COMPARATIVE STUDY OF CARDIOVASCULAR REACTIVITY TO COLD PAIN IN DYSMENORRHEIC WOMEN AND NON DYSMENORRHEIC WOMEN ACROSS MENSTRUAL CYCLE

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ABSTRACT: BACKGROUND: Dysmenorrhea is the most common gynecologic disorder among female adolescents, with a prevalence of 60% to 93%. Primary dysmenorrhea, painful menstruation without pelvic abnormalities, may be associated with vomiting, fatigue, back pain, headaches, dizziness, and diarrhoea. MATERIALS AND METHODS: This is a comparative and cross sectional Study. Thirty one dysmenorrheic women and non dysmenorrheic women between the age group of 18-26 years participated in this study. All participants satisfied inclusion and exclusion criteria and gave informed consent. We performed Cold Pressor Test on 1st, 14th and 21st day of menstrual cycle denoting the menstrual phase, late follicular phase and luteal phase on the participants. Radial pulse rate was recorded before and after the Cold Pressor test, expressed in beats per minute. Blood pressure was recorded in sitting position just before and after immersion using sphygmomanometer, expressed as mmHg. RESULTS: The SBP difference was highest in the dysmenorrheic women (10.52±2.68) when compared to non dymenorrheic women (8.52±1.93) on the 1st day which was statistically significant. The SBP change was lowest on the 14th day in the dysmenorrheic women (6.52±2.42) when compared to non dymenorrheic women (3.74±1.00) which is statistically significant. The DBP difference was highest in the dysmenorrheic women (4.90±1.54) when compared to non dymenorrheic women (4.06±0.63) on the 1st day which was moderately significant. The DBP change was lowest on the 14th day in the dysmenorrheic women (4.06±1.50) when compared to non dymenorrheic women (2.26±0.68) which is statistically significant. In dysmenorrheic women, there was difference in pulse rate when comparing the 3 episodes that is 1st, 14th day & 21st day. In non dysmenorrheic women, there was difference in pulse rate when comparing the 3 episodes that is 1st, 14th day & 21st day. CONCLUSIONS: We concluded that dysmenorrhieic women had increased cardiovascular response to experimental pain across menstrual cycle when compared to non dysmenorrhieic women which could be attributed to activation of Sympatho-adrenal medullary system.

KEYWORDS: Cold Pressor Test, Dysmenorrhea, Menstrual Cycle, Systolic Blood Pressure, Diastolic Blood Pressure.

INTRODUCTION: Dysmenorrhea is the most common gynecologic disorder among female adolescents, with a prevalence of 60% to 93%.¹ Primary dysmenorrhea is painful menstruation without pelvic abnormalities, may be associated with vomiting, fatigue, back pain, headaches, dizziness, and diarrhoea. Primary dysmenorrhea, a condition associated with ovulatory cycles, is due to myometrial contractions induced by prostaglandins originating in secretory endometrium, which results in uterine ischemia and pain.¹ Prostaglandins (PGs) are hormone-like compounds that
function as mediators of a variety of physiological responses such as inflammation, muscle contraction, vascular dilation, and platelet aggregation.\(^2\) The variations of autonomic functions and heart rate variability during menstrual cycle has been widely studied.\(^3\) Several studies have found variations in sympathetic activities across menstrual cycle which is attributed to changing milieu of ovarian hormones.\(^4\)

The cold pressor test (CPT) is an empirically validated test commonly used in research on stress, pain and cardiovascular reactivity. George E. Brown and Edgar A. Hines in 1932 introduced a test designed to detect latent states of hypertension by immersion of one extremity in ice water for 1-3 minutes.\(^5\) This test was called as Hines and Brown test.\(^5\) Later on name of this test was changed to cold pressor test. Cold pressor test is simple, provocative, non-invasive, reliable and cheap test to know autonomic status of body.

The Cold Pressor test is extensively used in cardiovascular research to elicit a blood pressure response.\(^5\) Our study would like to explore any differences in autonomic function in dysmenorrheic women when compared to non-dysmenorrheic women. The early detection of autonomic dysfunction would be beneficial.

