A Comparative Study between Different Phases of Menstrual Cycle Regarding Hemodynamic Response to Laryngeal Mask Airway and Intraocular Pressure Changes in Elective Ophthalmic Surgery

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Abstract: Objective: The aim of the study was to determine the effect of the different phases of the menstrual cycle on hemodynamic response to laryngeal mask airway and intraocular pressure changes in elective ophthalmic surgeries. **Methods:** 80 ASA I & II female patients were equally allocated in one of two groups: group 1 (follicular) and group 2 (luteal) according to the phases of the menstrual cycle. Patients received propofol and rocuronium and LMA was introduced. Hemodynamic variables and intraocular pressure were recorded before administration of I.V anesthetic and after LMA introduction. Rate pressure products were calculated as well as IOP measurements. **Results:** Rate pressure products values were significantly increased at the first minute after LMA introduction in group 2 (luteal) compared to group 1 (follicular) ($P < 0.001$). There was no significant statistical difference between the two groups regarding the intraocular pressure measurements. **Conclusion:** The phase of the menstrual cycle affects the hemodynamic response to LMA introduction being higher in the luteal phase than in the follicular phase, whereas the different phases have no significant effect on IOP measurements.
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1. Introduction

The normal menstrual cycle is divided into two phases; the follicular phase and the luteal phase[1]. Hormonal, physical and psychological fluctuations occur during the menstrual cycle.

The hormonal changes during the different phases affect the anesthetic, analgesic and antiemetic requirements according to the phase[1,2]. Pain perception can also differ during the different phases of the cycle[3]. Laryngoscopy and tracheal intubation stimulates somatic and visceral nociceptive afferents in the airway and can significantly increase arterial blood pressure and catecholamine levels.[4] Previous studies studied the effects of the phases of the menstrual cycle on the hemodynamic response to tracheal intubation[5].

In this study, we evaluated the effects of the follicular and luteal phases of the menstrual cycle on the hemodynamic response to laryngeal make airway, also their effects, if any, on the intraocular pressure in elective ophthalmic surgery.

2. Patients and Methods

After obtaining the approval of the Ethical Committee of the Research Institute of Ophthalmology and written informed consent, 80 female patients ranging from 18 to 42 years old, ASA physical status I & II, were scheduled to receive general anesthesia with laryngeal mask airway introduction for elective ophthalmic surgeries; (cataract extraction and intraocular lens (IOL) implantation) and enrolled in this study. Exclusion criteria were: the presence of neurological or psychiatric diseases, communication problems, history of combined oral contraceptive use, irregular menstrual cycle, amenorrhea, total abdominal hysterectomy, pregnancy, any medications (including analgesics) received 24 hours prior to surgery effecting either arterial blood pressure or heart rate, patients with diagnosed glaucoma or with a history of increased intraocular pressure (even if not symptomatizing) and lengthy ophthalmic procedures.

The patients were equally assigned in two groups, 40 each, according to the phase of their menstrual cycle. The patients who were on the 1st to 12th days after the 1st day of their last menstruation were considered to be in the follicular phase of the cycle and assigned to group 1 (follicular group). Those on the 20th to 24th days after the 1st day of their last menstruation were considered to be in the luteal phase of the cycle and assigned to group 2 (luteal group).

Laboratory measurement of estrogen and progesterone levels were not done, we only abided to the above mentioned calculation. To be more precise in determining the two phases distinctively, patients in the 13th to the 19th days of their last menstruation cycles were excluded (as luteinizing hormone peaks on the 13th day and progesterone starts to increase on the 18th day of the menstrual cycle). Also, patients on

the 24th or more day of their cycle were excluded as progesterone level starts to decrease on the 24th day of the cycle. Menstrual cycle duration was recorded[5].

On arrival to the operating theatre, patients were cannulated and received premedication with 0.03 mg/kg IV midazolam 15 minutes prior to induction of anesthesia. All patients in the two groups were monitored with continuous electro-cardiography, non-invasive arterial blood pressure manometer and pulse oximetry. Intraocular pressure (IOP) was measured by an ophthalmologist blinded to the study immediately before induction, immediately after induction, immediately after laryngeal mask airway (LMA) insertion and at 5 and 10 minutes after LMA insertion.

