

# The Effect of Premenstrual Syndrome and Menstrual Phase on Postoperative Pain

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**Background:** Premenstrual syndrome (PMS) is a common finding in luteal phase of menstrual cycle resulting in several changes in woman life including pain sensation.

**Objectives:** This study evaluated the alterations of postoperative pain sensation in those with and without a history of PMS.

**Patients and Methods:** A total of 140 women in in postoperative period were assigned to four groups regarding luteal or follicular phase of menstrual cycle and the history of PMS and were evaluated regarding scale of pain sensation and morphine demand in recovery room. To evaluate the difference among the groups, Mann Whitney U, Kruskal-Wallis, and Bonferroni tests were used.

**Results:** Patients with PMS presented higher pain sensation and analgesia request ( $P = 0.003$ ). Patients in luteal phase showed less pain and analgesia request in two out of five studied outcomes ( $P = 0.075$ ).

**Conclusions:** The most comfortable postoperative women were those in luteal phase without history of PMS group.

**Keywords:** Menstrual Cycle; Pain Perception; Postoperative Pain; Premenstrual Syndrome; Women

## 1. Background

Premenstrual syndrome (PMS) includes a spectrum of emotional and somatic symptoms observed in luteal phase of menstrual cycle, which are disappeared after menstruation (1, 2). American college of Obstetricians and Gynecologists (ACOG) described PMS in ten indexes (2). According to previous reports, the incidence PMS ranges from 19% to 90% (3-5). During menstrual cycle, fluctuation in sexual hormones results in attitude change and alteration in pain perception (6). Different studies reported some interactions between sex hormones and central nervous system (7-9), which might be linked to activity of serotonin and beta-endorphin (neurotransmitters) in the brain (10, 11).

Pain perception differs during menstrual cycle (12). It has been recommended that estrogens might have an influence on somatic sensory process (13). Some studies reported a significant effect of pain sensitivity with higher levels of progesterone (13, 14) and some other studies reported similar patterns for pain perception. There are reports of more complaint of pain in luteal phase of menstruation, which is suggested as the reason for functional changes in women during menstrual cycle (15).

Studies suggest that symptoms of other disorders get

worse right before the menstruation (16). Furthermore, there is an association between stress and PMS. Stress suppresses the hypothalamus proper functioning, its control on the pituitary gland, and regulating hormones (17). Researchers suggest that stress might have direct impact on PMS through altering levels of sex hormones. In addition, cortisol affects PMS symptoms. For many patients, surgery is a physical and psychologic stressful event. Moreover, the postoperative period might be accompanied by significant pain and discomfort. As any stress, it might be affected by patient's background including PMS history and the phases of menstrual cycle during the preoperative period (18).

## 2. Objectives

This study aimed to assess the alterations of postoperative pain perception regarding the history of PMS in the patients undergoing surgery during the luteal and follicular phase of menstrual cycles.

## 3. Patients and Methods

This cohort study included 140 women, mostly candidate of gynecologic surgery. Patient's menstrual period and serum progesterone level were determined.

In patients with regular menses, menstrual phase was clarified according to their last menstrual history and confirmed by serum progesterone level. Serum progesterone measurement was done few hours before surgery. In patients with irregular menstruation, serum progesterone level  $> 60.19$  nmol/L (20.5 mg/mL) was determined as the luteal phase and  $< 60.19$  nmol/L as follicular phase. Patients with oral contraceptive pill consumption, amenorrhea, menopause, history of bilateral oophorectomy, or those consuming psychiatric drugs were excluded. All reproductive-age women who were candidate of surgery by transverse incision, mostly in lower abdomen, were included. This study was approved by Ethic Committee of Shahid Beheshti University of Medical Sciences. After explanation of the study for patients and providing them with information regarding analgesia and operative management, they signed informed consent and entered the study. They answered to questions regarding their premenstrual symptoms and history of menstruation. Based on menstrual characteristics and filling the criteria of premenstrual syndrome according to ACOG (2), patients were categorized in four subgroups. Two main subgroups included positive or negative history of premenstrual syndrome and in each subgroup, phase of menstrual cycle was determined. Meeting at least one of emotional and one of physical symptoms out of ten criteria of ACOG were needed to confirm PMS. Beginning of symptoms must be five days before period for at least three menstrual cycles ending within five days after period (2). All patients were operated under general anesthesia with similar anesthetic drugs.

Pain sensation was determined according to visual analog scale (VAS) and recorded once after the operation, at the time of entry into the recovery room. VAS was used to determine degree of pain sensation in all patients and a fixed morphine dosage of 3 mg was prescribed regardless of patient weight in recovery room, if VAS scale was  $\geq 3$  (19). During the stay period in recovery room, if patient needed more analgesia, bolus morphine dose was prescribed again with 2-mg fixed dose and the dose and frequency were recorded. After transferring to gynecology ward, Patient-controlled analgesia (PCA) was used

according to patient's need and frequency of morphine usage during the first 24 hours was recorded. Regulation of PCA pump included background infusion of 0.8 mg/h, lock-out interval of 15 minutes, and bolus dose of 0.2 mg morphine.

