



AN APPROACH TOWARDS PREMENSTRUAL ASTHMA ALONG WITH BLOOD CELL COUNTS- VARIATION IN PULMONARY FUNCTION TESTS AND SOME HEMATOLOGICAL PARAMETERS IN DEFERENT PHASES OF MENSTRUAL CYCLE

Physiology

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ABSTRACT

Introduction- Menstrual cycle is a physiological process that occurs in women. It is characterized by periodic vaginal bleeding due to shedding of uterine mucosa. This has its own effect on various systems and metabolisms.

Objective- This study was attempted to understand the variations in respiratory parameters as well as hematological parameters in different phases of menstrual cycle.

Methodology- The present study was conducted on 55 healthy female volunteers within the age group of 18 to 24 years having regular menstrual cycle of 28±3 days from the female medical students of M. L. N. Medical College, Allahabad U.P. We analyzed various pulmonary function parameters and hematological parameters on three different phases of menstrual cycle (Menstrual phase-2nd day, Proliferative phase -12th day & Secretory phase-22nd day).

Results- In Pulmonary function test the mean FVC, FEV1, PEFR and FEV1/FVC ratio were significantly different and higher ($p < 0.01$ or $p < 0.001$) in both proliferative phase and secretory phase as compared to menstrual phase. Furthermore, the mean FVC, FEV1, PEFR and FEV1/FVC ratio were also found significantly ($p < 0.05$ or $p < 0.001$) different and higher in secretory phase as compared to proliferative phase. The mean TLC & PMN count increased with time i.e. highest in secretory phase followed by proliferative phase and least in menstrual phase. In contrast, mean Hb was highest in proliferative phase followed by secretory phase and menstrual phase. Conversely, mean eosinophils level was highest in menstrual phase followed by secretory phase and least in proliferative phase.

Conclusion- This study was a moderate attempt to determine regular variations in some specific pulmonary function parameters and hematological parameters, during different phases of menstrual cycle in normal healthy females and evaluate various conflicting reports on female subjects as well as to correlate pulmonary function test parameters and hematological parameters. Eosinophil count increases in menstrual and premenstrual phase. In this phase exacerbation of menstrual asthma has also seen.

KEYWORDS

Apical plug, Apexification, Biodentine, Calcium hydroxide, Open apex

INTRODUCTION:

Female reproductive phase comprises menstrual cycle which is an integral part of their lives. A normal menstrual cycle is dependent on the fluctuation in the ovarian hormones (oestrogen and progesterone) during different phases of menstrual cycle – menstrual, proliferative and secretory phases. The characteristic rhythmic changes in the rate of secretion of ovarian hormones produce corresponding changes not only in the reproductive system but in other organ systems as well.

It is suggested that lung functions exhibit not only diurnal variations but also show changes dependent on different phases of menstrual cycle¹. Women, for largely unknown reasons, are increasingly becoming more affected with inflammatory lung diseases such as asthma, chronic obstructive pulmonary disease and cystic fibrosis and are experiencing excess morbidity and mortality from these disorders after adjusting the smoking factor. It is being increasingly recognized that about a third to half of women experience worsening of asthma symptoms during the premenstrual or menstrual phase of their menstrual cycle.² Although men have higher prevalence of COPD than women, the increased rates of cigarette smoking in females in the last decade have been associated with steadily increasing rates of COPD in females.³

The epidemiologic data suggest that female gender is a significant risk factor for morbidity and mortality in inflammatory lung diseases and sex hormones may be important in their pathogenesis, though the mechanisms by which they act may differ between these disorders. Some of the investigators also proposed to supplement progesterone hormone along with other bronchodilators and found better results in female patients suffering from bronchial asthma with acute exacerbations.⁴

Thus the information on the effect of sex hormones on lung functions

are controversial and hence require further evaluation so as to enable the physicians to formulate better treatment regimes. Therefore, the present study was attempted to observe the variation in pulmonary functions during different (menstrual, proliferative and secretory) phases of the menstrual cycle in healthy adult females.

It is also now recognized that important systemic as well as hematological changes are accompanying the various phases of menstrual cycle.

It is suggested that stressful situations during ovulatory periods and menstruation may cause increased 17-hydroxy corticosterone levels with resulting eosinopenia⁵.

5–20% of women reporting severe dysmenorrhea may be associated with reproductive morbidities like infection. Thus estimation of leucocyte count is an important tool. 9–14% of reproductive-aged women have blood loss that exceeds 80 mL⁶ and prolonged and excessive bleeding may provoke or exacerbate anemia. Thus there arises a need to estimate Hemoglobin, Red Blood Cell count and ESR during the menstrual cycle.

