Lung function tests in different phases of menstrual cycle

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Abstract

Introduction: Menstrual cycle is an integral part of a woman’s life. During these different phases, rhythmic changes occur in the levels of ovarian hormones especially progesterone and estrogen. The goal of this study was to study the effect of the luteal and follicular phases of the menstrual cycle on bronchial reactivity (BR) in a group of women.

Material and Methods: The fifty girl medical students of first year MBBS of 18 – 24 years age were undertaken to study pulmonary function tests in different phases of menstrual cycle. Pulmonary function tests were taken between 8 – 10 th day of menstrual cycle, that is in follicular phase and again were recorded between 20 – 22 nd day of menstrual cycle that is in luteal phase by using spirometric technique. The results were expressed as Mean ± Standard Deviation (Mean± SD). Statistical analysis was done through Graph pad prism. Comparison of pulmonary function parameters in different phases of menstrual cycle was done by using one way ANOVA (Analysis of Variance) by bonferroni post-hoc test. Results: Anthropometric measurement of all subjects in which mean age was 19.45 ± 1.80 years, arm span was 157.25± 6.37 cm, chest circumference was 80.58 ± 7.69 cm, height was 149.07 ±4.64 cm , weight was 45.65±6.69 Kgs. Spirometric study found FVC, FEV1, and PEFR increase in luteal phase of menstrual cycle compared to follicular phase, which were statistically significant. Conclusion: We found better lung functions which were statistically significant in luteal phase as compared to follicular phase of our subjects indicating a possible role of progesterone causing β adrenergic stimulation / sensitization.

Keywords: Lung functions, Adolescent females, Progesterone, Luteal phase

Introduction

The increased vulnerability to inflammatory and autoimmune disease women experience after puberty is considered secondary to the different effect sex hormones have on the inflammatory defence system, and specifically on mast-cells (MC) [1,2] and eosinophils cells. Fluctuations of estrogens trigger the mast-cell degranulation, whilst testosterone and other androgens are credited to have a stabilizing effect. Perimenstrual fluctuations of sex hormones in women are considered responsible for the specific worsening of many different perimenstrual symptoms and of specific inflammatory [3], autoimmune [4,5] and pain related conditions, such as headache and pelvic pain [6-10]. It has been known for a long time that some female asthmatic patients experience an aggravation of asthma symptoms during the premenstrual or menstrual phases of their cycle. In particular, it has been hypothesized that hormonal fluctuations during the menstrual cycle play a significant role in the pathophysiology of asthma, resulting in periodic worsening of disease severity in adult females [10-12].

Therefore, the goal of this project was to study the effect of the menstrual cycle; specifically, the luteal and follicular phases and plasma sex hormone levels, on bronchial reactivity (BR) in a group of asthmatic women. In particular, sex hormone levels and mediators of bronchial smooth muscle contraction were evaluated.

Material and Methods

The present study was conducted on the fifty girl medical students of first year MBBS of 18 – 24
years age group. The subjects were selected from students studying in tertiary care teaching hospital attached with medical college in India. The subjects selected for the study were normal healthy young girls with no history of any disease, which could influence pulmonary function. The general and systemic examination of the subjects was done for all the systems with special emphasis on the respiratory system.

**Inclusion criteria**- Females of 18-24 years age group having regular menstrual cycle of 26 – 30 days.

**Exclusion criteria**- Age below 18 years and above 24 years age group, history of irregular menstrual cycle, subject on oral contraceptive pills and hormone replacement therapy.

**Equipments**- Spiro Excel Machine (Computerized spirometer) manufactured by Medicaid Systems, Chandigarh was used to measure the pulmonary Functions. The logic built into the Spiro Excel evaluates the patient/subject as an adult or a child male or female and selected the suitable set of equation for computation of predicted norms.

