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Indian Journal of Clinical Anatomy and Physiology

Journal homepage: https://www.ijcap.org/

Original Research Article

Effect of hormonal supplementation on pain tolerance in women– A comparative study

Bhavya Reddy V[1,*], M Sahithi[1], O Padmini[2]

[1]*Osmania Medical College, Hyderabad, Telangana, India*
[2]*Dept. of Physiology, Osmania Medical College, Hyderabad, Telengana, India*

ARTICLE INFO

Article history:
Received 24-04-2021
Accepted 25-07-2021
Available online 01-03-2022

Keywords:
Hormal supplementation
Cold intolerance

ABSTRACT

Introduction and Objectives: Gonadal hormones (oestrogen and progesterone) influences pain sensitivity, the former strongly influences nociceptive actions, whereas the latter prevents neuropathic pain. However, there is only little evidence on direct effect of hormonal based drugs on experimental pain response. Therefore the aim of the present study is to the difference in response to pain stimulus in terms of - pain threshold, pain tolerance, pain intensity, pain unpleasantness between women on OCP pills, normal menstruating women and age matched men using cold pressor test.

Materials and Methods: Total of 50 females (20-35 years age group) on COCP pills, 50 controls (normal menstruating women of 20-35 years age group) and 50 healthy males (20-35 years age group) were enrolled in the study as per the eligibility criteria. Cold pressor test was used as a stimulus source. The participants were instructed to hold their least dominant hand in the water bath (maintained between between 0°C and 2°C) 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.Statistical analysis of data was done using standard SPSS software. Data was represented as mean standard deviation. Chi-square test was done and p values <0.05 were considered significant.

Results: Average pain tolerance was significantly (p<0.00) higher in women on COCP (combined oral contraceptive pill) therapy compared to naturally menstruating women. But men and women on COCP pill therapy do not differ significantly in average pain tolerance. The average pain threshold did not differ significantly between any age groups. The average pain unpleasantness was less in females taking hormonal pills compared to men and naturally menstruating women establishing the role of increased levels of sex hormones in reducing the discomfort and unpleasantness. There was no significant difference in average pain intensity between men and normal women but it differed significantly between normal women and women on COCP therapy.

Conclusion: The use of COCP affects the pain reporting of subjects.

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1. Introduction

Gonadal hormones (Oestrogen and Progesterone) influence pain sensitivity, the former strongly influences nociceptive actions, whereas the latter prevents neuropathic pain. However, there is only a little evidence on the direct effect of hormonal based drugs on experimental pain response. Animal experiments have shown that the pregnancy induced analgesia, reported also in humans[1] is mediated by changes in circulating 17 Beta estradiol and progesterone that occurs

* *Corresponding author.*
E-mail address: bhavya.reddy0910@gmail.com (B. Reddy V).

https://doi.org/10.18231/j.ijcap.2022.003
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as a natural consequence of gestation[2,3] and further gonadal hormone administration to gonadectomized female and male rats similarly increases pain threshold.[4,5] Testosterone has also been shown to modulate pain sensitivity in mammals.[6,7]

Previous studies have reported that there is no association between pain and menstrual cycle in females.[8] However, there are also controversial reports stating that cyclical sex hormone levels do have an impact on pain response and pain threshold.[9–11] The data is inadequate on the different aspects of pain in women receiving Combined Oral Contraceptive Pills (COCP)compared to women not receiving COCP. Furthermore, the comparison has not been made with age matched males.

2. Aim

The aim of the present study is to investigate the effect of hormonal COCP on pain sensitivity response in women receiving COCP and comparing the same with naturally menstruating women and age matched males.

3. Objectives

1. To study the difference in response to pain stimulus in terms of following parameters - Pain threshold, Pain tolerance, Pain intensity, Pain unpleasantness, between women on COCP and normally menstruating women using cold pressor test.
2. To study the difference in patterns of pain perception between women on COCP pills and age matched males.

