RESEARCH ARTICLE

A study of pain perception by cold pressure test in young females during the different phases of menstrual cycle

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ABSTRACT

Background: Menstruation is a cyclic physiological phenomenon showing fluctuations of various gonadal hormones. Gonadal hormones (estrogen and progesterone) influence pain sensitivity, the former strongly influences nociceptive actions; whereas the latter prevents neuropathic pain. Some previous studies have shown changes in pain sensitivity during menstruation. However, there is only little evidence present on the effects of gonadal hormones on experimental pain sensitivity.

Aims and Objectives: The aim of the present study is to differentiate in sensation of pain stimulus in terms of - pain threshold, pain tolerance, pain intensity, pain unpleasantness in females with normal menstruation during different phases through using cold presser test.

Materials and Methods: A total of 55 normal healthy females were enrolled in the study as per the eligibility criteria. Cold presser test was used as a pain stimulus source. The participants were instructed to hold their least dominant hand in the water bath as long as possible and were requested to inform the first sensation of pain which denoted the participants’ pain threshold. Time from pain threshold to the point where participants could no longer cope with pain and indicate stop, was recorded as pain tolerance. At this point, participants were directed to note pain intensity and unpleasantness on the visual analogue scale.

Results: The results showed that high significant pain intensity, pain unpleasantness, and pain tolerance level were highly significant during the follicular phase than the luteal phase.

Conclusion: In our study, we concluded pain perception difference across different phases of menstruation in the form of high significant pain intensity, pain unpleasantness, and pain tolerance during the follicular phase due to the hormonal fluctuation and the differences in autonomic nervous system reactivity these would be the underlying mechanism for these findings.

KEY WORDS: Menstruation; Gonadal Hormone; Pain Threshold; Pain Tolerance; Pain Intensity; Pain Unpleasantness

INTRODUCTION

Menstruation is a cyclic physiological phenomenon showing fluctuations of various gonadal hormones. The female menstrual cycle consists of three phases. The follicular phase, ovulation, and luteal phase in which secretion of various hormone occurs. Many of females had pain-related complaints at various phases of menstruation like migraines.[1] Sex hormone level alteration in reproductive-aged females has found a rheumatoid arthritis, irritable bowel disease, and Fibro Myalgia.[2-4] Additionally, there is an increased risk of temporomandibular pain in females using oral contraceptive pills and also in females on hormone replacement therapy in post menopause.[5] Cyclical fluctuation of gonadal hormone may increase pain sensitivity in women in form of migraine, premenstrual pain syndrome could influence role of hormone on clinical evidence base.[6] Some animal experiments have shown that the pregnancy-induced analgesia, reported also in humans[7] is mediated by changes in circulating 17 Beta Estradiol and progesterone that occurs as a natural
consequence of gestation. And further Gonadal hormone administration to gonadectomized female and male rats similarly increases pain threshold. However, various pain studies conducted in females in way to find out pain response during menstruation showed nonspecific findings. Hence, the present study is conducted to know how pain sensitivity is related to different phases of menstruation by cold pressure test.

MATERIALS AND METHODS

Study Design

It is a case–control study conducted at our college among 1st and 2nd year MBBS students after taking ethical committee permission. The participants included 55 Healthy Female Volunteers. After explaining, all details of test informed and written consent were taken.

Inclusion Criteria

The following criteria were included in the study:
1. Females in age between 18 and 22 years
2. Females with regular menstrual cycle (28 ± 4 days)
3. Females with body mass index <28 kg/m².

Exclusion Criteria

The following criteria were excluded from the study:
1. Females with any gynecological diseases
2. Females with any endocrine diseases
3. Females on hormone therapy
4. Females with alcohol/any drug abuse
5. Females with any acute or chronic pain disorders
6. Females with dermatitis at the site of pain stimulation.

Procedure

Cold presser test was used as a stimulus source. Participants asked to immerse their dominant hand (writing) into a 2–4°C water bath up to their wrist in Palm down position. The water level is above 5 cm from Wrist. The water bath was shaken manually for every 30 s, to prevent water from warming up around the skin. The temperature in the tub was measured with a thermometer and care was taken not to reach above 2–4°C. The participants were instructed to hold their dominant hand in the water as long as possible and were requested to inform the first sensation of pain which denoted the participants’ pain threshold. Time from pain threshold to the point where participants could no longer cope with pain and indicate stop after repeated motivation, was recorded as pain tolerance. At this point, participants were directed to note pain intensity and unpleasantness on the visual analog scale (0–10), 0 means no pain and 10 means worst pain. Heart rate (HR), systolic blood pressure (SBP), and digital blood pressure (DBP) were taken using an automatic sphygmomanometer while SPO₂ through pulse oximeter. To avoid any possible recording bias all the measurements related to pain responses were done by 1st author (AV) and measurements related to cardiovascular reactivity were done by 2nd author (HSG).

