



## TO STUDY THE EFFECTS OF MENSTRUAL CYCLE ON HEMODYNAMICS DURING SPINAL ANESTHESIA

### Anaesthesiology

<b>Dr. Joginder Pal Attri</b>	Professor, Department of Anaesthesia, Govt. Medical College, Amritsar.
<b>Dr. Anita Madan</b>	Associate Professor, Department of Obstetrics and Gynaecology, Govt. Medical College, Amritsar.
<b>Dr. Anu Sharma</b>	Assistant Professor, Department of Anaesthesia, Govt. Medical College, Amritsar.
<b>Dr. Puneetpal Kaur</b>	Senior Resident, Department of Anaesthesia, Govt. Medical College, Amritsar.
<b>Dr. Sameeksha Arora</b>	Junior Resident, Department of Anaesthesia, Govt. Medical College, Amritsar.
<b>Dr. Leena Mahajan*</b>	Assistant Professor, Department of Anaesthesia, Govt. Medical College, Amritsar. *Corresponding Author

### ABSTRACT

**Background:** The hormonal levels of oestrogen and progesterone during the menstrual cycle affect various body systems. In this study, we investigated how these biphasic variations during menstrual cycle affects the circulatory function during spinal anesthesia and which phase was more stable to changes during anesthesia.

**Methods:** Sixty female patients of the age group 20 to 40 years of American Society of Anesthesiologists (ASA) Class I and II, who underwent infraumbilical surgeries under spinal anesthesia were the subjects of study and allocated into two groups of 30 each namely Group F (follicular) and Group L (luteal). Preoperative heart rate and blood pressure measurements were taken in supine and standing positions. Heart rate measurements as well as systolic, diastolic, and mean blood pressure measurements were taken upon entering the operating room, at the beginning of the spinal anesthesia and then every 5 minutes for 1<sup>st</sup> hour, every 10 minutes for 2<sup>nd</sup> hour, after every 20 minutes for 3<sup>rd</sup> and 4<sup>th</sup> hour and every 30 minutes for 5<sup>th</sup> and 6<sup>th</sup> hour.

**Results:** The heart rates of patients in the Group L were higher than those of patients in group F before and after anesthesia ( $P < 0.05$ ). Significantly more ephedrine was used during the first 30 min of spinal in the Group L than in the Group F ( $P < 0.05$ ).

**Conclusions:** The women in follicular group are able to compensate and tolerate the circulatory changes better. The surgeries should be planned during follicular phase for women wherever possible.

### KEYWORDS

Spinal anesthesia, Menstrual cycle, Follicle stimulating hormone, Luteinizing hormone

#### INTRODUCTION

There is an interplay of various hormones responsible for maintaining blood pressure homeostasis in our body. The variation in blood pressure in males and females manifests differently owing to the presence of testosterone in males and oestrogen and progesterone in females. The hormonal levels of oestrogen and progesterone in females during the menstrual cycle affect various body systems like the cardiovascular system. These fluctuating hormone levels affect the endometrium, causing the menstrual cycle to be divided into three phases: menstruation, the follicular and luteal phases. In females, oestrogen and progesterone receptors are widely distributed across various tissues and organs. Studies have found that the oestrogen  $\beta$  receptor<sup>1,2,3</sup> is widely distributed and this receptor helps to regulate biosynthetic functions in tissues and cells, blood flow in tissues and organs, and body temperature. Conversely, progesterone plays the opposite role. Oestrogen affects regulating the body's circulation via three mechanisms i.e. increasing the responsiveness of endothelium-dependent bradykinin-mediated vasodilation, norepinephrine-mediated vasoconstriction and upregulating nitric oxide (NO) synthase<sup>4</sup>, thereby, regulating the sympathetic nervous system activity by affecting norepinephrine synthesis alongwith the number and sensitivity of  $\alpha$ -adrenergic receptors. Conversely, progesterone weakens the responsiveness of endothelium-dependent vasodilation to oestrogen, so the hormonal levels during different phases of menstrual cycle shows a biphasic variation on hemodynamics of females.<sup>5</sup>