4. Materials and Methods

4.1. Study design

It is a case control study conducted in a specialty hospital under Upgraded Department of Physiology, Osmania Medical College. The participants included 50 females (20-35 years age group) on COCP pills, 50 controls (normal menstruating women of 20-35 years age group) and 50 healthy males (20-35 years age group).

4.2. Study period

2 months.

4.3. Inclusion criteria

1. Group 1- Female participants using combined oral contraceptive pill therapy were included and were requested to state if the previous pill cycle was taken correctly (on time and no misses).
2. Group 2- Females menstruating naturally and not taking any contraceptive pills or using any contraceptive devices were included.
3. Group 3- Healthy age matched males.

4.4. Exclusion criteria

1. Participants suffering from chronic diseases and those taking any analgesics at least 48 hours before the onset of study were excluded from the study.
2. Female participants using mini pill were excluded as it comprises only one hormone (progesterone).

4.5. Procedure

Cold pressor test was used as a stimulus source. Participants standardised their hand skin temperature by immersing their least dominant hand (non-writing) into a 32°C water bath (human body skin temperature) for 3 minutes. After 3 minutes, the participants were asked to immediately immerse their hand up to their wrist in an ice chilled water bath maintained between 0°C and 2°C.

The water bath was shaken manually for every 30 seconds, 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°C. The participants were instructed to hold their least 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, was recorded as pain tolerance. At this point participants were directed to note pain intensity and unpleasantness on the visual analogue scale.

4.6. Statistic analysis

Statistical analysis of data was done using standard SPSS software. Data was represented as mean standard deviation. Chi-square test was done and p values <0.05 were considered significant.

4.7. Implications

Several studies have proved that female hormones (oestrogen and progesterone) have definite effects on pain perception and tolerance. But there is no sufficient data on hormonal (COCP) supplementation effect on pain perception in women. At the end of the study we were able to draw a comparison between pain perception in women on COCP with normal menstruating women and add to the existing literature regarding the effect of hormonal supplementation on pain response. Further, this study also compares the pain sensitivity response in women and age matched males.

Data expressed are mean+ standard deviation. Analysis was done using standard SPSS software. COCP: Combined Oral Contraceptive Pill.

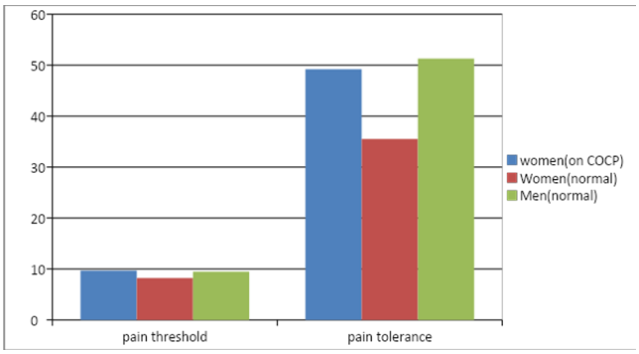
Table 1: Group differences in pain responses to the cold pressor test

	Women (on COCP)	Women (menstruating naturally)	Men
Pain Threshold (sec)	9.66±3.31	8.23±4.3	9.46±3.4
Pain Tolerance (sec)	49.2±21.38	35.5±11.82	51.3±23.8
Pain Intensity (mm)	59.2±6.25	68.5±6.99	62.8±5.81
Pain Unpleasantness(mm)	53.2±6.28	67.4±7.21	59.1±6.85

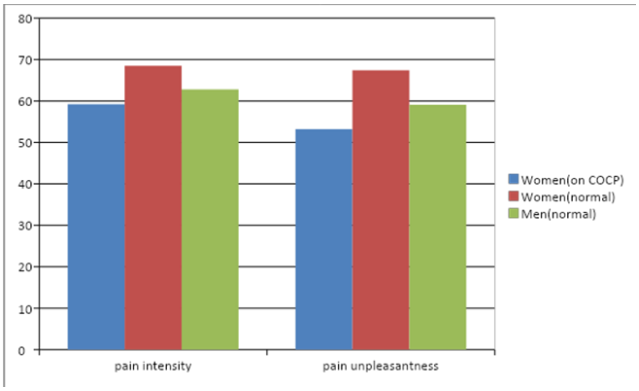
Table 2: Comparison of different parameters of pain between the groups. Values given in P

