

Study of Pain Perception in Different Phases of Menstrual Cycle

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ABSTRACT

Background: Pain is an unpleasant sensation induced by noxious stimuli which is detected by the peripheral afferent nociceptors. In most studies, women report lower pain threshold, more frequent pain and pain of longer duration as compared to men. Earlier studies in animals suggest that gonadal hormones can modulate sensitivity to nociceptive stimuli. Understanding the relationship between the menstrual cycle and pain can contribute significantly to our knowledge of pain processing in women. The present study was undertaken to find out the differences in pain perception during different phases of menstrual cycle.

Materials and Methods: The study was a cross sectional study, carried in 65 females in a tertiary hospital. It was aimed to evaluate the variation in the pain perception; pain threshold and pain tolerance in different phases of menstrual cycle i.e. menstrual, follicular, ovulation, early luteal and late luteal phase using cold pressor test.

Results: The pain threshold and pain tolerance was significantly increased during late luteal phase i.e there was a decrease in pain perception during late luteal followed by follicular phase.

Conclusion: The pain perception varied during different phases of menstrual cycle. This difference was might be due to change in the levels of gonadal hormones during different phases of menstrual cycle.

Keywords: Pain Threshold, Pain Tolerance, Gonadal Hormones, Menstrual Cycle.

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INTRODUCTION

The word "pain" comes from the Greek: poinē, meaning penalty.¹ International Association for the Study of Pain (IASP) has defined pain as '...an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'.¹

Sex differences in the perception of noxious experimental stimuli have been reported by various groups, with women exhibiting higher pain sensitivity than men.² Contradictory reports, however, exist. Fillingim and Maixner³ reviewed 34 human experimental studies and found sex related differences in only two-thirds of them. Recently, it has been observed pain as a physiological process and its perception varies amongst individual.⁴ A another study done by Guillermo A. Cecchi and Lejian Huang showed that a subjective percept such as pain displays a highly deterministic behaviour.⁵

Laura D. Wandner and Cindy D. Scipio also investigated new measures of race/ethnic and age related stereotypic attributions of pain sensitivity and willingness to report pain.⁶

Tashani et al and Alabas et al showed sex differences in pain. This study measured the responses of Libyan men and women to cold pressor pain and found Libyan women had higher pain sensitivity response to cold pressure pain than did Libyan men.⁷ Harman-Boehm et al have investigated the possible influence of menstrual cycle phase on fluctuations in more natural or usual pain experiences.⁸ Another study also shown increase in pain perception among females during their menstrual or perimenstrual period was significantly greater than their postmenstrual period.⁹ A. Ahmed, F. Khan, M. Ali, showed the effect of the menstrual cycle phase on post-operative pain perception.¹⁰ Dao et al noted that reproductive hormones may play a role in temporo-mandibular disorders. They found, in a pilot study, that women with myofascial pain of the masticatory muscles, not consuming oral contraceptive showed considerably more variance in pain estimates than those who used the pill. For the non-users, peaks of pain were observed at the menstrual and premenstrual phases of the menstrual cycle.¹¹

A number of reports have examined possible links between ovarian function and rheumatoid arthritis (RA) and other autoimmune diseases.¹² Both the experimental and clinical data suggest that the menstrual cycle may modulate pain, but there was a lack of consensus regarding which phase is associated with greater or lesser degrees of pain perception. The aim of the study was to find, any variations in pain perception (pain threshold and pain tolerance) during different phases of menstrual cycle using cold pressure test.

MATERIALS AND METHODS

The study was a cross sectional type of study. The study was carried out on 65 female resident doctors of age 23- 30 years from a tertiary hospital. Written informed consent was obtained from the participants and ethical Committee approval was taken before the start of the study. Subject with history of regular menstrual cycle of 28-30 days was included in the study. Individual with history of menorrhagia, metrorrhagia, dysmenorrhoea, breast feeding, chronic smoking, acute illnesses during past one month, chronic diseases such as diabetes mellitus, hypertension, chronic pain diseases like spondylitis, rheumatoid arthritis, neuritis and migraine, consuming medication such as oral contraceptive pills currently or until 6 months prior to study, consuming medicines like Tricyclic antidepressant, serotonin reuptake inhibitor, analgesics like paracetamol, NSAID's were excluded from the study. The participants were asked to note the daily basal body temperature using the thermometer just immediately after awakening but before undertaking any physical activity. Temperature was recorded from the onset of menstruation till the day when there was a rise of temperature of 0.5 degree

Fahrenheit or 0.24 degree Celsius above the temperature noted on 1st day of menstruation. The participant was instructed to inform the chief investigator about it on the same day. The participants were asked to report for the study on the following days for noting pain threshold & pain tolerance time. Menstruation phase reading was noted on the 2-4th day after the onset of menstruation, follicular phase on 10-12th day from the 1st day of menstruation, ovulation phase within 24 hours after rise of basal body temperature i.e. 0.5 degree Fahrenheit or 0.24 degree Celsius, early luteal phase on 2-4th day after ovulation, late luteal phase on 6-9th day after ovulation.

Method of Hand Cold Pressor Test

A container filled with cold water, maintained at 4 degree Celsius was used. Its temperature was recorded immediately before initiating the test. A water circulator was used to prevent the water near the subject's hand from warming. At the onset of the test, subjects were instructed to immerse their hand completely up to the wrist joint and to remain still.

Subjects were instructed to indicate when the sensations in their hand first become painful (pain threshold) and when they were no longer able to tolerate the pain (pain tolerance).

A maximum time limit of 5 minute was imposed on each participant but the participants were not informed prior of this time limit.

Statistical Analysis

The data was statistically analysed using Freidman non parametric repeated measure ANOVA to determine if there were significant ($P < 0.05$) differences in nociception responses (pain threshold and pain tolerance) during the different phases of menstrual cycle.

Table.1 Mean of pain threshold (seconds) in five phases of menstrual cycle

| Phase | Menstrual | Follicular | Ovulation | Early Luteal | Late Luteal |
|---------|-------------|-------------|-------------|--------------|-------------|
| Mean(X) | 55.538 | 60.292 | 51.661 | 58.969 | 69.384 |
| X + SD | 55.538+7.26 | 60.292+7.37 | 51.661+5.16 | 58.969+5.64 | 69.384+6.42 |

Table.2 Comparison of pain threshold of late luteal phase with other phases

| Phase | Menstrual | Follicular | Ovulation | Early Luteal |
|---------|-----------|------------|-----------|--------------|
| P-value | <0.001 | <0.001 | <0.001 | <0.001 |

Table.3 Comparison of pain threshold of follicular phase with other phases

| Phase | Menstrual | Ovulation | Early Luteal | Late Luteal |
|---------|-----------|-----------|--------------|-------------|
| P-value | <0.05 | <0.001 | >0.05 | <0.001 |

Table.4 Mean of pain tolerance in the five phases of menstrual cycle

| Phase | Menstrual | Follicular | Ovulation | Early Luteal | Late Luteal |
|---------|-----------|------------|-----------|--------------|-------------|
| Mean(X) | 184.584 | 201.138 | 112.953 | 177.984 | 212.507 |
| X+SD | 7.191 | 16.306 | 17.646 | 11.749 | 13.605 |

Table.5 Comparison of pain tolerance of late luteal phase with other phases

| Phase | Menstrual | Follicular | Ovulation | Early Luteal |
|---------|-----------|------------|-----------|--------------|
| P-value | <0.001 | >0.05 | <0.001 | <0.001 |

Table.6 Comparison of pain tolerance of follicular phase with other phases

| Phase | Menstrual | Ovulation | Early Luteal | Late Luteal |
|---------|-----------|-----------|--------------|-------------|
| P-value | <0.001 | <0.001 | <0.001 | >0.05 |

OBSERVATIONS AND RESULTS

The participants were of age 23-30 years with a mean age 26.69±1.667 yrs. Pain threshold and pain tolerance was measured using cold pressor test in the 5 different phases of menstrual cycle.

It was found that pain threshold during late luteal phase shows a significant difference with all other phases i.e. menstrual, follicular, ovulation and early luteal (P-value<0.001) while follicular phase shows a significant difference with menstrual phase (P-value <0.05), ovulation phase and late luteal with (P-value <0.001) and no difference with early luteal phase (P-value >0.05).

On Comparison of pain tolerance, late luteal phase shows a significant difference with menstrual, ovulation and early luteal phase (P-value<0.001) and shows no significant difference with follicular phase (P-value>0.05). Follicular phase shows a significant difference with menstrual, ovulation phase and early luteal (P-value <0.001).

DISCUSSION

In the present study it was found that there was a variation in the pain perception, with an increase in pain threshold and pain tolerance during late luteal (20-23rd day) and follicular phase (10-12th day). The variation in pain perception in the present study was might to be due to gonadal and hypothalamo-pituitary hormones, as there is change in the level of these hormones during the phases of menstrual cycle. A study done by Dao et al noted that reproductive hormones may play a role in temporomandibular disorders.¹¹ In the present study the increase in pain threshold and pain tolerance during late luteal phase might be due to increase in both progesterone and estrogen which occur approximately between 16th to 24th day of the menstrual cycle. Both progesterone and estrogen have a nociceptive effect and the increase in pain threshold and pain tolerance in the late luteal phase than other phases might be due to the additive effect of these hormones.^{13,14} Antinociceptive effect of estrogen was shown in the study carried out by done by Smith et al. The study showed a direct proportional relationship between the pain threshold and estradiol levels in women, high estrogen levels increase the number of opioid receptors, activating a state of analgesia. When the estrogen levels were low there was a reduction in the number of opioid receptors in areas of the brain associated with analgesia such as the thalamus, the nucleus accumbens and the amygdala, the areas associated with hyperalgesic responses.¹⁵ The mechanism by which progesterone produces antinociceptive response was unclear. A study done by Caba et al showed progesterone metabolites, acting through the GABA_A receptor, were responsible for the analgesic actions in female rats.¹⁶ The results of the present study is in concordance with the study done by Hellstrom et al and Lundberg et al.¹⁷ Another study carried out by Stening et al and Eriksson et al showed decreased pain threshold during late luteal phase compared to late follicular, the results was slightly contrast to the current study.¹⁸ The result might have varied due to the differences in the days on which the test was performed.

The increase in pain threshold and pain tolerance during follicular phase in the present study can be attributed to the rise in estrogen level which occurs during follicular phase. The estrogen levels start rising approximately on day 10 and peaks till day 14. The LH level is also low during this period which is known to have a nociceptive effect.¹⁹ A study done by Stening et al showed, when

estradiol levels are high, women are not very different from men in terms of the threshold of pain.¹⁸ As there is only increase in estrogen during follicular phase the pain threshold and pain tolerance is slightly less than the late luteal phase in the present study. Studies on pain perception often showed differences in their findings when pain perception was taken as measure. The division of phases or the days when the readings were noted vary amongst the studies and also the pain perception is a subjective finding that might results in the variation in the findings of various studies. This discrepancies among the studies showing variation in pain perception in different phases due to the effect of gonadal hormones can be removed after an hormonal study on a large sample and this will also help to categorise the menstrual cycle in to exact phases and thus might remove the conflicts between the results of the various studies and might predict the exact phase of the menstrual cycle when there is change in pain perception.

CONCLUSION

The pain perception (sensitivity) varied during different phases of menstrual cycle with decrease in pain perception during late luteal followed by follicular phase. This difference was might be due to the change in the levels of gonadal hormones during different phases of menstrual cycle. The discrepancies among the studies showing variation in pain perception during different phases due to gonadal hormones can be addressed by performing a hormonal study on a large sample.

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