Since the hormonal levels during different phases of menstrual cycle show a biphasic variation on hemodynamics of females.<sup>5</sup> So most of the studies were conducted that focused on how hormone levels affect the body during rest, stress or exercise. However, no report has addressed the effect of hormone levels on the circulation during anesthesia. In this study, we investigated how spinal anesthesia affect the circulatory function during the stages of the menstrual cycle i.e. these biphasic variations during spinal anesthesia and which phase was more stable to changes during anesthesia

#### METHODS:

Study participants

Sixty women aged between 20 to 40 years, who underwent a scheduled infraumbilical surgeries, were classified as American Society of Anesthesiology (ASA) I-II were initially selected. 30 were assigned to the Group F (follicular group: 6-12 days after their last menstrual period), and 30 were assigned to the Group L (corpus luteal: 16-24 days after their last menstrual period). All patients met the inclusion criteria. All patients' menstrual cycles ranged from 28 to 35 days, and none had used any cardiovascular or hormonal drugs for  $\geq 6$  months. Patients with histories smoking, mental illness, puncture site infection, peripheral nervous system disease, diabetes, spinal deformity, taking oral contraceptive pills or allergies to local anesthesia were excluded. The ethics committee of our hospital approved this study video no. 1219D26 dated 11/01/2021 and all patients signed an informed written consent form.

#### ANESTHESIA METHODS AND INDICATORS

All the patients were operated by experienced gynaecologists and the spinal anesthesia was provided by experienced anesthesiologists. Patient's age, height, body weight and menstrual cycle was recorded. Pre-anaesthetic checkup including detailed history of the patient and thorough general examination of the patient was carried out a day before the surgery and was recorded as per the performa attached. Patients were also explained about the procedure night before the surgery and were told to remain fasting from food and water for 8 hours before the procedure, and their blood pressures were measured from the supine and standing positions and recorded on the morning of the surgery. For that, patients assumed supine position in a quiet room, for 10 minutes before having their systolic, diastolic, mean blood pressure and heart rates ( $T_0$ ) measured. The patients were kept standing and 30 seconds later, their systolic, diastolic, mean blood pressure and heart rates were measured ( $T_1$ ). This was repeated twice to calculate an average. Patients were not infused before the operation without special circumstances. After entering the operating room, the patient assumed

supine position for 5 minutes. Venous access was secured and Ringer Lactate solution was started at 500 ml/ hr over the first hour. Systolic, diastolic, mean blood pressure and heart rates were recorded upon entering the operating room (T<sub>2</sub>), upon beginning of anesthesia (T<sub>3</sub>), at 5 minutes (T<sub>4</sub>), 10minutes (T<sub>5</sub>) and 15 minutes (T<sub>6</sub>) after receiving the anesthesia. The patients were moved to left lateral position and following all the sterile precautions, L3-L4 space was selected as the puncture site. The median approach was used for spinal puncture. After observing the free flow of cerebrospinal fluid 3ml of 0.5% hyperbaric bupivacaine was injected. The spinal needle was removed and patient was turned to supine position. If the blood pressure of patient fell below 20% of the baseline, 6mg of ephedrine was given intravenously. The drugs were given repeatedly, if needed.

**STATISTICAL ANALYSIS:**

The data from the present study was systematically collected, compiled and statistically analyzed using software IBM SPSS 21 (Armonk, NY:IBM Corp.) to draw relevant conclusions. Data was expressed as mean, standard deviation, number and percentages. The patient characteristics (non parametric data) were analysed using the 'Chi – Square tests' and the inter - group comparison of the parametric data was done using the 'Unpaired “t” test. The 'p' value was determined to finally evaluate the levels of significance. The p value of < 0.05 was considered as significant at 5% significance level; p < 0.01 was considered significant at 1% significance level and by taking a error 0.05.