Preoxygenation was done for 2 minutes with 5L/min fresh gas flow of 100% oxygen. After oxygenation, all patients were administered 3 mg/kg propofol over 30 seconds. After loss of eyelash reflex to touch, mask ventilation was started. Rocuronium 0.7 mg/kg was given and after around one and a half minutes, LMA was inserted and patients were instantly connected to be ventilator. Tidal volume, I:E (inspiration to expiration) ratio and RR (respiratory rate) were all calculated for each patient and were preset before patients were on the ventilator. Patients' systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), heart rate (HR) and SpO_2 (arterial oxygen saturation) were recorded at the following times: before administration of I.V. anesthetic and muscle relaxant, after administration of I.V. anesthetic and muscle relaxant, immediately after LMA insertion and at 1,2,3,4,5, and 10 minutes after LMA insertion before start of surgery.

Rate pressure product (RPP), which is calculated by the formula RPP = HR X systolic pressure was calculated for each time point and recorded.

After LMA insertion, anesthesia was maintained with 100% oxygen and 1.5% isoflurane. Ventilation was adjusted to maintain end-tidal Co_2 ($ETCo_2$) between 30 and 35 mm Hg. The surgery commenced after the data collection period (10 minutes after induction and LMA insertion). Atropine at a dose of 0.5 mg was given for bradycardia [HR < 50 beats per minute (bpm)]. 5 mg ephedrine was given if MAP decreased by 30% from the control value for a minimum of 1 minute and 1 μg/kg fentanyl was given if MAP increased by 30% from the control value for a minimum of 1 minute.

All these drugs were recorded if given. Complications related to LMA insertion such as laryngospasm, coughing or bronchospasm were also recorded. Primary outcome measures were the RPP changes in both groups while IOP changes were recorded as secondary outcome measures.

Statistical analysis

Numerical data were given as mean ± SD and were analyzed using the student's t-test. A p value < 0.05 was considered statistically significant.

3. Results

The 2 groups were comparable regarding the demographic data ($p > 0.05$) as shown in table (1).

Intraocular pressure recordings were comparable with no statistical significant difference at all time recordings (Table 2).

Table (1): Demographic Data

	Group 1 (follicular phase) (n = 40)	Group 2 (luteal phase) (n = 40)	*p* value
Age (years)	29.6±7.3	28.4±7.9	0.31
Weight (kg)	68.4±12.3	67.2±12.1	0.79
Height (cm)	165.5±4.8	163.9±4.2	0.88
Duration (days)	26.2±0.94	26.3±1.1	0.21

Table (2): Intraocular pressure measurements in the two groups at different time points

IOP (mmHg)	Group 1 (follicular phase) (n = 40)	Group 2 (luteal phase) (n = 40)	*p* value
Immediately before induction	13.2±1.1	13.4±1.3	0.33
Immediately after induction	13.4±1.5	13.7±1.2	0.41
Immediately after LMA insertion	14.1±1.6	14.3±1.5	0.37
5 min after LMA insertion	13.9±1.3	14.0±1.4	0.39
10 min after LMA insertion	13.5±1.2	13.8±1.3	0.38

Hemodynamic variables were comparable in the two groups before administration of I.V. anesthetic (propofol) ($P > 0.05$). RPP values at the first minute after LMA insertion were significantly higher in group 2 (Luteal phase) than in group 1 (follicular phase) (12.006±2063 mmHg. bpm, 9.801±1923 mmHg. bpm, respectively) ($p < 0.001$) (Tables 3 & 4).

SpO_2 and $ETCO_2$ values showed no statistical significant difference ($P > 0.05$) in the two groups. Only one patient received atropine in group 1 and two patients required fentanyl; one in group 1 and one in group 2. No patients required ephedrine. No patients developed any complications during LMA insertion.

