

Assessment of Pulmonary Functions during Various Phases of Menstrual Cycle in Healthy Young Girls

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Abstract: *Introduction:* Rhythm of menstrual cycle is controlled by Hypothalamus – pituitary – ovarian axis. It is well known that the asthma incidence is greater in boys during childhood and in girls during adolescence. This study was undertaken to confirm the probable effects of these hormones on the bronchial musculature that may explain exacerbation of symptoms during different phases of the menstrual cycle. *Aim and Objective:* Aim of the study is to carry out pulmonary function tests during menstrual, proliferative and secretory phase of menstrual cycle in young girls. *Methodology:* This study was conducted in a tertiary teaching college and hospital in Mumbai. The study involved the collection of data from 50 female volunteers after taking an informed consent. The volunteers were in the age group between 18 and 26 years and BMI of 18.5-22.9 kg/m². *Results:* Mean values of FVC were 2.64 ± 0.33, 3.12 ± 0.35 and 3.19 ± 0.46 liters in menstrual, proliferative, secretory phases respectively. Mean values of FEV1 in menstrual, proliferative, secretory phases were 2.32 ± 0.89, 2.58 ± 0.48 and 2.83 ± 0.53 liters respectively. Mean values of FEV1 /FVC (%) were 92.37 ± 8.20, 91.29 ± 6.36 and 90.67 ± 4.21 in menstrual, proliferative, secretory phases respectively. Mean values of PEFr in menstrual, proliferative, secretory phases were 5.79 ± 1.35, 6.19 ± 0.68 and 6.44 ± 0.56 (liters/sec). *Conclusion:* The difference in FVC, FEV1, PEFr and MVV values were significant in menstrual and proliferative phases, in menstrual and secretory phase and also in proliferative and secretory phase.

Keywords: pulmonary functions, asthma, menstrual cycle, secretory phase

1. Introduction

Monthly rhythmic changes in the rate of secretion of female sex hormones and corresponding physical changes in the ovaries, uterus and other sex organs characterizes normal reproductive years of the female. This rhythmic pattern is called the female monthly sexual cycle or menstrual cycle. [1]. Word menses originated from Latin word 'mensis' meaning a month. [2]

Rhythm of menstrual cycle is controlled by Hypothalamus – pituitary – ovarian axis. [3]. Various hormones like gonadotropin releasing hormone (GnRH), follicle stimulating hormone (FSH), luteinizing hormone (LH), Estrogen and progesterone regulate the menstrual cycle.

Menstrual cycle is divided into follicular phase, ovulatory phase, luteal phase and menstrual phase. Follicular phase starts with first day of menstruations and is followed by luteal phase from ovulation until menstruations restart. [4]

Chronic obstructive pulmonary disease (COPD) is one of the common diseases which is preventable and treatable chronic respiratory disease. Worldwide, it affects about 210 million people. Co-existence of other chronic respiratory diseases like asthma can adversely influence the prognosis of COPD. [5]

Asthma is a syndrome characterized by airflow obstruction and is manifested physiologically by widespread narrowing of airway that varies markedly and may be relieved spontaneously or as a result of treatment. [6] Overall prevalence rate of asthma increased from 41.9 (per 1000 population) in 2004–05 to 54.9 (per 1000 population) in 2011–12. [7]

Asthma incidence is greater in boys during childhood and in girls during adolescence. Hormonal differences and their changes during adolescence are found to be the responsible factors. Even some female asthmatic patients experience aggravation of asthma symptoms during the premenstrual or menstrual phase of their cycle. This has been referred to as perimenstrual asthma. Perimenstrual asthma has been documented in 30% to 40% of asthmatic women. Premenstrual and menstrual exacerbations of asthma may result from changes in level of female hormone in the blood. [8]. Our study was undertaken to confirm the probable effects of these hormones on the bronchial musculature that may explain exacerbation of symptoms during different phases of the menstrual cycle. The results of the studies like ours may help in some way to modify the therapy and lifestyle of the asthmatic women in the menstruating age group.

2. Aims and Objectives

Aim of the study is to carry out pulmonary function tests during menstrual, proliferative and secretory phase of menstrual cycle in young girls.

3. Materials and Methods

This study was conducted in a tertiary teaching college and hospital in Mumbai. The study involved the collection of data from 50 female volunteers after taking an informed consent. The volunteers were in the age group between 18 and 26 years and BMI of 18.5-22.9 kg/m². [9]

3.1 Inclusion criteria

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The volunteers were selected strictly based on predetermined inclusion criteria that include normal healthy young female volunteers falling in the age group of 18-26 years, having BMI between 18.5 and 22.9 kg/m², having regular menstrual cycle, those who signed informed consent and those who agreed to chart their body temperature.

