

## Assessment of the Perioperative Effect of Vasopressin in Patients Undergoing Laparoscopic Myomectomy a Double-Blind Randomized Study

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**Conflict of interest:** Nil

### **Abstract**

**Aim:** The present study was aimed to study the effectiveness vasopressin for the patients undergoing Laparoscopic Myomectomy.

**Methods:** The present study was conducted in the Department of emergency and Critical Care(Trauma and Emergency), IGIMS, Patna, Bihar, India, a study was conducted on 150 patients with uterine fibroid and American Society of Anesthesiologists (ASA) physical status I and II, undergoing elective laparoscopic myomectomy for 1 year.

**Results:** The two groups were almost similar in respect to their past surgical and medical history. The two study groups were comparable with respect to the number of uterine fibroids. There was no significant difference in the pre-operative haemoglobin level in the two study groups. There is no statistical significance in the two groups with a 'p' value of > 0.05. The mean pre-operative Hb and mean post-operative haemoglobin in patients of group A was 11 (SD 1.124) and 10.4 (SD 1.485) respectively with a 'p' value of 0.06.

**Conclusion:** Intra-operative blood loss was significantly more in cases where no measure was adopted for controlling blood loss. Use of vasopressin resulted in reduction of blood loss. Technically, the use of vasopressin is a safe and simple procedure. Vasopressin being cheap and easily available can be used routinely while doing myomectomy whether laparoscopic or abdominal.

**Keywords:** Vasopressin, Laparoscopic Myomectomy, hemorrhage, blood transfusion

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### **Introduction**

Uterine leiomyomas (myomas or fibroids) are the most common type of pelvic tumours in women. [1] When a uterine myoma develops, the normal anatomy of

uterine blood vessels is disturbed, and the vessels run in abnormal directions. Myomectomy causes vascular damage regardless of the direction of the incision

and results in severe blood loss. [2] Vasopressin is a synthetic analogue of the anti-diuretic hormone. It causes vasoconstriction through its action on V1 receptors and anti-diuresis through V2 receptors in the kidney. Intramyometrial injection of vasopressin causes vasoconstriction, stimulates the uterine contractions and therefore it reduces the blood loss during surgery. [3-6]

The traditional procedure performed is abdominal myomectomy, which is the treatment of choice in reproductive age group as myomas are most prevalent in reproductive years. Myomectomy can also be performed laparoscopically or by hysteroscopic resection in certain conditions. Since myomectomy was first performed by Washington and John Atlee in 1844, [7] it has come a long way, but even today, the biggest complication of myomectomy remains excessive blood loss during surgery which may require conversion of myomectomy to hysterectomy. Control of bleeding during myomectomy not only reduces the blood loss but also facilitates to get into the correct plane of dissection and minimized the use of energy sources, prevents tissue necrosis and leads to better healing.

Vasopressin is a synthetic analogue of the anti-diuretic hormone. It causes vasoconstriction through its action on V1 receptors and anti-diuresis through V2 receptors in the kidney. Intramyometrial injection of vasopressin causes vasoconstriction stimulates the uterine contractions and therefore it reduces the blood loss during surgery. [8] Vasopressin produces generalized constriction of blood vessels including coronary vasculature when given at higher doses. The effects include reduced cardiac output and heart rate resulting from vasoconstriction.

When infiltrated, vasopressin reduces hemorrhage, which is the most common complication during gynecological surgery, through its vasoconstrictive and uterine contraction effects, shortens the

duration of surgery, and prevents additional complications such as infection.<sup>9</sup> However, vasopressin was reported to be associated with severe complications such as bradycardia, arrhythmias, pulmonary edema, and cardiac arrest. [10] The present study was aimed to study the effectiveness vasopressin for the patients undergoing Laparoscopic Myomectomy.

## **Materials and Methods**

The present study was conducted in the Department of emergency and Critical Care(Trauma and Emergency), IGIMS, