Trakia Journal of Sciences, Vol. 12, Suppl. 1, pp 376-380, 2014
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Available online at:
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ISSN 1313-7050 (print)
ISSN 1313-3551 (online)

PAIN PERCEPTION TO THE COLD PRESSOR TEST IN REPRODUCTIVE-AGE WOMEN: RELATION TO MENSTRUAL PHASE AND COMPARISON WITH MEN

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ABSTRACT

PURPOSE. To evaluate the response to cold pressor pain in normally menstruating women during the two phases of the menstrual cycle and in comparison to men. METHOD. 60 volunteers, separated in two groups of women (in follicular phase - gr. 1, n = 18; and in luteal phase – gr. 2, n = 21) and men - gr.3 (n = 21), were subjected to cold pressor test. Latency to first feel pain (pain threshold) and latency to withdraw the arm from the icy water (pain tolerance) were recorded. Participants completed questionnaires assessed health, anger and stress state. RESULTS. The data revealed statistically significant differences ($F = 8.12$, $p<0,001$) between women in two groups, and men, in pain tolerance. Women reported significantly more pain symptoms than did men. Women in follicular phase displayed longer pain tolerance than did women - in luteal. CONCLUSIONS. 1. Men tolerated more pain than women. Moreover, attitudes and role expectations are likely to play key roles in this difference, since no gender difference was found for pain threshold. 2. The menstrual phase difference assessed seems to be dependent on the serum concentration of estrogen as far as possible that this hormone level is high in follicular phase.

Key words: cold pressor test, pain tolerance, pain threshold, sex differences, menstrual phase

INTRODUCTION

The most current human findings regarding sex differences in experimental pain indicate greater pain sensitivity among females compared with males for most pain modalities (1). Compared with men, women display enhanced sensitivity to most forms of experimentally induced pain.

The majority of studies show that women are more sensitive than men to experimentally induced cold pain as evidenced by lower pain tolerance (2, 3).

The aim of the study was to compare perception of pain, induced by the cold pressor test in women and men and women's response to cold nociceptive irritant in dependence of menstrual cycle. We decided to examine and compare our data with these of Hellström & Lundberg (4) and several other investigators (5, 3).

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METHODS

Subjects. Sixty healthy volunteers: 39 female - students, aged between 19 and 37 years, with regular menstrual cycle (28 ± 4 days), without hormonal treatment during the past 12 months, separated in two groups: gr.1. - in follicular phase and gr. 2. - in luteal phase and 21 men, aged 27 (SD = 4) years) were included. Exclusion criteria were use analgesics, and for women not taken oral contraceptives. In all the study, we strongly observed the rules of the the local ethical committee at Trakia University and the principles of the Declaration of Helsinki (1964). An informed consent was obtained from all participants before initiation of the experimental procedures. They were informed

that they could discontinue the study whenever they wanted and without giving any reason for their decision.

Experimental procedure.
Cold pressor test. The dominant hand was immersed up to the wrist in ice-chilled water (4 ± 0.5°C). The participants were instructed to hold their hand in the water as long as possible. Before each cold water immersion, the experimenter read a standardized script describing the procedures to the participant and measured blood pressure and heart rate. Latency to first feel pain (pain threshold, PThr) and latency to withdraw the arm from the cold water (pain tolerance, PTol) were recorded (4- 6).

Questionnaires. Participants completed questionnaires about their socio-demographic background and three scales: Subjective health assessment scale (7), Optimism and Negative Expectations Inventory (8) State-Trait Anger Expression Inventory (9).

Statistical analysis. All statistical analyses were performed using SPSS v. 12.01, (SPSS, Chicago, IL). Analysis of variance (ANOVA) was used to determine the significance of differences between groups. To analyze differences in pain measures within groups paired t- tests were used. Differences were considered significant when $p < 0.05$. Two different models were used, which was to evaluate pain sensations in relation to sex, and the different menstrual phases.

