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Cross-sectional Study

Hemodynamic stability during menstrual cycle in women undergoing elective surgery

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ABSTRACT

Objective: Hemodynamic changes occur in almost one-third of patients undergoing spinal anesthesia, which are likely to effect vital organ. The aim of this study is to determine the hemodynamic effect of spinal anesthesia during different phases of menstrual cycle.
Methods: This is a descriptive cross-sectional study, two hundred and seventy-three patients who underwent spinal anesthesia for elective surgery were enrolled in this study. Of all the patients, 141 patients were in the luteal phase and 132 patients were in the follicular phase of their menstrual cycle. Analytical epidemiological study was conducted using questionnaires. Blood pressure and heart rate of patients before, immediately after, and 1 h after spinal anesthesia were recorded, and the data were analyzed using SPSS software.
Results: In the follicular phase before anesthesia, systolic blood pressure (SBP) was 127.5 ± 3.9, diastolic blood pressure (DBP) was 80.3 ± 6.2 mmHg and heart rate (HR) was 82.0 ± 8.5bpm, while, immediately after the induction of anesthesia following recordings were measured; 109.7 ± 9.13, 71.8 ± 2.8 mmHg and 70.0 ± 8.10bpm, respectively. In the luteal phase, it was 126.9 ± 3.12, 81.6 ± 9.3 mmHg and 80.2 ± 4.4bpm, and 122.0 ± 9.12, 78.6 ± 8.5 mmHg and 75.9 ± 6.5bpm respectively before and immediately after anesthesia, these changes in the menstrual phase was significant ($P < 0.001$). In the follicular phase an hour after spinal anesthesia, the mean SBP was 100.3 ± 3.9, DBP was 71.2 ± 7.5, MAP was 87.0 ± 4.7 mmHg and HR 67.5 ± 5.7bpm and following was seen in luteal phase; 115.4 ± 1.8, 75.9 ± 2.3, 97.3 ± 3.5 mm Hg and 74.0 ± 7.4bpm, respectively. These values were significantly lower in the follicular phase ($P < 0.001$).
Conclusion: Spinal anesthesia in the luteal phase as compared to the follicular phase of the menstrual cycle shows less variation in hemodynamic parameters.

Introduction

Spinal anesthesia is safe and commonly used anesthetic method [1] however, is known to be associated with hypotension in 1/3rd of the non-obstetric surgeries and 50% of the obstetric ones. A drop in arterial blood pressure, as a result, is also characterized by nausea and vomiting, reduced consciousness and can also lead to aspiration [2–4]. This cause of this hypotension is the drop in systemic vascular resistance and Bezold-Jarisch reflex [5]. Changes in hemodynamic parameters can lead to damage to vital organs and mortality [1,6,7]. Many factors influence the hemodynamic changes following spinal anesthesia, these include age, sex, height, weight, history of medical conditions (such as diabetes mellitus, hypertension, anemia), block level at T5 or higher and the use of drugs such as opioids and regional anesthesia [8,9].

One of the factors that are believed to cause hemodynamic changes in different phases of menstrual cycle are regular monthly changes in the secretion of female hormones and corresponding changes in the ovaries and sexual organs [10,11]. The average women sexual cycle is 28 days and ovulation occurs approximately for 14 days [12,13]. The first day of bleeding is considered as the first day of the menstrual cycle [14]. The endometrial menstrual cycle consists of four main stages: menstrual bleeding, proliferative phase, ovulation phase, and secretory phase [15, 16].

The ovarian menstrual cycle has two main stages: follicular phase

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(first half), and the luteal phase (second half) [17]. Several studies have shown the effects of menstrual cycle on factors such as hemodynamic changes [18–20], including changes in blood pressure and heart rate during laryngoscopy, nausea and vomiting, pain on injection of anesthetics such as propofol, and sore throat after laryngoscopy [21,22]. It is also reported that heart rate is higher during luteal phase however, the variation is lesser than follicular phase [23,24]. Therefore, this study is designed to investigate the relation between the two stages of menstrual cycle (luteal and follicular) and their effects on hemodynamic alterations as a result of spinal anesthesia during elective surgeries.

Methods

This is a descriptive cross-sectional study enrolled all women who were referred (XXX) who underwent elective surgery under spinal anesthesia (as per our criteria, defined below).