Ovarian hormones also alter the immune system like depression of the suppressor T cell activity). Human & animal studies suggest that there is a change in the distribution of immune cells during different phases of menstrual cycle. The ovulation phase of the menstrual cycle is the marker for fertilization and it may have unique hematological values. This study compares the hematologic values in the ovulation and luteal phases of the menstrual cycle.

MATERIAL AND METHOD

The purpose of the present study was to find any variation in specific pulmonary function test parameters and in hematological parameters different phases of menstrual cycle and if there was any significant

correlation between pulmonary and hematological parameters in reference to premenstrual asthma.

The study was conducted in the Clinical Physiology lab of the department of Physiology, and department of Pathology, Motilal Nehru medical college, Allahabad over a period of one year (Aug, 2014 to July, 2015) after approval from institutional ethical committee. This group included apparently healthy female medical students of Motilal Nehru medical college, Allahabad between the ages of 18 to 24 years.

Contraceptive pills users, lactating women, H/O diabetes mellitus, Cases suffering from cardiovascular abnormalities, Psychiatric illness, Irregular periods, heavy Dysmenorrhoea, Oligomenorrhoea, Polymenorrhoea were excluded from the study.

The study protocol was explained to the subjects and oral and written informed consents were obtained. Prior to that all: age, height, weight were measured. A demonstration was given to the subject before performing the tests.

The first sample was taken on 2nd day of onset of menstruation (Menstrual phase) Second sample during 12th day of Proliferative phase, and the third sample was collected 22nd day during (Secretory Phase). All samples were taken at 10 am to avoid diurnal variations. The parameters analyzed were Hb, Total RBC count (Hayem's fluid) Total Leucocyte Count (Turk's fluid), Absolute Eosinophil Count (Pilot's fluid) & Differential leucocyte Count (DLC) of neutrophils, Arneht Count by Tallybar method, eosinophils, basophils, lymphocytes, monocytes. Total Platelet count (1% ammonium oxalate) was done by haemocytometer. Bleeding time (Duke's method), clotting time (capillary glass tube method).

Pulmonary parameters were recorded by spirometer SPIROEXCEL PC based pulmonary function test. Forced expiratory volume in one second FEV1, and forced vital capacity FVC and FEV1/FVC, of each subject was recorded in sitting position. Subjects were asked to take in a deep breath and exhale forcefully into the tube while closing the nostrils. Three recordings were taken for each test in the interval of two minutes. The best out of three were taken for consideration and the values were expressed in liters/minute.

STATISTICAL ANALYSIS

Sample sizes were taken by Nonrandomized Judgemental Study and has been taken maximum possible number. Data collected from these tests were subjected to SPSS software analysis. Statistical analysis was done by Student's t-test. Comparison of data was done by using ANOVA. The p value of <0.05 indicates statistically significant. The results were expressed as Mean ± SEM (Standard error of mean).

Groups were compared by repeated measures one way analysis of variance (ANOVA) and the significance of mean difference between the groups was done by Tukey post hoc test. A two-tailed (α=2) p value less than 0.05 (p<0.05) was considered statistically significant. Analyses were performed on STATITICA (Windows version 6.0) software.

Results

A. Pulmonary function test

The mean levels of all the pulmonary function test parameters were lowered in menstrual phase as compared to both proliferative phase and secretory phase. Comparing the mean levels of each pulmonary function test parameter between the three groups (or periods), ANOVA revealed significantly (p<0.05 or p<0.01 or p<0.001) different levels of FVC, FEV1, and FEV1/FVC ratio among the groups.

Further, Tukey test revealed that the mean FVC, FEV1, and FEV1/FVC ratio were significantly different and higher (p<0.01 or p<0.001) in both proliferative phase and secretory phase as compared to menstrual phase (Table 2). Furthermore, the mean FVC, FEV1, PEFR and FEV1/FVC ratio were also found significantly (p<0.05 or p<0.001) different and higher in secretory phase as compared to proliferative phase.