RESULTS

Sex differences.

Pain tolerance(PTol). 8 men and 2 women reached the 7 min cut-off limit without lifting up their hands. The PTol for these participants was recorded as 420 sec. A paired t-test for women and men showed a significant effect of the gender, $t_{(27)} = 2.90$, $p<0.05$ in pain tolerance. The data revealed statistically significant differences between women in two menstrual phases, and men, in pain tolerance, $F_{(1,38)} = 8.12$, $p<0,01$ **(Figure 1)**. Men tolerated more pain than women, as performed by the time of latency of withdraw the arm from the cold water upon cold pressor test.

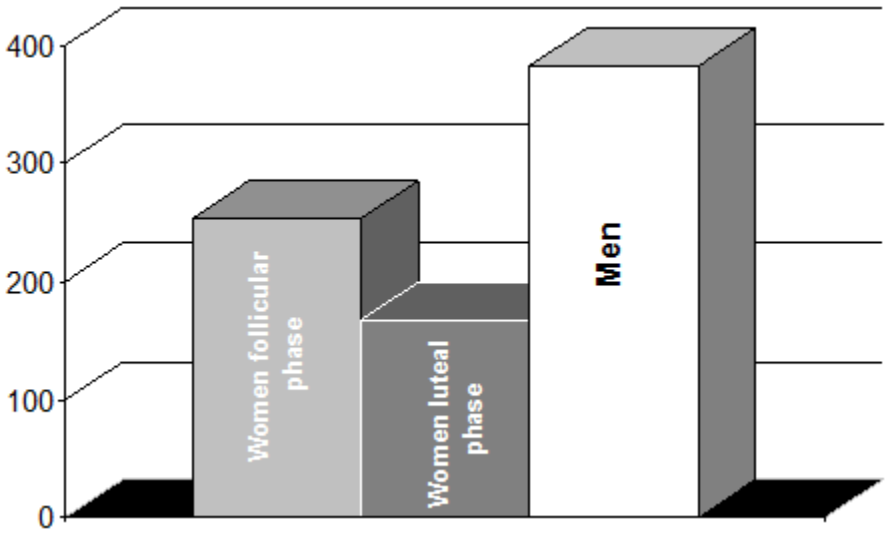

Figure 1. Mean values in pain tolerance (latency to withdraw) between menstrual phases for women and men. $F_{(1.38)} = 8.12$, $p<0.001$

Relationship between menstrual phase and pain sensation. Statistically there was significant difference in pain tolerance between menstrual phases for women. Women in follicular phase displayed longer pain tolerance **(Figure 2)**. The time of influence in the cold pressor stimulus (latency to withdraw) was significantly reduced ($p<0.05$) during the luteal phase compared with the follicular phase.

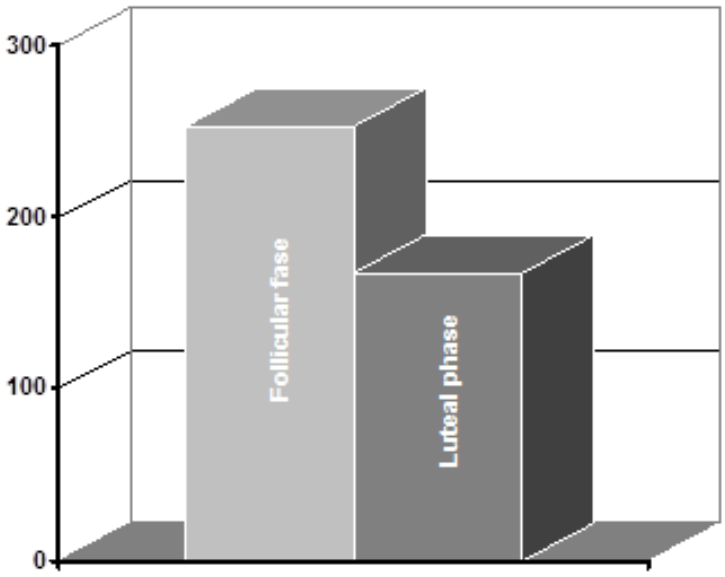

Figure 2. Mean values in pain tolerance between menstrual phases for women. $t_{(27)} = -1,67$, $p<0.05$