Data were presented by mean and standard deviation (SD), median, and range. Mann Whitney U test was used to evaluate the difference among the groups. To evaluate the difference between the combinations of the groups, Kruskal-Wallis test and the multiple comparisons was considered by Bonferroni method. The modification of the effect of menstrual phase by PMS status was evaluated by General linear model. P value  $< 0.05$  was considered as statistically significant. All statistical analysis was performed by SPSS 21.0 (IBM Co., Somers, NY, USA).

#### 4. Results

Six out of 140 patients were excluded due to ambiguity in menstrual phase and serum progesterone level. Mean age of patients was  $41 \pm 7$  year (median, 42; range, 19-59). A total of 116 patients (87.2%) were operated by transverse incision in lower abdomen for hysterectomy, myomectomy, or cystectomy. Six patients (4.5%) had transverse incision in subcostal area for open cholecystectomy and 11 (8.3%) were operated by low-midline incision for hysterectomy.

Overall, 95 patients had positive history for PMS and 38 had negative history; patients with positive history of PMS showed significantly higher pain and analgesia request than other patients (Table 1).

At the second step and regarding the menstrual phase, 79 and 64 patients were respectively assigned to luteal phase and follicular phase. Five determined outcomes including recovery room VAS, number of morphine request in recovery room, total morphine dose consumption in recovery room, number of PCA usage for morphine during first 24 hours, and total number of morphine request (including recovery room and PCA) were compared between two groups of luteal and follicular phase (Table 2). Pain and analgesia request were less in luteal phase group in comparison to follicular phase in all outcomes (Table 2).

**Table 1.** Comparison of Patients in Five Outcomes Regarding History of Premenstrual Syndrome <sup>a, b</sup>

Outcome	History of PMS				P Value
	Positive		Negative		
Recovery VAS	9.2 $\pm$ 2	10 (3-10)	7.9 $\pm$ 3.3	10 (1-10)	0.057
Number of Morphine Request in Recovery Room	1.4 $\pm$ 0.7	1 (0-3)	1.4 $\pm$ 1.7	1 (0-10)	0.288
Total Morphine Dose in Recovery Room, mg	4.8 $\pm$ 2.1	5 (0-10)	3.7 $\pm$ 2.4	3 (1-10)	0.007
Number of PCA Usage During the First 24 Hours	10.8 $\pm$ 6.9	10 (0-20)	7.6 $\pm$ 7.2	4.5 (0-10)	0.006
Total Number of Morphine Request (Recovery Room + First 24 Hours)	12.1 $\pm$ 7	11 (0-23)	8.6 $\pm$ 7.3	5 (0-22)	0.003

<sup>a</sup> Values are presented as mean  $\pm$  SD and median (range).

<sup>b</sup> Abbreviations: PMS, premenstrual syndrome; VAS, visual analogue scale; and PCA, Patient-controlled analgesia.

**Table 2.** Comparison of Follicular and Luteal Phase Patients Regarding Five Outcomes<sup>a, b</sup>

Outcome	Luteal Phase		Follicular Phase		P Value
Recovery Room VAS	8.7 ± 2.6	10 (3-10)	8.9 ± 2.4	10 (1-10)	0.627
Number of Morphine Request in Recovery Room	1.3 ± 0.8	1 (0-3)	1.4 ± 1.2	1 (0-10)	0.477
Total Morphine Dosage Recovery Room, mg	4.4 ± 2.5	4 (0-10)	4.5 ± 2	5 (0-10)	0.507
Number of PCA Usage in First 24 Hours	8.5 ± 6.8	8.5 (0-20)	10.8 ± 7.2	10 (0-20)	0.062
Total Number of Morphine Request (Recovery Room + First 24 Hours)	0.9 ± 7	10 (0-22)	12.1 ± 7.3	11 (0-23)	0.075

<sup>a</sup> Values are presented as mean ± SD and median (range).

<sup>b</sup> Abbreviations: VAS, visual analogue scale; and PCA, Patient-controlled analgesia.