Inclusion criteria of this study was: women between 16 and 45 years of age who had not used hormonal or cardiovascular medicines for ≥6 months, ones with regular menstrual cycle of 28–35 days, no prohibition for the use of spinal anesthesia and patients classified under ASA class I. The surgeries include repair of inguinal hernia, femoral neck fixation orthopedic, urologic surgeries. Only those with a biochemically confirmed ovulation during the measurement session of the luteal phase were included for further analysis. Participants were ≥5 months postpartum.

Patients with the history of mental illness, smoking or drinking, irregular menstrual cycle, using contraceptive, pregnant or lactating, presenting diabetes, allergy to anesthesia and those who did not consent to participate in the study were excluded.

Each of the participant underwent two laboratory sessions, this session was timed to coincide with the follicular phase (Days 12–15) and the luteal phase (Days 21–24). The phases were determined based on the self-report of the onset of menses along with urine luteinizing hormone test and modulation was made to allow individual cycle length differences. While neither the participants nor experimenter were blind to the menstrual phase, sessions were counterbalanced to allow for equal representation of the two phases on both testing occasions, and both sessions were attended simultaneously in a day. The study questionnaire contains demographic data; (weight, height) cardiovascular disease, hypertension, menstrual cycle phase, type of surgery, spinal anesthesia level, systolic and diastolic blood pressure, mean arterial pressure and number of heart beats per minute (before, immediately after, and 1 h after spinal anesthesia every 5 min), body mass index, and the total amount of ephedrine administered were recorded in a questionnaire.

The patients were taken to the operating room and venipuncture was performed. Ringer lactate solution of 3–5 ml per kilogram of body weight within 15 min was infused to the patient, the patient's blood pressure and heart rate was measured and recorded using the devices provided by SAADAT, Iran. Then, L3-L4 or L4-L5 spinal anesthesia in a sitting position with a 25-gauge needle, with 4 mg of 5% isobaric marcaine was administered. Anesthesia level was recorded by cotton Swab and the blood pressure and heartbeat was measured in the first 10 min for every 1 min, and then every 5 min until the end of surgery. A drop in the systolic blood pressure less than 90 mmHg or diastolic blood pressure less than 60 mmHg signified hypotension, which was treated using 5 mg ephedrine. The total amount of ephedrine needed was calculated and recorded. Liquid preservative based on the 4-2-1 (per ten kg first, 4 cc per kilogram of body weight; 2 cc per kilograms for second, and 1 cc per kilogram of body weight; for the rest of the body weight) was infused. For heart rate less than 60 beats per minute, 0.5 mg IV of atropine every 3–5 min was used for the treatment of bradycardia.

Excluded criteria

Patients who do not complete their spinal anesthesia levels were higher than those of T10, and anesthetic drugs to patients who have had surgery.

Anesthesia was administered by an anesthesiologist and blood pressure of all patients were measured by a device. Intraoperative monitoring devices included pulse oximetry, ECG, heart rate and blood pressure, respectively. In the questionnaire, systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were assessed.

The data were analyzed using software SPSS v.19 by statistical consultant. Repeated measures analysis of variance was used to analyze the data. P-value < 0.05 was reported to be statistically significant.

This study was approved by the Research Ethics Board (XXX).

Unique identifying number researchregistry:8012.

The methods are stated in line with STROCSS 2021 guidelines [25].

Results

Two hundred and seventy-three were included in the study, of whom 132 women were in the follicular phase, while 141 were in the luteal phase. Table 1 shows the demographic data; the average age of the patient in the follicular and luteal phase was 31 ± 2 and 31 ± 4 years respectively, whereas, average height was reported as 166 ± 2 and 165 ± 4 cm respectively, and BMI was 24 ± 4 and 23 ± 5 respectively.