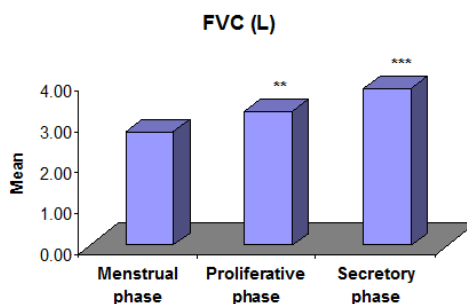
Table 1: Pulmonary function test parameter levels (Mean ± SD, n=55) at three different phases of menstrual cycle in undergraduate female students

Parameters	Menstrual phase	Proliferative phase	Secretory phase	F value (2,162 DF)	p value
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FVC (L)	2.77 ± 0.43	3.26 ± 0.65	3.81 ± 0.90	31.59	<0.001
FEV1 (L)	2.09 ± 0.66	2.72 ± 0.50	3.52 ± 0.92	55.46	<0.001
FEV1/FVC (%)	75.13 ± 18.67	84.95 ± 15.54	92.51 ± 10.39	17.95	<0.001

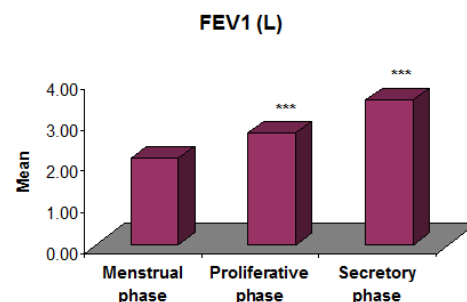
Table 2: For each parameter, comparison (p value) of mean difference between the groups by Tukey test

Comparisons	FVC	FEV1	FEV1/FVC
Menstrual phase vs. Proliferative phase	0.001	<0.001	0.002
Menstrual phase vs. Secretory phase	<0.001	<0.001	<0.001
Proliferative phase vs. Secretory phase	<0.001	<0.001	0.025



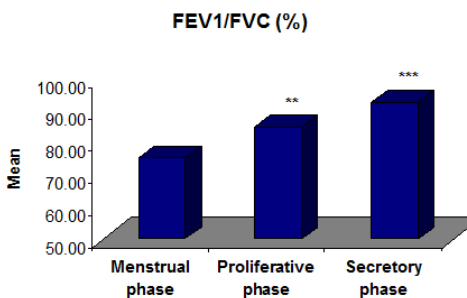
p<0.01 or *p<0.001- as compared to Menstrual phase

Fig. 1. Mean FVC at three different periods.



***p<0.01- as compared to Menstrual phase

Fig. 2. Mean FEV1 at three different periods.



p<0.01 or *p<0.001- as compared to Menstrual phase

Fig. 3. Mean FEV1/FVC ratio at three different periods.

B. Hematological parameters

Like, pulmonary function test parameters, the mean levels of hematological parameters also varied between the periods. The mean TLC & PMN count increase with time i.e. highest in secretory phase followed by proliferative phase and least in menstrual phase.

Comparing the mean levels of each hematological parameter between

the three groups, ANOVA revealed significantly ($p < 0.05$ or $p < 0.01$ or $p < 0.001$) different levels of all the parameters among the groups.

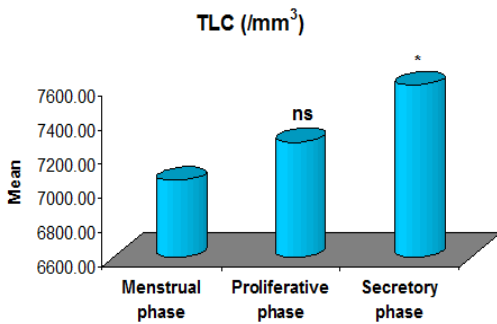
Further the mean TLC & PMN were significantly ($p < 0.05$ or $p < 0.01$ or $p < 0.001$) different and higher in secretory phase as compare to menstrual phase. In contrast, the mean Hb was significantly ($p < 0.001$) different and higher in proliferative phase as compared to both menstrual phase and secretory phase. Conversely, the mean Eosinophils was significantly ($p < 0.01$ or $p < 0.001$) different and higher in menstrual phase as compared to both proliferative phase and secretory phase and also higher significantly ($p < 0.05$) in secretory phase as compared to proliferative phase.

Table 3: Hematological parameter levels (Mean \pm SD, n=55) at three different phases of menstrual cycle in undergraduate female students

Parameters	Menstrual phase	Proliferative phase	Secretory phase	F value (2,162 DF)	p value
TLC (/mm ³)	7045 \pm 1026	7271 \pm 1067	7600 \pm 1333	3.23	0.042
PMN (%)	65.20 \pm 3.83	66.07 \pm 2.87	68.11 \pm 7.29	4.84	0.009
Eosinophils (%)	5.64 \pm 2.10	3.31 \pm 1.67	4.31 \pm 2.30	18.01	<0.001

