HAEMATOLOGICAL AND ELECTROCARDIOGRAPHIC VARIATIONS DURING MENSTRUAL CYCLE

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Background: Menstruation coupled periodic bleeding from the blood vessels, at the time of shedding of the uterine mucosa has directed interest, more especially in the haematological changes during different phases of menstrual cycle. **Methods:** The present study was carried out on 30 healthy female medical students in the age group of 18 to 23 years with the normal menstrual cycle of 30 ± 3 days. The various haematological parameter and electrocardiography were studied on the 2nd, 11th, 14th and 22nd day of menstrual cycle. **Result:** The study reveals that the total leukocyte count and total platelet count significantly increased (p<0.001) around mid-cycle, however total eosinophil count significantly decreased (p<0.05) during the same period. Differential leukocyte count, bleeding time, clotting time, heart rate, P-R interval and Q-T interval did not show any significant change during different phases of menstrual cycle, although some mild changes were observed. **Conclusion:** This study was a moderate attempt to determine regular variation in the different haematological parameters and ECG during the different phases of menstrual cycle in normal healthy females and evaluate conflicting reports on the subjects.

Keywords: Menstrual cycle, electrocardiography

INTRODUCTION

Menstruation is a phenomenon which has appeared very late in evolution and is confined to us and our closest cousins, the primates like monkey and apes. In contrast females of subhuman species show oestrous cycle in which sexual activities occur cyclically at a particular time of a year.

The menstrual cycle is a repetitive phenomenon occurring during the reproductive life of a female that involves a patterned sequence of structural, functional and hormonal changes in the reproductive system. The only visible external sign is periodic discharge of blood along with degenerated uterine endometrium from vagina. The vaginal bleeding, which occurs for 3–5 days every month is rightly called menstruation (menstrualis, monthly) because, strangely enough, it's periodicity of 30±3 days almost coincides with that of our calendar month. Start of this cyclical phenomenon's marks the beginning of active reproductive life in a female. This is linked and controlled by cyclical fluctuations in the levels of FSH, LH of pituitary and sex hormones oestrogen and progesterone.

Hardly any organ in the body remains unaffected by these large hormonal fluctuations. It is also now recognized that important systemic as well as haematological changes are accompanying the various phases of menstrual cycle. Repeated cyclical haemorrhages and variations in the oestrogen and progesterone level in the blood during menstrual cycle could affect the blood volume, cardiac activity and may also affect electrocardiographic pattern.

MATERIAL AND METHODS

The present study was carried out on 30 healthy female medical students in the age group of 18–23 years with the normal menstrual cycle of 30±3 days. Cases of irregular periods, chronic disease and with history of drug affecting the menstrual cycle were not included.

The purpose and methodology of the study were fully explained to all of them for their full cooperation and their relaxed mental condition was pre-requisite for appropriate results. The different parameters were done under the following phases of menstrual cycle:

(a) Menstrual phase (2nd day)
(b) Proliferative phase (9 days after 1st sample)
(c) Mid-cycle (14th day)
(d) Secretory phase (8 days after 3rd sample)

Blood samples were drawn from anticubital vein (3.5 ml) in a wax coated or plastic vial containing EDTA as anticoagulant. In order to avoid diurnal variation blood was collected in the morning time at 8:00 AM Counting of Total leukocyte count (Turk's fluid), Total platelet count (1% ammonium oxalate) and Absolute Eosinophil count (Pilot's fluid) was done by haemocytometer, bleeding time by Duke's method, clotting time by capillary glass tube method, and differential leukocyte count by tally-bar method.

The ECG was recorded by using an electrocardiograph machine. The subjects were asked to lie comfortably in supine position over a table. The 4 limb leads were attached to the respective limb of the subject. The ECG was recorded generally in Lead II for the sake of simplicity. Heart rate, P-R interval and Q-T interval could also be determined from the ECG. For

Statistical analysis Student's *t*-test was applied to determine the significance of values.