A Hemodynamic indices before and immediately after spinal anesthesia:
   a Systolic blood pressure (SBP); The average SBP in the follicular phase before and immediately after anesthesia was 127.5 ± 3.9 mmHg and 109.7 ± 9.13 mmHg respectively, and 126.9 ± 3.12 and 122.0 ± 9.12 respectively in luteal phase group, which was not seen to be statistically significant (Table 2 and Fig. 1).
   b Diastolic blood pressure (DBP); The average DBP in the follicular phase before and immediately after anesthesia was 80.3 ± 6.2 and 71.8 ± 2.8 mmHg respectively, and 81.6 ± 9.3 and 78.6 ± 8.5 mmHg respectively in the luteal phase. This represents a further drop in DBP immediately after receiving spinal anesthesia in the follicular phase of the menstrual cycle, which is statistically significant ($P < 0.001$) (Table 2 and Fig. 2).
   c Heart rate (HR): HR in the follicular phase before and immediately after anesthesia was 82.0 ± 8.5 and 70.0 ± 8.10 beats per minute and 80.2 ± 4.4 and 75.9 ± 6.5 beats per minute, respectively in the luteal phase group. Heart rate significantly declined in the follicular phase following the induction of spinal anesthesia ($P < 0.001$) (Table 2 and Fig. 3).

B Hemodynamic indices an hour after spinal anesthesia:
   a SBP in the follicular phase and luteal phase an hour after spinal anesthesia was 100.3 ± 9.6 mmHg and 115.4 ± 1.8 mmHg, respectively. The SBP was significantly lower in the follicular phase ($P < 0.001$) (Table 1 and Fig. 1).
   b DBP in the follicular phase and luteal phase an hour after spinal anesthesia was 71.2 ± 7.5 mmHg, and 75.9 ± 2.3 mmHg, respectively, which was also significantly different ($P < 0.001$). (Table 1and Fig. 2).
   c MAP in the follicular phase and luteal phase an hour after spinal anesthesia, was 87.0 ± 4.7 mmHg, and 97.3 ± 3.5 mmHg, respectively. This show, the MAP was significantly less in the follicular phase ($P < 0.001$) (Table 1).

Table 1
Demographic data of follicular phase and Luteal phase.

	Luteal Phase (n = 141)	Follicular Phase (n = 132)
Age (y)	31 ± 2	31 ± 4
Height (cm)	166 ± 2	165 ± 4
Body mass index (kg · m−2)	24 ± 4	23 ± 5
Parity (median and range)	1 (1–2)	1 (1–3)

Table 2
Average hemodynamic indices before, immediately after and 1 h after spinal anesthesia in the subjects on the basis of menstrual phase.

Phase	Number of patients	Measuring time	SBP	DBP	MBP	HR
Follicular	132	Before anesthesia	127.5 ± 3.9	80.3 ± 6.2	–	82.2 ± 8.5
		After anesthesia	109.7 ± 9.13	71.8 ± 2.8	–	70.0 ± 8.10
		One hour after anesthesia	100.3 ± 3.9	71.2 ± 7.5	87.0 ± 4.7	67.5 ± 5.7
Luteal	141	Before anesthesia	126.9 ± 3.12	81.6 ± 9.3	–	80.2 ± 4.4
		After anesthesia	122.0 ± 9.12	78.6 ± 8.5	–	75.9 ± 2.3
		One hour after anesthesia	115.4 ± 1.8	75.9 ± 2.3	97.3 ± 3.5	74.0 ± 7.4
P value			P < 0.05	P < 0.001	P < 0.001	P < 0.001

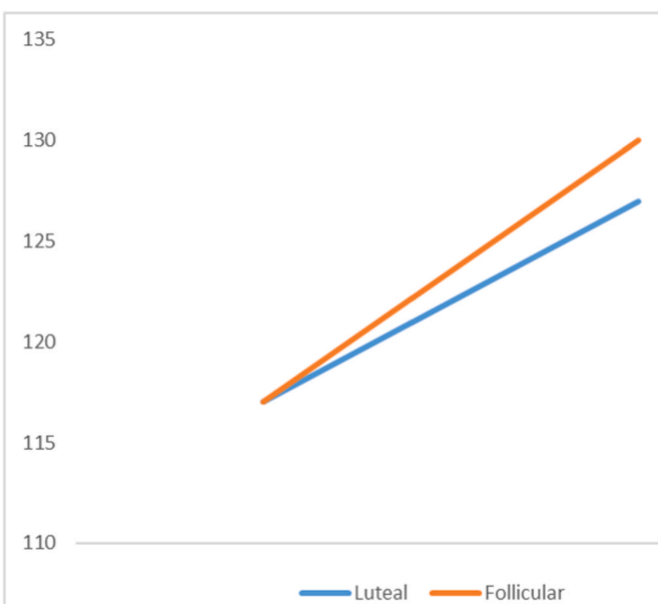

Fig. 1. Average Systolic Blood Pressure (mmHg) for the follicular and luteal Phase.

d HR in the follicular phase and luteal phase an hour after spinal anesthesia, was 67.5 ± 5.7 and 74.0 ± 7.4 bpm respectively. The HR was significantly less in the follicular phase ($P < 0.001$) (Table 1 and Fig. 3). The result indicates less alterations hemodynamic response in the luteal phase an hour after spinal anesthesia is performed.