3.2 Exclusion criteria

Volunteers having age <18 and >26 years, BMI of <18.5 and >22.9 kg/m², irregular menstrual cycle, and having known allergy, chronic obstructive lung disease (COPD), restrictive lung diseases, cardiovascular disease, psychiatric illness, medical or surgical illness; those using oral contraceptive pills (OCP), hormone replacement therapy (HRT) and those who were smokers, alcohol and drug abusers were excluded from the study. A detailed history about the presence of any allergy was obtained and volunteers having skin rash, cutaneous erythema, flushing, rhinitis, hoarseness of voice, difficulty in breathing were excluded from the study.

Before starting the procedure, all the subjects were asked to fill up the proforma containing age in completed years, gender, dietary habits, history of smoking (active/passive, duration), history of recurrent respiratory tract infections, other major disease, family history of COPD, allergy; detailed history regarding the menstrual cycle (last menstrual period -LMP, regularity of menses, duration of menses, any unusual symptom or sign associated with the menses) was obtained.

A brief general examination including general appearance and built, signs of pallor, state and condition of pharynx, soft palate and tonsils, complete pulse examination, blood pressure and temperature were done. A complete blood count and a chest x-ray were offered to confirm any anemia, allergy or respiratory illness. Pulmonary function tests (PFTs) were carried out in the department of General medicine at a tertiary care hospital where the study was conducted. Respiratory and cardiovascular system examinations were conducted prior to each pulmonary function testing and suspected volunteers were excluded from the study. Written informed consent was signed by all of them.

The tests were conducted over two successive cycles in each volunteer. The average of each of the tests was determined for each of the volunteer separately and this mean value was taken for statistical analysis of the study. To maintain the uniformity for each volunteer, the recording of the data was done in the same designated room, at the same stipulated time (morning hours) of the day, on the same instrument, by the dedicated investigator and near about same temperature (maintained by the Air conditioner).

Confidentiality of each volunteer was maintained by assigning a number to each volunteer, which coincides with the page number in the general record book. Thus the anthropometric measurements (height, weight) and personal history of the volunteers including last menstrual period (LMP), regularity of menses, duration of menses, etc can be obtained and assessed conveniently. The data, so obtained, was entered in the separate sheet as per the number assigned.

Atmospheric temperature was recorded. MIR spirometer with Winspiro - pro 4.4 software was calibrated for the temperature, atmospheric pressure and volume [10]. Patient's information like age, sex, height, weight, date of performing the test and the atmospheric temperature was entered in the spirometer. Each volunteer was instructed in a language she can understand and encouraged to carry out the maneuver smoothly.

The volunteers were made to sit in a room for about 10 minutes and relax prior to the recording. PFTs were carried out with volunteer in sitting position with legs uncrossed. Nose clip was put on her nose. She was asked to perform tidal breathing and after that to execute forceful expirations as fast as possible the end of a deep and full expiration through sterile mouthpiece. Trial performances were given before recording the final data.

In each volunteer, recording during the menstrual cycle was done as follows:

- during the first or second day of the menstrual cycle,
- 9th and 10th day of the proliferative or follicular phase,
- 14th to 16 the day of menstrual cycle (ovulation),
- 22nd to 24th of the secretory/luteal phase.

Following parameters of the PFTs were taken into the consideration.

- 1) Forced vital capacity (FVC) (liters)
- 2) Forced expiratory volume in the first second (FEV1) (liters)
- 3) FEV1% (FEV1/FVC ratio)
- 4) Peak expiratory flow rate (PEFR) (Liters/second)
- 5) Maximum voluntary ventilation (MVV) (Liters/minute)

4. Statistical Analysis

Various groups were compared by one-way analysis of variance (ANOVA) test, and the Tukey's post hoc test was applied for significance of mean difference between the groups was done by. The data were summarized as mean±SD (standard deviation). A two-tailed ($\alpha = 2$) p value less than 0.05 ($p < 0.05$) was considered statistically significant.

5. Results

Mean age of the 50 female participants was 21.54±1.42 years, mean height was 155.36±7.11 cm, mean weight was 51.21±6.83 Kg and mean body mass index (BMI) was 21.52±2.31 Kg/m². Mean values of FVC were 2.64 ± 0.33, 3.12 ± 0.35 and 3.19 ± 0.46 litres in menstrual, proliferative, secretory phases respectively. Mean values of FEV1 in menstrual, proliferative, secretory phases were 2.32 ± 0.89, 2.58 ± 0.48 and 2.83 ± 0.53 litres respectively. Mean values of FEV1 /FVC (%) were 92.37 ± 8.20, 91.29 ± 6.36 and 90.67 ± 4.21 in menstrual, proliferative, secretory phases respectively. Mean values of PEFR in menstrual, proliferative, secretory phases were 5.79 ± 1.35, 6.19 ± 0.68 and 6.44 ± 0.56 (litres/sec) respectively and mean values of MVV in menstrual, proliferative, secretory phases were 86.32±15.59, 92.44±21.14 and 98.95±31.86 (litres/min)

respectively.

