrual cycle is only possible by the successive positive and negative co-ordination existing between the reproductive hormones. In most women the luteinizing hormone (LH) pulse amplitude begins to increase after ovulation takes place (20) and reaches its peak during ovulation (21). Our study corroborates a previous findings, which states that LH is low during the early follicular phase and begins to rise by the mid-follicular phase due to the positive feedback from the rising estrogen levels (22).

It is evident from a study that an increase of follicle stimulating hormone (FSH) is noticed during the last few days of the menstrual cycle (23). Reports say FSH levels begin to decline after menses due to the negative feedback of estrogen (23, 24-26). Our study too supports this view.

During the first 14 days of the (follicular phase) menstrual cycle estrogen is high and progesterone is low (27) and a decrease of estradiol and progesterone is noticed in the late luteal phase (28). The same trend was noticed in our study subjects also.

Blood prolactin level is related to the physiological phase of the cycle and to the age of the subjects (7). Our study supports an earlier study, which states that a broad mid-cycle peak of prolactin and serum luteal phase values are higher than the follicular phase values (29). An earlier report says thyroid stimulating hormone (TSH) was found to be unchanged throughout the normal menstrual cycles (30), but a peak level of TSH is measured in the ovulatory phase of our study subjects.

Estrogen and serotonin are the two critical vital substances to sustain mental health in women. One report says the feelings of well being and happiness is decided by serotonin (10). A significant level of increase of serotonin is noticed in preovulatory, ovulatory and luteal phases compared to the menstrual phase of our subjects.

Lead produces various health hazards including reproductive problems in women. Reports say blood lead levels may increase as estrogen levels decrease and more amount of lead is eliminated during menses (9, 10). Our study fully supports this view.

V. Conclusion

The menstrual phase specific increase or decrease of reproductive hormones such as estrogen, progesterone, testosterone, LH and FSH are imminent for the normal menstrual cycle. The present study also confirmed the positive and negative feedback control of these master controllers in menstrual cycle. In addition to the elimination of mucous, shrouded epithelium, impure blood and unfertilized ovum, it also eliminates lead with menses and protect the menstruating women from lead related hazards.

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