Discussion

In this study, we investigated the relationship between luteal and follicular phases of menstrual cycle with different hemodynamic response after spinal anesthesia.

In a study by Arabi et al., effect of anesthesia on hemodynamic parameters was studied on 77 women at follicular and luteal phase of menstrual cycle [26]. In the study, 38 women were in the luteal phase, and 39 women were in the follicular phase. Systolic blood pressure after intubation in the follicular phase was 138.4 ± 20, and in the luteal phase it was127.7 ± 18 (mm Hg), which was significantly different ($P < 0.001$). The heart rate after intubation in the luteal phase was 90.7 ± 12 which was significantly higher than the follicular phase, 85.3 ± 11 ($P = 0.05$). As a result, less changes in hemodynamic parameters were observed in the luteal phase. The results of Vahabi et al., study showed that blood pressure and heart rate after spinal anesthesia in the luteal phase is less than the follicular phase [27]. Although, there was difference in the type of anesthesia used in the two studies, it can be still marked that hemodynamic alteration as a result of anesthesia can be different in the different phases of menstrual cycle. As a result, due to less changes in hemodynamic parameters in the luteal phase and reduce perioperative cardiovascular complications [28], it can be conjectured that elective surgeries in women who are of childbearing age, should be performed at this time [29].

In a study conducted by Hanci et al., the effects of the menstrual cycle phases on hemodynamic parameters in response to tracheal intubation and laryngoscopy were evaluated [30]. They found that the product of heart rate and blood pressure RPP (Rate Pressure Product), a minute after intubation were significantly higher in the luteal phase compared with the follicular phase, nonetheless, our study reported

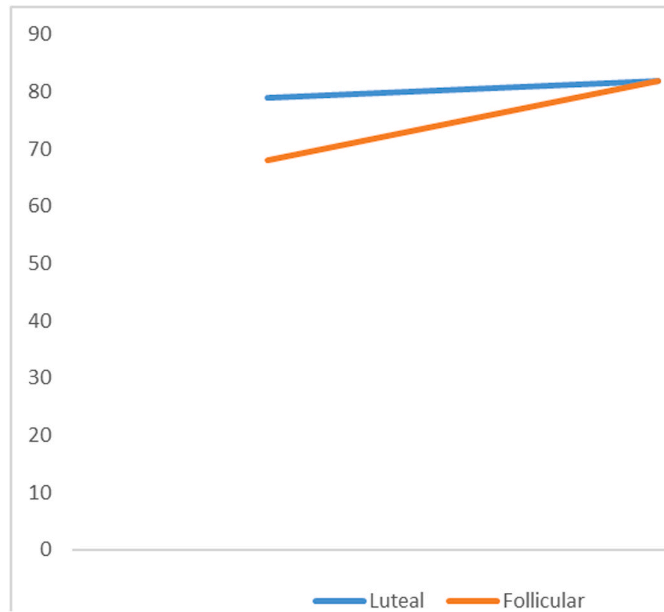

Fig. 2. Average Diastolic Blood Pressure (mmHg) for the follicular and luteal Phase.

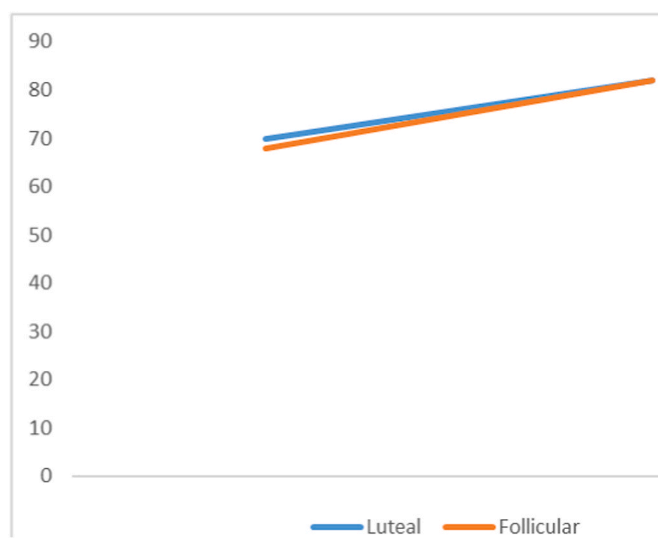

Fig. 3. Average Heart Rate (bpm) for the follicular and luteal Phase.