**RESULTS:**

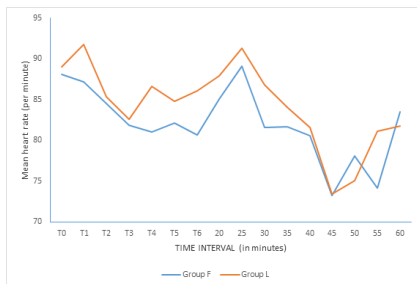
General patient information

No significant differences were found in demographic profile of the patients. (P>0.05).

**Table No.1 Changes In Heart Rate In Group F And Group L (luteal)**

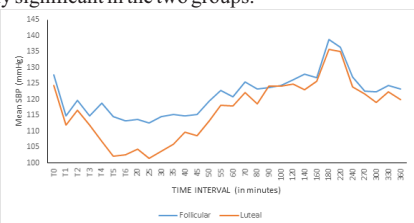
Time interval	Group F (follicular)		Group L (luteal)		t-value	p-value
	Mean	SD	Mean	SD		
T0 (supine)	88.07	8.71	89.03	5.85	-0.54	0.31
T1 (standing)	87.20	5.89	91.73	7.39	-1.47	0.04

In table no.1, no significant difference was observed between the Group L and Group F for the heart rate measurements taken in the supine position (T<sub>0</sub>). After the patients moved from the supine to standing position (T<sub>1</sub>), the mean heart rate of the Group F was 87.20±5.89 and the Group L was 91.73±7.39 i.e. Group L having significantly higher heart rate than that of the Group F (p<0.05). No significant difference in blood pressure change was observed for the standing position between the two groups (p>0.05).

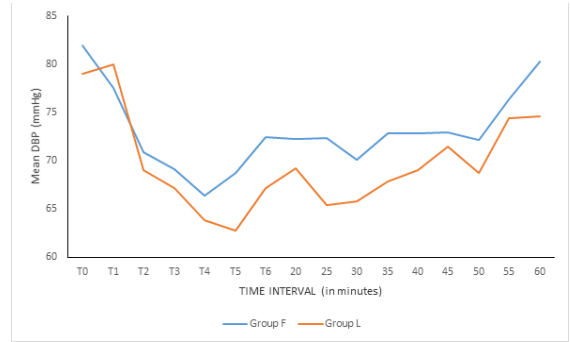


**Figure 1: Changes In Heart Rate In Group F And Group L (luteal)**

In figure no.1 no significant differences in blood pressure or heart rate were found when patients entered the operating room as shown at T<sub>2</sub>, T<sub>3</sub>. There was increase in heart rate seen in Group L at T<sub>4</sub>, T<sub>6</sub> time interval and 30, 55 min after the start of anesthesia (p<0.05) which was statistically significant in the two groups.



**Figure 2: Systolic Blood Pressure In Group F (follicular) And Group L (luteal)**



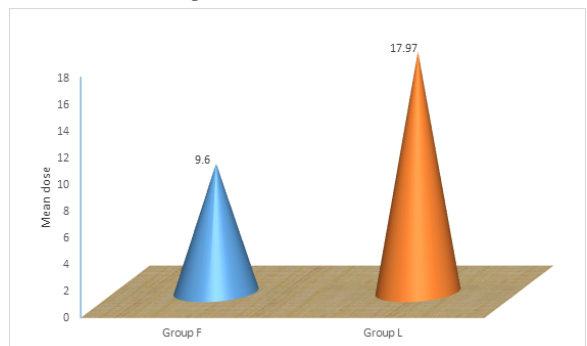
**Figure 3: Diastolic Blood Pressure In Group F (follicular) And Group L (luteal)**

In figure no.2, the fall in systolic blood pressure at T<sub>4</sub>, T<sub>5</sub>, T<sub>6</sub> time intervals and 20, 25, 30, 35, 45, 50 minutes after the start of anesthesia was more in the Group L as compared to Group F the difference being statistically significant (p<0.05).

In figure no.3 The fall in diastolic blood pressure at T<sub>4</sub>, T<sub>5</sub>, T<sub>6</sub> time intervals and 25, 35, 45, 50, 60 min after the start of anesthesia was more in the Group L as compared to Group F the difference being statistically significant (p<0.05).