Technical features of Spiro excel machine.- Flow meter Bi-directional digital turbine Range for flow measurement 0.03 -20 L/Sec. Range for volume measurement 10 L Accuracy of measurement ± 3% or 50 ml Dynamic resistance @ 12 L/Sec <0.7 cm H2O/ L/Sec. Mouthpieces 31 and 21 mm Power Supply No external supply required, works on 5V from CPU Dimensions 160 x 50 x 25 mm Weight 100 gm

**Method of collection of data**- After explaining the aims and objectives of study written consent was taken from all the subjects.

All the subjects were given Proforma containing name, age in completed years, gender and dietary habits (whether vegetarian or non-vegetarian), history of smoking, whether active or passive and its duration, history of recurrent respiratory infections or significant past history of any other disease, family history of COPD (asthma or emphysema) and history of allergy, to be filled up. We recorded the menstrual history which specifically included date of last menstrual period (LMP), duration of menses, date of last three consecutive menstrual cycles. Data of all the subjects was acquired in the following three phases of menstrual cycle.

1. Menstrual phase
2. Proliferative phase
3. Secretory phase

Subjects were asked to report three times on the 2nd or 3rd, 10th-12th and 20th-22nd days of menstrual cycle. These days were calculated from LMP dates that were filled in the proforma. Pulmonary function tests were carried out of the subjects in the sitting position before lunch and values of different parameters were recorded.

**Procedure for test administration**

PFT were performed in calm and comfortable environment in 2 Steps.
1. Preparation
2. Test administration

**Preparation**

- It was ensured that the subjects were not wearing items of apparel that were tight or restrictive (e.g. necktie, buttoned shirt collar, tight belt etc.).
- Clean, disinfected mouthpiece was provided to every subject for the procedure.

**Test administration**

- Clear and simple instructions were given to the subject followed by a demonstration.
- Nose was closed during the manoeuvre by nose clips.
- Mouthpiece was positioned in such a way that the subject's chin was slightly elevated and neck was extended.
- The subject was asked to exhale into the mouthpiece of Spiro Excel machine as forcefully as possible after deep inspiration. The test was repeated three times and the highest values were considered for analysis.
- In the manoeuvre each subject was motivated and encouraged to give her best performance.

**Statistical Analysis**- The results were expressed as Mean ± Standard Deviation (Mean ± SD). Statistical analysis was done through Graph pad prism. Comparison of pulmonary function parameters in different phases of menstrual cycle was done by using one way ANOVA (Analysis of Variance) by bonferroni post-hoc test.
Results

The mean cycle length of all the subjects was in the range of 28±2 days. Anthropometrical results of all the subjects are exhibited in table no. 1.

Table No 1: Shows the anthropometric parameters of all the subjects (n= 50).

| Parameters               | Mean ± SD   |
|--------------------------|-------------|
| Age (years)              | 19.45 ± 1.80|
| Arm span (cm)            | 157.25±6.37 |
| Chest circumference(cm)  | 80.58±7.69  |
| Height (cm)              | 149.07±4.64 |
| Weight (kg)              | 45.65±6.69  |

Above table shows anthropometric measurement of all subjects in which mean age is 19.45 ± 1.80 years, arm span is 157.25± 6.37 cm, chest circumference is 80.58 ± 7.69 cm, height is 149.07 ±4.64 cm, weight is 45.65±6.69 cm.

Table No 2: Exhibits the results of all pulmonary function tests Standard deviation.

| Parameters | Follicular phase | Luteal phase | P value |
|------------|-----------------|--------------|---------|
| FVC(L/SEC) | 2.01± 0.40      | 2.16± 0.37   | 0.001   |
| FEV1(L/SEC)| 1.44±0.40       | 2.16±0.37    | 0.001   |
| FEV3(L/SEC)| 2.13±0.55       | 2.19±0.54    | 0.721   |
| PEFR(L/SEC)| 3.43±0.50       | 4.00±1.28    | 0.001   |
| MVV(L/MIN) | 90.21±6.91      | 90.36±30.06  | 0.028   |

Significant p≤ 0.05

It is clear that FVC, FEV1, and PEFR show statistically increase in luteal phase of menstrual cycle compared to follicular phase. Which is statistically significant.

