

Original Article

# Hormonal contraceptive pill effect on pain sensitivity response

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## Abstract

**Background and Aim:** Estrogen strongly influences nociceptive actions, whereas progesterone prevents the neuropathic pain. However, there is only a little evidence on the direct effect of hormonal-based drugs on the experimental pain sensitivity response. Therefore, the aim of the present study was to investigate the effect of hormonal combined oral contraceptive pill (COCP) on pain sensitivity.

**Methods:** A total of 45 participants (15 men [control], 15 women [using COCP], and 15 women menstruating naturally) were subjected to cold pressor test. Participants relaxed their least dominant arm in a 32°C water bath (3 min) and then the hand was plunged into an ice slurry bath (0°C–2°C). The time taken for the participant to report the pain was recorded as pain threshold. The time from pain threshold to the participant no longer able to tolerate the pain was recorded as pain tolerance. Pain intensity and pain unpleasantness were recorded using the visual analog scale.

**Results:** The pain tolerance was significantly greater ( $P = 0.02$ ) in women using COCP compared to control women (women not on COCP) and men. The pain unpleasantness was significantly decreased ( $P = 0.04$ ) in COCP women compared to control women (women not on COCP) and men.

**Conclusion:** Women using COCP have more tolerance and less unpleasantness to the pain threshold. They appear to respond differently than women menstruating naturally to cold pressor pain, which may be due to psychological, social, or environmental factors that need to be evaluated in future studies.

**Key words:** Cold pressor test, combined oral contraceptive pill, pain intensity, pain response, pain threshold, pain tolerance, pain unpleasantness

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## INTRODUCTION

Currently, the male sex hormone, testosterone, and its effects on nociceptive response have not been fully elucidated.<sup>[1]</sup> Comparatively, female sex hormones (estrogen and progesterone) have been studied worldwide, suggesting an influence of endogenous hormonal fluctuation throughout the females 28-day menstrual cycle on pain sensitivity.<sup>[2,3]</sup> Previous studies have reported that there is no association between pain and menstrual cycle in females.<sup>[4]</sup> However, there are also controversial reports saying that sex hormones do have an impact on pain response and pain threshold.<sup>[5,6]</sup>

The previous study has also shown that sex hormones have an influence on some of the pain-specific conditions such as temporomandibular joint disorders.<sup>[3]</sup> However, the data are inadequate on the different aspects of pain in women receiving combined oral contraceptive pill (COCP) compared to women not receiving COCP. Furthermore, the comparison has not been made with age-matched males. Therefore, this study was conducted

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to assess the difference in pain parameters in women receiving COCP with women not receiving COCP and with males.

## MATERIALS AND METHODS

### Participants

This study was approved by Leeds Beckett University Ethics Local Committee. Forty-five participants were divided into three groups: Group 1: 15 women using COCP, Group 2: 15 women menstruating naturally, and Group 3: 15 men [Table 1].

### Inclusion criteria

Group 1: Female participants using contraceptive pill therapy were included if they used a combined pill comprising estrogen and progesterone and were requested to state if the previous pill cycle was taken correctly (on time and no misses). Users of the mini-pill were eliminated, as it comprises only one hormone (progesterone) and is taken continuously with no breaks, unlike the combined pill, which more closely resembles the natural menstrual cycle (21 days on the pill, 7 days break).

**Table 1:** Comparison of age, height, and body weight of three groups (n=15) in each group

	Men	Women (not receiving COCP)	Women (receiving COCP)	P
Age (years)	23.60±6.4	22.1±2.8	20.8±0.9	0.18
Height (cm)	117.8±7.4	162.3±6.8	165.7±6.0	0.00*
Weight (kg)	79.8±13.4	62.7±9.9	64.5±9.0	0.00*

Data expressed are mean±SD. Analysis was done by one-way ANOVA and *post hoc* by Tukey-Kramer test. *P*<0.05 considered significant. SD: Standard deviation, COCP: Combined oral contraceptive pill

Group 2: Females menstruating naturally and not taking any contraceptive pills or using any contraceptive devices.