	Women (on COCP)		Women(normal)		Men	
	Men	Women (normal)	Men	Women (on pill)	Women (normal)	Women (on pill)
Average pain Threshold	0.84	0.31	0.22	0.31	0.22	0.84
Average pain Tolerance	0.08	0.00*	0.00	0.00	0.00	0.08
Average pain Intensity	0.54	0.02*	0.06	0.02	0.06	0.54
Average Pain Unpleasantness	0.19	0.00*	0.01	0.00	0.01	0.19

Significant differences (P) using chi-square test, *represents P<0.05.



Graph 1: Significant difference in Pain threshold and tolerance between women on the pills and naturally menstruating women. (Units expressed in Seconds)



Graph 2: Significant difference in Pain Intensity and Unpleasantness between women on COCP (combined oral contraceptive pills) and women menstruating normally. (Units in millimetres)

5. Results

Average pain tolerance was significantly (p<0.00) higher in women on COCP (combined oral contraceptive pill) therapy compared to naturally menstruating women. But men and women on COCP pill therapy do not differ significantly in average pain tolerance. The average pain threshold did not differ significantly between any age groups. The average pain unpleasantness was less in females taking hormonal pills compared to men and naturally menstruating women establishing the role of increased levels of sex hormones in reducing the discomfort and unpleasantness. There was no significant difference in average pain intensity between men and normal women, but it differed significantly between normal women and women on COCP pill therapy.

6. Discussion

The results differed significantly(p<0.05) between naturally menstruating women and women on hormonal pill therapy. But there was no significant difference between men and women taking COCP pills. The differences in average pain threshold are not significant for all the three study groups (Graph 1). However, women menstruating naturally found pain more unpleasant compared to women using contraceptive pills (Table 1, Graph 2), possibly due to increased circulating hormone levels enabling women using COCP pill therapy to cope up better with pain or potentially mask pain. The average pain tolerance in females normally menstruating was significantly (p<0.00) lower than females on pill therapy (Graph 1). Interestingly the average pain tolerance in females on COCP pill therapy was less than normal males but not to a significant extent[9] (Table 1, Graph 2). This is in accordance with most literature

on gender difference.[9] Finally, my study emphasizes the influence of hormones on the opioid analgesic system. However, personality factors also may play a role in modifying pain responses in both genders.[10]

7. Conclusion

This study highlights the fact that the use of hormone based contraceptive drugs affect the pain reporting of subjects and hence health care professionals should make a note of women who are using hormonal contraceptives while eliciting pain sensation for varied reasons.

8. Limitations of the Study

1. In this study the subjects were only age matched. They were not height and body weight matched.
2. Only one type of stimulus (cold was used
3. Pain responses are known to vary across menstrual cycles due to differences in blood hormonal levels. In this study the female participants belonged to different menstrual phases.

The above limitations could be minimised for a better analysis of the subject.

9. Conclusion

Cold stimulus was utilised to study pain threshold, tolerance, intensity and unpleasantness in normally menstruating women, women on COCP pill therapy and normal age matched males. Significant increase in pain tolerance was noted in females on pill therapy as compared to normal females, though less than normal males, indicating influence of sex hormones on pain pathway.

10. Source of Funding

None.

11. Conflict of Interest

The authors declare no conflict of interest.

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Author biography

Bhavya Reddy V, Final Year MBBS

M Sahithi, Final Year MBBS

O Padmini, Professor

Cite this article: Reddy V B, Sahithi M, Padmini O. Effect of hormonal supplementation on pain tolerance in women– A comparative study. *Indian J Clin Anat Physiol* 2022;9(1):9-12.