RESULTS

Table-1 shows total leukocyte count (TLC) of the 30 healthy female medical students in the age group of 18 to 23 years during different phases of menstrual cycle. TLC shows a significant (p<0.001) rise from menstrual phase to proliferative phase and a maximum level occurring around mid-cycle. Thereafter it significantly declined (p<0.001) during secretory phase.

Table-1 also shows Total eosinophil count that did not show significant variation during proliferative phase and secretory phase, although it shows a significant (p<0.05) fall around mid-cycle.

In addition table-1 shows significant rise (p<0.01) of total platelet count during proliferative phase. Thereafter, it reached to a peak during mid-cycle, which is highly significant (p<0.001) and slight fall in the count were observed during secretory phase.

Table-2 shows the Differential leukocyte count reveals that all types of leukocyte show hardly any variation during the different phases of menstrual cycle, except in case of eosinophil, which show a significant (p<0.01) decreased around mid-cycle.

Bleeding time and Clotting time did not show any significant change during different phases of menstrual cycle. Bleeding time and clotting time were least around mid-cycle, and thereafter they increased during secretory phase.

Heart rate did not show consistent pattern during different phases of menstrual cycle. Electrocardiogram shows no change in P-R interval, however maximum Q-T interval was found to be during proliferative phase whereas Q-T interval was shorter in the secretory phase.

DISCUSSION

The human menstrual cycle involves a complex and regular change in female anatomy and physiology over an approximate monthly time period. The menstrual cycle, that is the interval between the onsets of two successive menstruations, is under the control of hypothalamic-pituitary-ovarian (HPO) axis. The endometrium is stimulated and regulated by ovarian steroid hormones, oestrogen and progesterone, which in turn is controlled by an integrated HPO axis through release of FSH and LH. The ovary plays a pivotal role in the menstrual cycle. It combines the gametogenic and steroidogenic functions in a unique manner (Longman).

Several studies[1,2] are in general agreement with the fact that the leukocyte count increased during the mid cycle and decrease during secretory phase. Although some are[3,4] exhibit a mild increase in total leukocyte count around mid cycle, yet no significant changes were observed.

Many opinions regarding the cause of fluctuation in leukocyte levels during the menstrual cycle have been presented. The changes in the circulating leukocyte count during the menstrual cycle is associated with the presumptive changes in blood oestrogen and the possibility that they are influenced by blood gonadotrophic hormone at the time of ovulation, or by blood progesterone or body temperature during the latter half of the cycle, cannot be excluded. These observations are in contrary to some studies[5,6] in which they did not find any change in the number of circulating leucocytes in relation to the menstrual cycle. According to them menstrual blood loss does not affect the complete blood count.

Numerous studies have been undertaken to examine the effects of different phases of the menstrual cycle on differential leukocyte counts but results have often been inconclusive and contradictory.[5,6] But in the present study differential leukocyte count reveals that all types of leukocyte show hardly any variation during the different phases of menstrual cycle, except in case of eosinophil, which shows a significant decrease around mid-cycle. Similarly basophil show decreased count around mid-cycle and secretory phase versus the menstrual phase. These midcycle and premenstrual falls are probably due to migration of the cells from the peripheral blood into the rupturing follicle of the ovary and into the ischemic premenstrual endometrium.[7]

Table-1: Total leucocyte count during different phases of menstrual cycle

Parameter	Menstrual Phase (2nd day)	Proliferative Phase (11th day)	Mid-cycle (14th day)	Secretory Phase (22nd day)
Total Leucocyte Count/mm^3	5953.33±1.35	6005±1.13	6675±1.11***	5740±1***
Total Eosinophil Count/mm^3	159.17±61.75	157.5±53.39	123.33±62.60*	150±80.14
Total Platelet Count (lac/mm^3	2.31±0.63	2.75±0.78**	3.09±0.64***	2.35±0.49