Group 3: Men under 35 years of age.

### Exclusion criteria

Participants suffering from chronic diseases and those taking any analgesics at least 48 h before the onset of the study were excluded from the study.

### Procedure

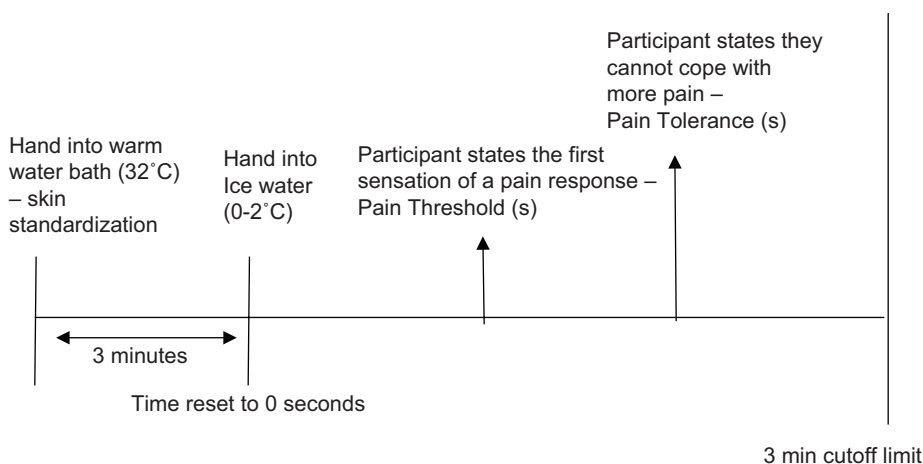
Participants standardized their hand skin temperature by immersing their least dominant (nonwriting) hand into a 32°C water-bath, (human body skin temperature), for 3 min. After 3 min, the participant was directed to plunge this hand directly into the ice slurry bath maintained between 0°C and 2°C [Figure 1]. Participants were requested to inform their first sensation of a pain response, which denotes the participant's pain threshold. Time from pain threshold to the point where participants could no longer cope with pain and indicated stop was recorded as pain tolerance. At this point, participants were directed to note their pain intensity and unpleasantness on the visual analog scale.

### Statistical analysis of data

Analysis of data was done using SPSS software version 16.0 (SPSS Inc., Chicago, IL, USA). Data were represented as a mean ± standard deviation. The analysis was done by one-way ANOVA and *post hoc* by Tukey-Kramer test. *P* < 0.05 was considered statistically significant.

## RESULTS

Within the cohort of 45 participants, there was no significant difference between the groups in age (*P* = 0.18).



**Figure 1:** A representation of one individual cold pressor task cycle. This cycle is repeated once in the familiarization phase and twice in the experimental phase

However, there was a statistically significant difference between the groups with respect to weight ( $P = 0.00$ ) and height ( $P = 0.00$ ) as men are taller and heavier than females [Table 1]. There was no significant difference in average pain threshold between the groups. The average pain tolerance of female receiving COCP was significantly reduced compared to men ( $P = 0.01$ ) though it was not significant compared to females without pill. Similarly, the average pain tolerance was significantly increased in females receiving pill ( $P = 0.01$ ) compared to female without pill. The average pain intensity was not significant for any of the groups. The average pain unpleasantness in female receiving COCP was significantly less when compared to women not receiving pill [Tables 2, 3 and Figure 2].

## DISCUSSION

This study found no significant differences in pain threshold or pain intensity between women using COCP therapy and women menstruating naturally. However, women menstruating naturally found pain more unpleasant compared to women using COCP, possibly due to increased circulating hormone levels enabling women using COCP to cope up better with pain or potentially mask pain. Furthermore, results indicate a statistically significant