Pain phteshold(PThr). There was no significant gender difference in latency to first feel pain (PThr), as measured by the time until the pain was reported **(Table 1).**

Data from Questionnaires. Women reported significantly more stress symptoms ($p<0.05$) than did men **(Table 2).**

Table 1. *Cold pressor test. Mean Values and Standard Deviation(SD) in Perceived Pain for men and women at Pain Threshold and Pain Tolerance*

	Men		*Women in follicular phase*		*Women in luteal phase*		
Perceived Pain	***M***	***SD***	***M***	***SD***	***M***	***SD***	***F***
Pain threshold	48,8	8,23	42,4	13,33	57,1	27,06	,195
Pain tolerance	384,3	20,21	253,7	47,61	167,6	43,87	8,12*

*) $p<0,01$

Table 2*. Mean values (M) and Standard Deviations (SD) for Stress and Anger levels during the experiment, Frequencies and Intensities in Common Pain Symptoms.*

	Men		*Women*		
	M	***SD***	***M***	***SD***	***t***
Stress symptoms	29.0	3,06	35,9	2,49	-2,17*
Anger	384,3	20,21	167,6	43,87	8,12*

*) $p<0,05$

DISCUSSION

The first finding of the present study was that Men tolerated more pain than women, as performed by the time of latency of withdraw the arm from the cold water upon cold pressor test. On the other hand, no significant gender difference was found in pain threshold. The previous data suggest that gonadal hormones play complex roles in pain perception, which may be either pronociceptive or antinociceptive, depending on the hormone profile. The gender difference, showing higher pain tolerance in men than in women, is consistent with findings of Hellström & Lundberg (4) and several earlier

findings (10). Jones et al (11) observed sex-related differences for cold pain tolerance but not threshold. It appears that sex differences in cold pain are consistent, particularly for suprathreshold measures such as tolerance. Moreover, attitudes and role expectations are likely to play key roles in this difference, since no gender difference was found for pain threshold.

1. The present study provides evidence that pain responses vary across the menstrual cycle and that these differences are probably related to differences in hormone levels. The time of influence in the cold pressor stimulus (latency to withdraw) was significantly reduced during the luteal phase compared with the follicular phase. The follicular phase is characterized by high estrogen levels. These results support the conclusion of Hellstrom & Lundberg (2000) that "Women were less sensitive to pain at a time when circulating estrogen levels generally are high". Moreover, experimental (12, 13) and clinical data have reported a clear antinociceptive role of estrogens (14, 15) probably by means of the role of estrogens to play in the regulation of opiate expression (16, 17). Several other investigators (18, 5) find that the results of both animal and human experiments are inconsistent. Since sex hormone levels were not measured in the present study, the influence of other factors associated with the two phases of the menstrual cycle can not be excluded.

CONCLUSION

1. Men tolerated more pain than women, as as performed by the time of latency of withdraw the arm from the cold water upon cold pressor test. Moreover, attitudes and role expectations are likely to play key roles in this difference, since no gender difference was found for pain threshold.

2. Pain tolerance evoked by the cold pressor test, is increased during the follicular phase in normal menstruating women. This menstrual phase difference seems to be dependent on the serum concentration of estrogen as far as possible that this hormone level is high in follicular phase. Successive measurements of estrogens and progesterone are necessary in order to determine the role of sex hormones in women's pain perception.

Acknowledgments. This study was supported by Grant 8/2013 from the Medical Faculty, Trakia University, Stara Zagora, Bulgaria.

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