Table 1: Lung function parameters in different phases of menstrual cycle

Parameters	Menstrual phase	Proliferative phase	Secretory phase
FVC (L)	2.64 ± 0.33	2.72 ± 0.35	3.19 ± 0.46
FEV1 (L)	2.32 ± 0.89	2.58 ± 0.48	2.83 ± 0.53
PEFR (L/s)	5.79 ± 1.35	6.19 ± 0.68	6.44 ± 0.56
FEV1/FVC (%)	92.37 ± 8.20	91.29 ± 6.36	90.67 ± 4.21
(MVV) (L/m)	86.32 ± 15.59	92.44 ± 21.14	98.95 ± 31.86

Table 2: Comparison of lung function parameters in menstrual and proliferative phase

Parameters	Menstrual phase	Proliferative phase	P value	t-Value
FVC (L)	2.64 ± 0.33	2.72 ± 0.35	<0.001	5.92
FEV1 (L)	2.32 ± 0.89	2.58 ± 0.48	<0.001	6.13
PEFR (L/s)	5.79 ± 1.35	6.19 ± 0.68	<0.001	5.02
FEV1/FVC (%)	92.37 ± 8.20	91.29 ± 6.36	>0.005	0.74
(MVV) (L/m)	86.32 ± 15.59	92.44 ± 21.14	<0.005	4.87

Table 3: Comparison of lung function parameters in menstrual and secretory phase

Parameters	Menstrual phase	Secretory phase	P value	t-Value
FVC (L)	2.64 ± 0.33	3.19 ± 0.46	<0.001	13.87
FEV1 (L)	2.32 ± 0.89	2.83 ± 0.53	<0.001	13.12
PEFR (L/s)	5.79 ± 1.35	6.44 ± .56	<0.001	09.11
FEV1/FVC (%)	92.37 ± 8.20	90.67 ± 4.21	>0.05	2.24
(MVV) (L/m)	86.32 ± 15.59	98.95 ± 31.86	<0.05	11.45

Table 4: Comparison of lung function parameters in proliferative and secretory phase

Parameters	Proliferative phase	Secretory phase	P value	t-Value
FVC (L)	2.72 ± 0.35	3.19 ± 0.46	<0.001	9.34
FEV1 (L)	2.58 ± 0.48	2.83 ± 0.53	<0.001	8.48
PEFR (L/s)	6.19 ± 0.68	6.44 ± .56	<0.001	7.31
FEV1/FVC (%)	91.29 ± 6.36	90.67 ± 4.21	>0.05	1.27
(MVV) (L/m)	92.44 ± 21.14	98.95 ± 31.86	<0.05	8.05

6. Discussion

It can be observed from the results that difference in FVC, FEV1, PEFR and MVV values were significant in menstrual and proliferative phases (table 2), in menstrual and secretory phase (table 3) and also in proliferative and secretory phase (table 4).

The probable reason for increase in lung function during secretory phase of menstrual cycle is higher level of progesterone causing hyperventilation. Hyperventilation is induced through both medullary centre (central mechanism) and peripheral receptors. Also the periodic hyperventilation improves the muscle strength. This explains improvement in FEV1/FVC ratio. [11] [12]

Progesterone is known to cause relaxation of smooth muscles and resulting in broncho-dilatation and decrease in airway resistance. This explains the improvement in FEV1 and PEFR during luteal phase. [12] [8] Estrogen might have smooth muscle relaxant effect in proliferative phase. It is

proven that the degree of bronchodilators required were less in patient receiving intramuscular progesterone. [13] It is also mentioned in the literature that asthmatic females used to become symptomatic and worsen just before menstrual bleeding, which can be correlated to the fall in the level of progesterone [13] [14]. Progesterone also decreases the resistance offered by the small bronchioles which may explain that females taking oral contraceptive pills have significant increase in pulmonary functions [11] [15] [16].

Increase in MVV in secretory phase can be explained by smooth muscle relaxation, hyperventilation effect along with beta adrenergic stimulation effect of the progesterone [3].

Mast cells, also known as unicellular glands, are known to be influenced by estrogen and progesterone [17] [18]. It causes degranulation, release of several mediators including histamine, proteases, metalloproteins, pro-angiogenic factors etc. It has been reported that there is increased sensitivity of adenosine monophosphate receptors to the sex hormone during secretory phase. Thus lower threshold activated mast cells release various mediators and cause bronchoconstriction [17]. This explains that asthma and other diseases involving mast cells have higher incidences in women than in men during mid-adulthood [19]. It is also found that physiological stress and increased level of steroid hormones in blood during secretory phase result in rise in eosinophil count [20] [21].

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