*** p<0.001, ** p<0.01

Table-2: Differential leucocyte count during different phases of menstrual cycle

Parameters	Menstrual Phase (2nd day)	Proliferative Phase (11th day)	Mid-cycle (14th day)	Secretory Phase (22nd day)
Neutrophils(%)	58.63±8.39	56.07±7.62	59.17±6.7	57.57±8.31
Lymphocytes (%)	33.7±7.81	36.07±7.78	33.97±6.6	35.6±7.77
Monocytes (%)	4.73±1.46	4.83±1.62	5.2±1.12	4.3±1.31
Eosinophils (%)	2.63±1.06	2.53±0.97	1.93±0.98**	2.43±1.43
Basophils (%)	0.3±0.46	0.37±0.55	0.17±0.37	0.17±0.37

The eosinophil count significantly (p<0.05) drops at mid-cycle and then its level increases during secretory phase are in agreement with the observations made by several authors.[8] According to them eosinopenia during mid-cycle (14th day) is a result of physiologic stress and one might expect a simultaneous increase in levels of steroid hormones in blood.[9,10] Contrarily, conflicting reports about blood eosinophil levels in relation to menstrual cycle[4,11] show no significant change in absolute eosinophil count on any day under consideration.

A mid-cycle peak elevation in platelet count, which followed by a gradual decline may be due to leuteal hormone's which inhibiting the spleen from releasing platelets.[12,13] Some are believed that absorption of necrotic endometrium caused a systemic reaction with a postmenstrual increase of platelets.[14] Some found that the platelet count was elevated significantly during mid-cycle. The cause of this peak of platelet lies in the physiological stress mechanism occurring in the wake of ovulation with an alarm reaction and discharge of corticosteroids, as injections of corticotrophin is followed by an increase in platelet count.[15]

Thus, the variations in the levels of platelet during different phases of menstrual cycle may be explained by variations in the levels of ovarian hormones, menotoxin (toxic reaction), and toxic resorption of necrotic material from raw endometrial surface, or due to an endocrine reaction via the spleen on haemopoietic system, or due to corticosteroids. However, in contrary to above findings some studies are reported mild changes in platelet count, but no statistically significant changes to be observed during different phases of menstrual cycle.[5]

As the bleeding time is correlated with the platelet levels, we found that during menstrual phase platelet count decreased and bleeding time increased, whereas around mid-cycle platelet count increased and bleeding time decreased. Balasubramaniam[15] reported the shortening of bleeding time during the mid-cycle. The shortening of bleeding time around mid-cycle could be due to increase in platelet count. But the shortening of clotting time during the mid-cycle, though not significantly correlated with the platelet peak. The shortening of clotting time could be due to increased progestational compounds affecting clotting factors. Our observations are in contrary to some studies[16,17] in which no alteration was found in bleeding time and clotting time during different phases of menstrual cycle.

Some of the fluctuations encountered in ECG during menstrual cycle may be attributed directly or indirectly to the hormonal disturbances (Katz 1947). Heart rate did not show consistent pattern during different phases of menstrual cycle. In fifteen subjects heart rate significantly (p<0.001) increased, whereas in thirteen subjects it decreased during secretory phase. In rest of two subjects' heart rate remain constant during the whole menstrual cycle. The inconsistent change in heart rate shows that it is influenced by many other factors apart from hormonal disturbances.

The results of thirteen subjects are in agreement with observation of Banerjee[18] who demonstrated decreased heart rate during secretory phase. It is correlated with changes in levels of circulating hormones and may be due to changes in serum electrolytes levels. Whereas the results of fifteen subjects are in agreement with observation of Machiko[19] who reported significantly increased heart rate during secretory phase. They concluded that the parasympathetic activity decreases and sympathetic activity increases during secretory phase of the normal menstrual cycle. But no significant change was observed in P-R interval and in the Q-T interval among the four phases of menstrual cycle. However the maximum Q-T interval found during proliferative phase whereas Q-T interval was shorter in the secretory versus the menstrual phase.[20,21] It is suggested that oestrogens may influence the duration of cardiac repolarization.

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