significant changes in the follicular phase. This difference could be as a result of the time of obtaining results in the two studies, since Hanci et al., obtained the outputs a minute after intubation whereas, our study recorded then an hour later. Lin and Li [23]reported that among patients undergoing spinal anesthesia for gynecological surgery, hypotension is significantly more in patients in luteal phase as compared to those in follicular. To it, elevation in the heart rate was also significantly more in luteal phase [31,32].

Fu et al., studied the effects of menstrual cycle on the kidneys and adrenal system, and hemodynamic response during orthostatic tachycardia syndrome as a result of prolonged standing [33]. The results of the study suggested that renin-angiotensin aldosterone system is effective during menstrual cycle as well as the hemodynamic status during orthostatic tachycardia syndrome in patients with orthostatic tachycardia. Due to higher levels of estrogen and progesterone in the mid-luteal phase, resulting in a further increase in the level of hormones in adrenal system and kidney, retention volume in circulation is probably created leading to the better tolerability in patient's long-term standing [34]. There was also an intravascular volume in the luteal phase because this phase has more stable hemodynamic variables [35].

Another study by Choudhury et al. [36], on parasympathetic nervous activity in different phases of the menstrual cycle in healthy women, reported that levels of estrogen and progesterone were measured, The results of the study is as follows: Valsalva maneuver and standing heart rate changes are not significant, but the heart rate response to deep breathing significantly decreased in the luteal phase compared to the follicular phase ($P < 0.05$). Generally, heart rate decreased significantly in the luteal phase compared with the follicular phase, the results of the study indicated a higher parasympathetic activity in the late luteal phase, which is also similar with the result obtained in our study [37].

Leicht et al., assessed the changes in heart rate and sex hormones during the menstrual cycle in young women [38]. In the study, 20 women with a regular menstrual cycle (10 in luteal phase and 10 in follicular phase) were studied. Heart rate showed no significant changes in the different phases of the menstrual cycle ($P < 0.05$). The study demonstrated that progesterone changes heart rate variability (HRV), which could also reflect the results from this study.

In the present study, the changes in the two phase of menstrual cycle led to changes in heart rate, and mean arterial pressure which was not significant, however, the changes in the luteal phase was lesser as compared to that of follicular (75.4 ± 3.2 in the luteal phase and 81.7 ± 2 in the follicular phase; $P < 0.05$). These results indicate that the luteal phase compared with the follicular phase is associated greatly with hypotension during spinal anesthesia.Women are likely to have stronger compensatory abilities during follicular phase, owing to the elevation in the estrogen levels. Despite, menstrual cycle is not a significant factor to choose the time of the surgery, this parameter can be of greater significance in women with hemodynamic and cardiovascular anomalies, which can also help surgeons and clinicians to predict possible intraoperative outcomes.

Conclusion

However, our study did not measure the levels of progesterone and estrogen. Data regarding the plasma levels of norepinephrine is also not presented in this study. Comparative studies including women with circulatory abnormalities, preoperative and postoperative analysis and greater number of samples can help researchers to draw a better and meaningful conclusion.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Please state any sources of funding for your research

No funding was secured for this study.

Author contribution

Dr. Sepideh Vahabi: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Siavash Beiranvand and Dr.Roghaye Mousavi: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Dr.Arash Karimi and Dr. Masoumeh Ghafarzadeh: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Please state any conflicts of interest

The authors deny any conflict of interest in any terms or by any means during the study.

Consent

Not applicable.

Registration of research studies

1. Name of the registry: Lorestan University of Medical Sciences
2. Unique Identifying number or registration ID:
   Hyperlink to the registration (must be publicly accessible):

Guarantor

Sepideh Vahabi.

Availability of data and material

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Provenance and peer review

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104649.

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