Discussion

In our study we found that, there was increase in FVC values in successive phases from menstrual to secretory phase. The FVC values of proliferative phase was significantly higher compared to menstrual phase (p <0.001). Likewise the values of FVC were significantly higher in secretory phase as compared to proliferative phase (p<0.001). There are many similar studies with comparable results likewise.

Menstrual cycles are considered to be the chief protagonists in the clinical scenario of inflammation and pain [13-15]. Mast cells (MC) are present in the endometrium and myometrium and are predominantly localized to the basal layer [16]. Mast cells (MC) are upregulated in response to a wide range of stimuli, including neurogenic factors, fluctuating oestrogen levels and menstrual blood in the tissue [6]. Once activated, MC degranulate and release a range of inflammatory mediators which perpetuate the immune response [6]. Sex hormones regulate MC functionality and distribution in several tissues [17-19], both in physiological and pathological conditions. In this regard, a relationship between female sex hormones, MC and development of asthma and allergy has been suggested [20,21]. Furthermore, the presence of sex steroid receptors on MC indicates that sex hormones may exert their biological effects by binding to these receptors [21].

Alessandra Graziottin et al [22] found that PMA incidence is reported to vary between 19 and 40% of asthmatic women. The presence of PMA has been related to increases in asthma-related emergency department visits, hospitalizations and emergency treatment including intubations. This paper will focus on the pathophysiology of hormone triggered cycle related inflammatory/
allergic events and their relation with asthma. We reviewed the scientific literature on Pubmed database for studies on PMA. Key word were PMA, mastcells, estrogens, inflammation, oral contraception, hormonal replacement therapy (HRT), and hormone free interval (HFI).

Dratva J et al [23] found that the prevalence of BHR was 13% (fall of ≥20% in FEV1 up to a maximal cumulative dose of 2 mg), and 6% had asthma. A total of 143 women had undergone methacholine challenge within the risk window.

We observed a significant increase in BHR within the window of risk (odds ratio [OR], 2.3; 95% CI, 1.27-4.29). A cyclic association pattern was confirmed by trigonometric functions. Effect modification by asthma status and oral contraceptive use was found, with lower OR in subjects without asthma and OR <1 in women using OCs.

Sathish V et al[24] summarize the potential for sex steroids as useful biomarkers and therapeutic targets in these lung diseases as a basis for future translational research in the area of gender and individualized medicine.

Elizabeth A et al [25] found that Potential beneficial effects of estrogens on the systemic cardiovascular system with regard to hypertension would suggest a protective contribution of female sex steroids against the development or progression of PH. Indeed, in experimental animal models of PH, estradiol attenuates or inhibits development of the disease. However, this protective nature is not realized clinically, thus forming the basis for an “estrogen paradox” in PH.

Furthermore, compared with the systemic vasculature, less is known on the role of other steroids (progesterone, testosterone, and DHEA) in the development or modulation of PH.

Several excellent reviews regarding sex steroids in the pulmonary vasculature cover these topics [26,27,28,29,30].

Here, we briefly summarize what is known, and not known, and highlight the need for further consideration of sex steroid signaling in regard to PH.

Fuseini H et al[31] women have an increased asthma prevalence compared to men. Further, women are more likely to have severe asthma and a later onset of asthma compared to men. Here, we review clinical and animal studies that have defined the role of sex hormones in airway inflammation, smooth muscle contraction, mucus production, and airway mechanics associated with asthma pathogenesis.

Understanding that the menstrual fall of estradiol and progesterone triggers asthmatic crises in vulnerable women may suggest new preventive strategies which are pathophysiologically oriented. This include stabilizing estradiol and progesterone/progestins levels and reducing the hormone free interval (HFI), when OC is considered.

Conclusion

Higher values of lung functions during proliferative and secretory phases can be attributed to the higher concentrations of sex hormones specially progesterone because in most of the studies progesterone is known to cause relaxation of bronchial smooth muscle. Our study also suggests possible role of sex hormones especially progesterone in treating asthmatic females or at least reduction in the doses of bronchodilators can be done while concomitantly using progesterone. However further prospective controlled studies are needed to test this working hypothesis.

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