The fall in mean blood pressure recorded at T<sub>3</sub> (start of anesthesia), T<sub>4</sub> (5min), T<sub>5</sub> (10min), T<sub>6</sub> (15min) time intervals and 25, 30, 35, 60 min after the start of anesthesia was more in the Group L as compared to Group F the difference being statistically significant (p<0.05)

**Table No. 2 Dose Of Ephedrine:**



In table no. 2, the amount of ephedrine used in the luteal group within 40 min after starting anesthesia was significantly greater than that used in the follicular group (P<0.05). Hypotension occurred more often in the luteal group than in the follicular group.

**DISCUSSION**

The purpose of the study was to compare the effects of different phases of menstrual cycle on hemodynamics during spinal anesthesia on hemodynamics of 60 female patients, in the age group of 20-40 years, of ASA grade I and II scheduled for elective infraumbilical surgeries of duration 30-120 minutes under spinal anesthesia randomly divided into two groups of 30 each after obtaining written informed consent. No significant difference was observed between the luteal and follicular groups for the heart rate measurements taken in the supine position (T<sub>0</sub>). As shown in table no.1, after the patients moved from the supine to standing position (T<sub>1</sub>), the heart rate of the luteal group was significantly higher than that of the follicular group. However, in both the groups' heart rates decreased after the start of anesthesia whereas, the heart rates of patients in the luteal phase were higher than those of the patients in the follicular phase as seen in figure no.1. Hypotension was observed in 15(50%) patients in Group F (follicular) and 28(93.33%) patients in Group L (luteal) which was statistically significant (p <0.05)

Hypotension, as seen in table no.2, occurred more often in the luteal group than in the follicular group. The amount of ephedrine used in the luteal group within 40 min after starting anesthesia was significantly greater than that used in the follicular group (p < It; 0.05). The mechanism behind increased HR in luteal phase is because of increase

in progesterone level which inhibits the action of estrogen, thereby, increasing sympathetic flow. Decrease in HR in follicular group is because increased oestrogen increases vagal tone and inhibits sympathetic flow. The present study concluded that women in follicular group showed more hemodynamic stability as compared to luteal phase i.e patients are able to compensate and tolerate the circulatory changes better in follicular phase. There are various hormones responsible for maintaining blood pressure homeostasis in our body which work together depending upon various factors like age, sex, altitude, posture, stress, illnesses (acute and chronic). The rise and fall in blood pressure in both the sexes manifests differently owing to the different hormones i.e. testosterone in males and oestrogen and progesterone in females. During follicular phase, there is a rise in estrogen level which inhibits the sympathetic outflow and in turn, increases vagal tone. The estrogen in the body also promotes the sensitivity of vessel vasoconstriction, so during this phase the heart rate and blood pressure do not increase. In luteal phase, there is rise in progesterone level which in turn inhibits the effects of estrogen hormone leading to increase in sympathetic flow<sup>6,7,8</sup> and decreased sensitivity of vessels to vasoconstriction<sup>1</sup>, therefore, increased heart rate<sup>9</sup> and blood pressure.

Some studies were conducted to see the effect of menstrual cycle on circulation during spinal anesthesia. In 2018 Hua Lin et al, studied the effect of menstrual cycle on circulation during combined spinal epidural anesthesia.<sup>5</sup> This study included 6 females scheduled for gynaecological surgery and divided into follicular and corpus luteal groups. They found that the heart rates of luteal group were higher than that in follicular phase<sup>2</sup> both during pre and post operative period. The use of ephedrine was more in luteal group than in follicular group, so they concluded that hemodynamics were more stable during follicular phase than luteal phase.

The limitation of the study was that the gynaecologists prefer to perform the surgery in follicular phase during which chances of bleeding are more because of pelvic congestion and increase vascularity owing to increased progesterone and estrogen levels.

## CONCLUSION

The study concluded that women in follicular group showed more hemodynamic stability as compared to luteal phase i.e they are able to compensate and tolerate the circulatory changes better in follicular phase. So, we recommend that the surgeries should be planned during follicular phase for women wherever possible for achieving more stable hemodynamics during intra-operative period.

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