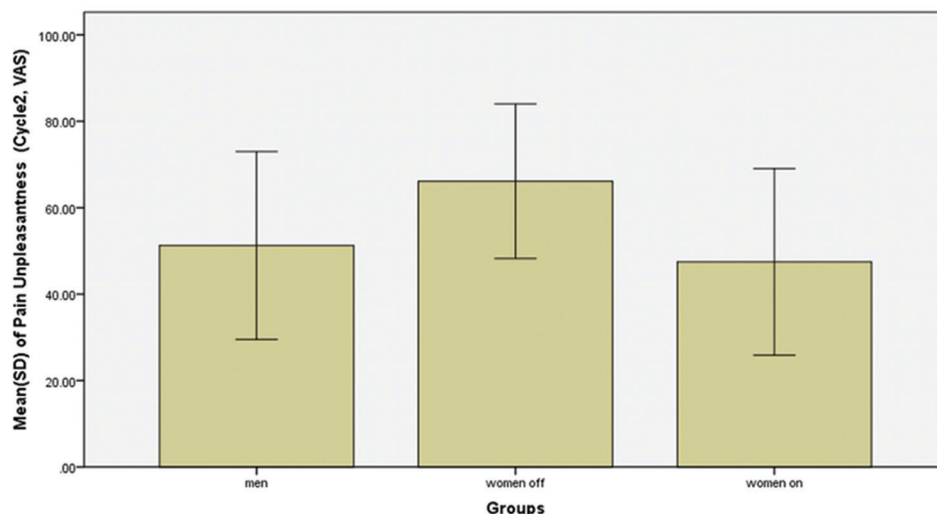
difference between men and both women groups suggesting the key influential factor is sex and gender.

The extent to which the significant differences between the groups are singly due to the COCP is largely inconclusive despite that the results slightly proposing that circulating blood hormones between naturally menstruating women and women using the COCP may be a key influence on at least some pain sensitivity measurements. Both the women groups in this study had significantly lower pain tolerance than men. This is in accordance with the most literature on sex and gender differences. Klatzkin *et al.*<sup>[4]</sup> investigated an ethnically diverse sample of participant including African, American, Caucasian, Indian, Asian, and Hispanic participants and found women were significantly more sensitive to cold pressor pain than men ( $P < 0.01$ ). These findings suggest that there are significant differences in pain unpleasantness; with women menstruating naturally experience the most unpleasant pain sensation and women using COCP experience the least. We found no differences between the two group of women and men in their pain pressor threshold, thus confirming the findings of previous studies<sup>[5-8]</sup> which shows no significant difference in pain threshold between women on or off the COCP and men.

**Table 2:** Group differences in pain responses to the cold pressor tasks over two cycles

	Men	Women (menstruating naturally)	Women (on COCP)	P
Pain threshold (s)	33.0±9.4	32.5±8.0	36.5±13.4	0.53
Pain tolerance (s)	61.2±37.2	39.1±15.7	35.4±16.5	0.02*
Pain intensity (mm)	53.5±18.2	57.9±15.7	56.2±21.3	0.81
Pain unpleasantness (mm)	52.5±17.3	62.0±16.8	46.7±19.9	0.04*

Data expressed are mean±SD. Analysis was done by one-way ANOVA and *post hoc* by Tukey-Kramer test.  $P < 0.05$  considered significant. COCP: Combined oral contraceptive pill



**Figure 2:** Pain unpleasantness. Significant difference between women off the pill and women on the pill ( $P = 0.03$ ). Women on the pill experience the least unpleasant pain sensation ( $46.7 \pm 20.8$  s). Women off the pill experience the most unpleasant pain sensation ( $62.0 \pm 17.9$  s)

**Table 3:** Comparison of different parameters of pain between the groups

Dependent variable	P
Average pain threshold (s)	
Men	
Women off the pill	0.88
Women on the pill	0.37
Women off the pill	
Men	0.88
Women on the pill	0.30
Women on the pill	
Men	0.37
Women off the pill	0.30
Average pain tolerance (s)	
Men	
Women off the pill	0.03*
Women on the pill	0.01*
Women off the pill	
Men	0.03*
Women on the pill	0.69
Women on the pill	
Men	0.01*
Women off the pill	0.69
Average pain intensity (mm)	
Men	
Women off the pill	0.52
Women on the pill	0.69
Women off the pill	
Men	0.52
Women on the pill	0.81
Women on the pill	
Men	0.69
Women off the pill	0.81
Average pain unpleasantness (mm)	
Men	
Women off the pill	0.16
Women on the pill	0.38
Women off the pill	
Men	0.16
Women on the pill	0.03*
Women on the pill	
Men	0.38
Women off the pill	0.03*