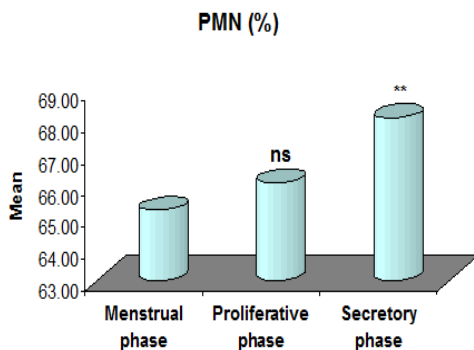
Table 4: For each parameter, comparison (p value) of mean difference between the groups by Tukey test

Comparisons	TLC	PMN	Eosinophils
Menstrual phase vs. Proliferative phase	0.559	0.634	<0.001
Menstrual phase vs. Secretory phase	0.031	0.007	0.002
Proliferative phase vs. Secretory phase	0.291	0.085	0.027



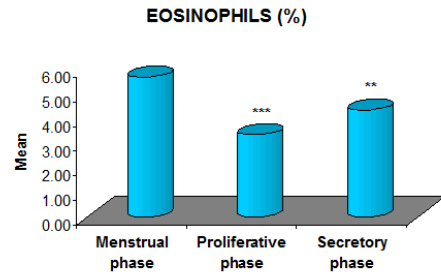
^{ns} $p > 0.05$ or ^{*} $p < 0.05$ - as compared to Menstrual phase

Fig. 4. Mean TLC at three different periods.



^{ns} $p > 0.05$ or ^{**} $p < 0.01$ - as compared to Menstrual phase

Fig. 5. Mean PMN at three different periods.



^{**} $p < 0.01$ or ^{***} $p < 0.001$ - as compared to Menstrual phase

Fig. 6. Mean eosinophils at three different periods.

Discussion-

Periodical change occurs in anatomical architect and hormonal fluctuation during menstrual cycle in females. It is also very much known to have a fluctuation in their hormone concentration. These hormones influence autonomic & metabolic activities.

In our present study the mean levels of all the pulmonary function test parameters were lowered in menstrual phase as compared to both proliferative phase and secretory phase. Comparing the mean levels of each pulmonary function test parameter between the three groups (or periods), ANOVA revealed significantly ($p < 0.05$ or $p < 0.01$ or $p < 0.001$) different levels of FVC, FEV1, and FEV1/FVC ratio among the groups.

This present study shows that respiratory parameters of women in reproductive age group show significant variations during different phases of menstrual cycle which could be due to the hyperventilation caused by increased levels of progesterone in the luteal phase as suggested by Das et al and Rao et al.^{8, 9} Progesterone induces hyperventilation through both the central medullary and peripheral receptors. According to Bayliss D.A and Millhorn D.E the respiratory response to progesterone is mediated at hypothalamic sites through an oestrogen (E2) dependent progesterone receptor (PR) mediated mechanism requiring RNA and protein synthesis i.e., gene expression. The neural mechanisms underlying the stimulation of respiration by progesterone are similar to those mediating its reproductive effects.¹⁰

On the other hand, Williams JS et al, Chong et al and Bruno da Silva et al observed that there were no significant differences in different phases of menstrual cycle for any spirometric variables and concluded that menstrual cycle phases did not influence ventilatory responses at rest.^{11,12,13}

This present study does not agree with these studies.

In the present study Like, pulmonary function test parameters, the mean levels of all the hematological parameters also varied between the periods. The mean TLC & PMN increase with time i.e. highest in secretory phase followed by proliferative phase and least in menstrual phase. Conversely, mean eosinophils level was highest in menstrual phase followed by secretory phase and least in proliferative phase.

In our present study there is an increase in neutrophil count percentage values during Secretory phase when compared to other phases, this changes is due to hormonal imbalance in ovary [kannan et al 2013]¹⁴. Some studies suggested that estrogen increases granular proliferation. Increase in 17 beta estradiol concentration in circulatory pool of blood, in Secretory phase promotes granulopoiesis, which in turn increases the granulocyte numbers.

Several studies are in general agreement with the fact that the leucocyte count increased during the follicular phase and decreased during luteal phase. Although some exhibit a mild increase in total leucocyte count around follicular, yet no significant changes were observed. The changes in the circulating leucocyte count during the menstrual cycle is associated with the presumptive changes in blood estrogen 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^{15,16} in which they did not find any change in the number of circulating leucocytes in relation to the menstrual cycle.

Conclusion-

In the present study results, we found that there is a significant increase in some specific pulmonary function tests variables in secretory phase as compared with menstrual phase that is better pulmonary functions which might be due to hormonal fluctuations or the bronchodilatory effects of progesterone.

There was also an increase in neutrophil count in secretory phase of menstrual cycle when compared to proliferative phase. It is also proved in few studies with increase in 17 beta estradiol concentrations in secretory phase promotes granulopoiesis which in turn increases the WBC count. 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.

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