**MATERIALS AND METHODS:** It was a comparative and Cross Sectional Study.

**Participants:** In this study we included two groups. Group a consisted of 31 Women with history of dysmenorrhea who were volunteers. Group B consisted of 31 Healthy women with no history of dysmenorrhea. The subjects of the study were informed about the project both in writing and in person and a written consent was obtained from all the subjects. We included women from the age group 18-26 years. Maximum number of subjects was in the age group of 19-20yrs in the three groups. Mean age for women was 18.77±1.26 years and for men was 18.68±13.25 years. It was statistically similar in both the groups with p-value of 0.940.

**Inclusion Criteria:** We included Nulliparous and unmarried women from the age group 18-26 years with history of regular menstrual cycles.
- Cycles for last 3 months should range from 25-30 days.
- The subjects should have no on-going hormonal treatment.
- The criteria for dysmenorrheic women are that clinical history of cramp like pain for past 3 Months, diagnosed by a gynaecologist.\(^6\)

**Exclusion Criteria:**
- We excluded subjects with history of bone injury in non-dominant hand.\(^6\)
- The subject should not have history of tingling, numbness sensation in the hands.
- The subject should not be taking medicines for pain relief.\(^6\)
- The subject should not have history of any urogenital pathology.

A typical menstrual cycle of 28 days can be divided into three phases. The follicular phase begins on the first day of menses and lasts 10-14 days. About 22-36 h before ovulation, a peak in estradiol level occurs, followed by a peak in luteinizing hormone level 10-12 h before ovulation. The phase after ovulation is called the luteal phase, which lasts for 14 days. Hence we performed CPT on 1st, 14th and 21st day of menstrual cycle denoting the menstrual phase, late follicular phase and
luteal phase. The subject is asked to lie down for 10 minutes and radial pulse rate was recorded and expressed in beats per minute Blood pressure was recorded in sitting position just before immersion using sphygmomanometer and expressed as mmHg. Systemic examination including respiratory, cardiovascular, abdominal and central nervous system was done.

A circulating water bath (designed locally) was used to immerse the non–dominant hand of the subject (palm down, up to 5 cm above wrist level). Water was maintained at 0-20°c using crushed ice. A thermometer was used to measure the temperature. Pulse and blood pressure were recorded manually before and immediately after the cold pressor task (CPT).

**STATISTICAL ANALYSIS:** Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Post-hoc Tukey test has been used to find the pairwise significance and Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale with in each group.

**RESULTS:**

**SBP Change before and after the Test:** The SBP difference was highest in the dysmenorrheic women (10.52±2.68) when compared to non dymenorrheic women (8.52±1.93) on the 1st day which was statistically significant. The SBP change was lowest on the 14th day in the dysmenorrheic women (6.52±2.42) when compared to non dymenorrheic women (3.74±1.00) which is statistically significant (Table 2)

| SBP(mm Hg) | Group I | Group II | Overall P value | Pairwise significance |
|------------|---------|----------|-----------------|-----------------------|
|            |         |          |                 | Group I-II  | Group II-III |
| 1st day    | 10.52±2.68 | 8.52±1.93 | 0.008***        | 0.007**    | 0.639       |
| 14th day   | 6.52±2.42  | 3.74±1.00 | <0.001**        | <0.001**   | <0.001**    |
| 21st day   | 9.03±2.30  | 6.58±1.73 | <0.001**        | <0.001**   | 0.002**     |

Significance

| 1st day-14th day | <0.001** | <0.001** | -     | -     | -     |
| 1st day-21st day | 0.005**  | <0.001** | -     | -     | -     |
| 14th day-21st day| <0.001** | <0.001** | -     | -     | -     |

Table 2: Comparison of difference in SBP(mm Hg) in three groups studied
DBP Difference before and after the Test: The DBP difference was highest in the dysmenorrheic women (4.90±1.54) when compared to non dysmenorrheic women (4.06±0.63) on the 1st day which was moderately significant. The DBP change was lowest on the 14th day in the dysmenorrheic women (4.06±1.50) when compared to non dysmenorrheic women (2.26±0.68) which is statistically significant. (Table 3)

| DBP (mm Hg) | Group I | Group II | Overall P value | Pairwise significance |
|-------------|---------|----------|-----------------|-----------------------|
| 1st day     | 4.90±1.54 | 4.06±0.63 | 0.010**        | 0.030* 0.978          |
| 14th day    | 4.06±1.50 | 2.26±0.68 | <0.001**       | <0.001** <0.001**     |
| 21st day    | 4.13±1.71 | 3.48±0.89 | 0.148          | 0.127 0.470           |