\*Significant differences using Tukey's *post hoc* analysis in one-way ANOVA SPSS function, \*represents  $P < 0.05$

This study highlights the fact that the use of hormonal-based contraceptive drugs may slightly affect the pain reporting, and hence health-care professionals while eliciting the history of pain should make a note of those women in pain who are using hormonal contraceptive.

**Limitations of the study**

Methodological variations between the study presented here and other studies will indisputably impact on the findings, and therefore concluding statements should be met with caution. One of the major limitations of this study is that the levels of different hormone levels in the plasma were not estimated. Another limitation is that the sample size does not justify dividing the women according to their menstrual cycle phase. There is evidence that pain responses vary across the menstrual cycle and that these differences are related to differences in hormone levels.<sup>[9]</sup>

However, we made sure in our experiment that all female participants were not at menstruation phase as the pain thresholds for all the physical stressors increased after menstruation.<sup>[9]</sup> Another major limitation is that though the participants in the study were age-matched, they were not body weight matched. Moreover, we have investigated only one type of innocuous stimuli, i.e., the cold pressor task, rather than a battery of different stimuli including heat and mechanical stimuli. It is recommended that whenever possible different types of stimuli are used in an experimental investigation.<sup>[10]</sup>

**CONCLUSION**

The COCP reduced pain unpleasantness but had no effect on pain threshold or pain intensity. A significant gender difference in cold pressor task was observed with women being more sensitive to pain.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Teepker M, Peters M, Vedder H, Schepelmann K, Lautenbacher S. Menstrual variation in experimental pain: Correlation with gonadal hormones. *Neuropsychobiology* 2010;61:131-40.
2. Sherman JJ, LeResche L. Does experimental pain response vary across the menstrual cycle? A methodological review. *Am J Physiol Regul Integr Comp Physiol* 2006;291:R245-56.
3. LeResche L, Mancl L, Sherman JJ, Gandara B, Dworkin SF. Changes in temporomandibular pain and other symptoms across the menstrual cycle. *Pain* 2003;106:253-61.
4. Klatzkin RR, Mechlin B, Girdler SS. Menstrual cycle phase does not influence gender differences in experimental pain sensitivity. *Eur J Pain* 2010;14:77-82.
5. Kowalczyk WJ, Evans SM, Bisaga AM, Sullivan MA, Comer SD. Sex differences and hormonal influences on response to cold pressor pain in humans. *J Pain* 2006;7:151-60.
6. Thorn BE, Clements KL, Ward LC, Dixon KE, Kersh BC, Boothby JL, et al. Personality factors in the explanation of sex differences in pain catastrophizing and response to experimental pain. *Clin J Pain* 2004;20:275-82.
7. Fillingim RB, Ness TJ. Sex-related hormonal influences on pain and analgesic responses. *Neurosci Biobehav Rev* 2000;24:485-501.
8. Grewen KM, Light KC, Mechlin B, Girdler SS. Ethnicity is associated with alterations in oxytocin relationships to pain sensitivity in women. *Ethn Health* 2008;13:219-41.
9. Stening K, Eriksson O, Wahren L, Berg G, Hammar M, Blomqvist A. Pain sensations to the cold pressor test in normally menstruating women: Comparison with men and relation to menstrual phase and serum sex steroid levels. *Am J Physiol Regul Integr Comp Physiol* 2007;293:R1711-6.
10. Greenspan JD, Craft RM, LeResche L, Arendt-Nielsen L, Berkley KJ, Fillingim RB, et al. Studying sex and gender differences in pain and analgesia: A consensus report. *Pain* 2007;132 Suppl 1:S26-45.