**Table 3.** Comparison of Four Groups Regarding Five Outcomes<sup>a, b, c</sup>

Groups	I		II		III		IV		P Value	IVSII	IVSIII	IVSIV
Recovery VAS	8.5 ± 3	10 (3-10)	8.7 ± 2.5	10 (3-10)	7.6 ± 3.5	10 (1-10)	9.5 ± 1.5	10 (3-10)	0.109			
Number of Morphine Request in Recovery Room	1.1 ± 0.7	1 (0-3)	1.4 ± 0.8	1 (0-3)	1.6 ± 2	1 (0-10)	1.4 ± 0.6	1 (0-3)	0.529			
Total Morphine Dosage Recovery Room, mg	4 ± 2.6	3.5 (0-10)	4.6 ± 2.5	4 (0-9)	3.5 ± 2.3	3 (0-9)	4.9 ± 1.7	5 (0-10)	0.028	> 0.99	0.569	0.031
Number of PCA Usage in First 24 Hours	6.1 ± 6	3 (0-20)	9.4 ± 6.9	10 (0-20)	8.4 ± 7.7	5 (0-20)	11.9 ± 6.8	11 (0-20)	0.009	> 0.99	0.611	0.02
Total Number of Morphine Request (Recovery Room + First 24 Hours)	7.2 ± 6.1	4 (0-21)	10.6 ± 7.2	10.5 (0-22)	9.4 ± 8	5.5 (0-22)	13.3 ± 6.7	12 (1-23)	0.005	> 0.99	0.486	0.015

<sup>a</sup> Values are presented as mean ± SD and median (range).

<sup>b</sup> Abbreviations: PMS, premenstrual syndrome; VAS, visual analogue scale; and PCA, Patient-controlled analgesia.

<sup>c</sup> Study groups are as follows: (I) luteal-PMS negative, (II) luteal-PMS positive, (III) follicular-PMS negative, and (IV) follicular-PMS positive.

At the third step, four groups of luteal-PMS negative (I), luteal-PMS positive (II), follicular-PMS negative (III), and follicular-PMS positive (IV) were compared regarding five predetermined outcomes (Table 3).

Statistically significant difference was detected among four groups regarding three outcomes including total morphine dosage in recovery room, number of PCA usage, and number of morphine request (Table 3). Post hoc analysis revealed significant difference between group I (luteal phase-PMS negative) and group IV (follicular phase-PMS positive) (Table 3). Effect modifier analysis revealed that existence of PMS might influence VAS difference in different menstrual phase in recovery room, with a borderline significance ( $P = 0.086$ ).

## 5. Discussion

In the present study, patients with PMS showed more pain and morphine request. It seems reasonable that patients in luteal phase tolerate postoperative pain better than follicular phase, and hence, surgeons might schedule operation time in luteal phase. In subgroup analysis, significant difference in three out of five outcomes was detected, which was the result of significant difference between two groups of luteal phase-PMS negative and follicular phase-PMS positive. This suggests the idea that

the most comfortable patients were in luteal phase without history of PMS and surgeons could schedule their operation in women's luteal phase in order to provide more comfortable postoperative period for patients. Our data showed more pain and morphine request in follicular phase of menstrual cycle in three out of five outcomes (Table 2).

In some studies increased progesterone level of luteal phase resulted in lower dosage needed for anesthesia (20). On the other hand, some studies showed decreased pain sensation in follicular phase (21, 22). There seems to be a controversy over pain sensation and analgesic requirement in different phases of the menstrual cycle (21-25). In a study, lower pain according to VAS was found in luteal phase of menstrual cycle (23). In a study morphine request was similar in luteal and follicular phase (25). Several studies found weak association between menstrual phase and postoperative pain (13, 24, 25).

Studies suggest the role of patient's psychologic factors in pain perception (26). Some studies intimate the idea that up to 40% of women with symptoms of PMS have a significant decline in serum levels of beta-endorphin (9). It has also been reported that mood changes and low serum beta-endorphin levels could result in different effects of menstrual cycle phase on postoperative pain perception (27).

The controversy observed in review of literature regarding influence of menstrual phase on pain perception might arouse the concept of ignoring the PMS as an effective and common parameter, sometimes with prevalence of 70%, in these studies. Borderline significance ( $P = 0.086$ ) of effect modification analysis of PMS effect on VAS difference during menstrual phase in recovery room support this idea.

ACOG recommendations for reduction of PMS symptoms include exercise, relaxation techniques, rich complex carbohydrate and low sugar diet, low fat and salt diet, and emotional support (2). Preparation of patients with PMS via known remedies for PMS symptom relief probably result in more comfort in postoperative period. The issue of preparation with antidepressants, change of diet, exercise, and other changes and their exact effect might be studied in future researches.

Some limitations of the study should be mentioned. Firstly, 17 out of 140 cases under study were operated by midline or subcostal incision. Postoperative pain might be affected by the incision itself. Secondly, pain sensation was recorded by VAS just once in recovery room; nevertheless, analgesic demand records by PCA were alternative indicator of pain sensation. Thirdly, although patients were conscious, they were encountered with VAS for the first time in postoperative period in recovery room. It might be better to instruct them on VAS before operation.

In conclusion, women would experience less pain and analgesia request in postoperative period if they were operated in luteal phase with no history of PMS. This predictive parameter of more postoperative pain might guide surgeon to prepare patients with history of PMS in preoperative period.

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