Statistical Analysis

All data were represented as mean ± standard deviation. Comparisons were using students unpaired t test and P < 0.05 was considered statistically significant.

RESULTS

Various findings of our study are shown in Tables 1-3. Table 1 shows finding of pain threshold and tolerance between the follicular and luteal phase of the menstruation. The mean pain threshold is significantly higher in follicular phase compared with luteal phase (P < 0.001). The Table 2 shows finding of pain intensity and unpleasantness between the follicular and luteal phase of the menstruation. The mean pain intensity and unpleasantness are significantly higher in follicular phase compared to luteal phase (P < 0.001) and Table 3 shows comparison of HR, DBP, SBP respiratory rate, and SPO₂ between follicular and luteal phase which is again statically significant.

DISCUSSION

Menstruation is cyclic phenomenon occurred on influence of various gonadal hormones. The present study has shown that mean pain threshold, pain intensity, and pain unpleasantness are significantly higher in follicular phase compared to luteal phase (P < 0.001).

| Table 1: Pain threshold and tolerance between follicular phase and luteal phase |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Parameters                  | Follicular phase (mean±SD)  | Luteal phase (mean±SD)      | t-value           | P-value             |
| Pain threshold (seconds)     | 9.46±3.4                    | 8.23±4.3                    | 1.664             | 0.0990              |
| Pain tolerance (seconds)     | 25.56±7.97                  | 17.68±7.24                  | 5.427             | <0.001**            |

**P<0.001

| Table 2: Pain intensity (mm) and pain unpleasantness (mm) through visual analog scale between follicular phase and luteal phase |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Parameters                  | Follicular phase (mean±SD)  | Luteal phase (mean±SD)      | t-value           | P-value             |
| Pain intensity (mm)         | 62.8±5.81                   | 59.2±6.25                   | 3.129             | 0.0023*             |
| Pain unpleasantness (mm)    | 59.1±6.85                   | 53.2±6.28                   | 4.708             | <0.001**            |

*P<0.01, **P<0.001
value significantly higher in follicular phase as compared to luteal phase of menstruation. We also found increased SBP and DBP during the luteal phase as compared to follicular phase of menstruation. The similar type high pain threshold in follicular phase was found reported by Hapidou and Decatanzaro.[14] Teepker et al. noted in 32 women with normal menstrual rhythm have increased pain threshold for cold between 1 and 14 day of menstruation,[15] on contrarily Hellström and Lundberg denoted increased pain threshold in second part of Menstruation.[16] Stening et al.[17] noted that follicular phase has prolonged activation time for hand cold pressure test when compared with Luteal Phase. Whenever Kowalczk et al.[18] noted no any significant changes in pain threshold in various phase of menstruation. In our study, we found high Pain tolerance in follicular phase. Rajni et al.[19] and Hapidou and Decatanzaro.[20] reported similar finding with our study. However, Stening et al.[21] have not noted any significant changes in 16 students. It is difficult to explain that why pain perception alters with various phase of menstruation. Some previous study denoted ovarian sex steroid hormone produced antinociception as an opioid mediated and results from the activation of spinal cord kappa and delta opiate receptors.[22] Many estrogen receptors are opioidergic and showing high opioid transcription on 17 Beta estradiol administration.[23] On the other side, one animal study showed that Estradiol does not modulate sensitivity of analgesic opioids effects in adult organism.[24] another animal studies noted that LH surge diminished analgesic effect of morphine may result from desensitization of brain opiate receptors.[25] Thus, one can speculate that hormonally induced (ovulation) opiate receptor desensitization could enhance pain sensitivity among females during luteal phase.

In our study, we found increased SBP and DBP during the luteal phase as compared to the follicular phase which is similar to Mendapara study[26] due to increase circulating catecholamine levels.

### Strength of Study
In our study, we used standardized methodology for pain evaluation and strictly following in the coherence of menstruation phases.

### Limitation of Study
In our study, we do not assess hormonal level only menstruation phases consider.

### CONCLUSION
We concluded from our study that pain sensitivity varies across the menstrual cycle due to hormonal fluctuation and differences in autonomic nervous system reactivity, these would be the underlying mechanism for these finding.

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### REFERENCES


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**Table 3: Heart rate, diastolic blood pressure, systolic blood pressure, respiratory rate, and SPO₂ between follicular phase and luteal phase**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Follicular phase (mean±SD)</th>
<th>Luteal phase (mean±SD)</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>76±7.02</td>
<td>73±7.78</td>
<td>1.415</td>
<td>0.1598</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>73.94±7.86</td>
<td>78.26±6.28</td>
<td>2.949</td>
<td>0.0039*</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>116.53±8.71</td>
<td>123.9±8.88</td>
<td>4.770</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>SPO₂</td>
<td>98±1.2</td>
<td>97±1.0</td>
<td>4.748</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>13±1.56</td>
<td>15±1.69</td>
<td>6.449</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

*P<0.01, **P<0.001


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