Table (3): Systolic blood pressure (SBP), diastolic Blood pressure (DBP), heart rate (HR recordings in both groups at different time points

	SBP		DBP		HR	
	Group 1 (follicular)	**Group 2 (luteal)**	**Group 1 (follicular)**	**Group 2 (luteal)**	**Group 1 (follicular)**	**Group 2 (luteal)**
Baseline	110±5	115±3	70±3	74±1	75±3	80±1
After propofol	105±4	113±3	65±2	72±1	76±2	79±1
After muscle relaxant	98±2	106±2	63±2	71±1	75±3	78±1
1 min after LMA insertion	121±6	138±2	71±3	80±2	81±2	87±1
2 min after LMA insertion	110±3	121±2	67±3	77±1	79±1	83±1
3 min after LMA insertion	107±3	115±1	65±2	76±1	77±1	82±1
4 min after LMA insertion	106±2	113±1	64±2	75±1	75±1	81±1
5 min after LMA insertion	109±2	112±1	63±1	75±1	74±1	80±1
10 min after LMA insertion	109±1	112±2	62±2	74±1	74±1	80±1

Values are mean ± SD HR values are in beats per minute (bpm) SBP, DBP value are in mmHg

Table (4): Rate pressure product (RPP) changes in both groups at different time points

Rate pressure product (RPP)	**Group 1 (follicular phase) (n = 40)**	**Group 2 (luteal phase) (n = 40)**
Baseline	8.25±970	9.200±953
After propofol	7.980±789	8.927±972
After muscle relaxant	7.350±771	8.268±883
1 min after LMA insertion	*9.801±998	*12.006±1001
2 min after LMA insertion	8.690±926	10.043±999
3 min after LMA insertion	8.239±877	9.430±901
4 min after LMA insertion	7.950±783	9.153±993
5 min after LMA insertion	8.066±853	8.960±981
10 min after LMA insertion	8.066±853	8.960±981

RPP values are in mmHg bpm. * $p < 0.001$

4. Discussion

In previous studies, it was found that in healthy women, plasma norepinephrine levels and sympathetic activity were significantly higher in the luteal phase than in the follicular phase[6-8]. Other studies revealed that venipuncture and propofol injection pain was higher in the luteal phase compared to the follicular phase[9-11]. This finding was referred to the increased progesterone and decreased oestrogen levels[6,10]. A previous study done by **Volkan *et al.*** studied the effects of the phases of menstrual cycle on the hemodynamic response to laryngoscopy and tracheal intubation. They found that the RPP at 1 minute after tracheal intubation significantly increased in the luteal phase compared to the follicular phase (14.686 ± 2278 mmHg. bpm and 11.167±2069 mmHg. bpm, respectively)[5].

In our study, our primary hypothesis was to detect if there was a different outcome on using a laryngeal mask airway instead. Our results showed the same significant effect, being higher in the luteal phase compared to the follicular phase, but our results were still lower compared to Volkan et al. study. In our study, RPP values at 1 minute after LMA introduction were 12.006 ± 2063 mmHg. bpm in the luteal phase and 9.801 ± 1923 mmHg bpm in

the follicular phase. The explanation for the lower RPP in our study compared to Volkan's is that the hemodynamic response is lower with LMA introduction compared to laryngoscopy and tracheal intubation. Still yet, there was a significant difference between the 2 groups, hence related to the same causes mentioned by the previous authors.

As the study was performed in ophthalmic surgeries, an IOP measurement was done to reveal if the different phases of the menstrual cycle affected the IOP as well. But, there was no significant difference between the two groups.

In conclusion, we suggest that in elective ophthalmic surgeries, it is advisable to perform the operation in the follicular phase rather than the luteal phase where there is significant increased RPP response to LMA introduction. Also, using an LMA is more advisable than laryngoscopy and tracheal intubation as RPP response is still lower as compared to previous studies. Therefore, further studies comparing the two techniques could be considered to reach the best anesthetic regimen.

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