Significance

- 1st day-14th day 0.021* <0.001** - - -
- 1st day-21st day 0.037* 0.005** - - -
- 14th day-21st day 0.873 <0.001** - - -

Table 3: Comparison of difference of DBP (mm Hg) in two groups
Pulse Rate Difference before and after the Test: There was not much difference in pulse rate on 1st day between all the groups. In dysmenorrheic women, there was difference in pulse rate when comparing the 3 episodes that is 1st, 14th day & 21st day. In non dysmenorrheic women, there was difference in pulse rate when comparing the 3 episodes that is 1st, 14th day & 21st day. (Table 4)

| Pulse(bpm) | Group I      | Group II     | Overall P value | Pairwise significance Group I-II |
|------------|--------------|--------------|-----------------|----------------------------------|
| 1st day    | 9.23±0.67    | 8.74±0.96    | 0.016*          | 0.110                            |
| 14th day   | 5.48±0.63    | 5.39±0.80    | <0.001**        | 0.901                            |
| 21st day   | 7.19±0.75    | 7.26±0.86    | <0.001**        | 0.959                            |

Significance

1st day-14th day <0.001** <0.001** - -
1st day-21st day <0.001** <0.001** - -
14th day-21st day <0.001** <0.001** - -

Table 4: Comparison of Pulse rate in three groups studied

DISCUSSION: The present study focuses on cardiovascular responses to experimentally induced pain in dysmenorrheic women and non dysmenorrheic women across menstrual cycle. Our results clearly demonstrated significant differences in cardiovascular responses before and after Cold pressor test. In healthy human subjects, CPT triggers an increase in BP. This may be due to an increased Cardiac Output during the initial period of the test with little increase in muscle sympathetic nerve activity, while an increase in this activity elevates peripheral resistances in the later period. Previous studies have demonstrated that the autonomic regulation of the heart in women varies across menstrual cycle. Previous study supports our findings that dysmenorrheic women have elevated Doppler indices in uterine arteries across the menstrual cycle. In a normal individual there is a delicate balance between sympathetic and parasympathetic divisions of autonomic nervous system. Activation of sympathetic division signifies sympathetic predominance and reduction of parasympathetic activity. Variation in cardiovascular response that is increased SBP and DBP change...
in the dysmenorrheic women is attributed to the activation of the sympathetic-adrenal-medullary axis (SAM axis) by painful stress. Two major physiological systems play an important role in stress response the catecholamine-producing Sympatho adrenal Medullary system and the cortisol-releasing hypothalamic-pituitary-adrenal (HPA) axis. When stressors act on the SAM system, BP, HR are promoted besides inducing peripheral vasoconstriction.

Some studies have shown that there appears to be a correlation between the hormonal levels in female hypothalamo pituitary-gonadal axis and the ANS control of their cardiac activity. Mehta et al have studied the autonomic functions in the different phases of menstrual cycle and reported significantly higher SBP and increased sympathetic activity in luteal phase compared to menstrual and follicular phases without significant differences in parasympathetic activity.

Estrogen has a significant action of increasing vagal and reducing sympathetic activity by enhancing the cholinergic muscarinic activity at both central and peripheral levels. Progesterone levels will be higher during luteal phase which will raise the SBP by increasing the fluid and salt retention. Pain induced during mental stress also causes the release of catecholamines into the systemic circulation.

Limitations of the Study: The study has a small sample size. We have included only 31 subjects. Hormonal assays could have been included for better evaluation.

CONCLUSIONS: We concluded that dysmenorrheic women had increased cardiovascular response to experimental pain across menstrual cycle when compared to non dysmenorrheic women which could be attributed to activation of Sympatho adrenal medullary system. Pain induced mental stress also causes increase in the levels of catecholamines in systemic circulation would result in increased cardiovascular response. Early detection of autonomic dysfunction before onset of any cardiovascular diseases in dysmenorrheic women would be beneficial in prevention of the same.

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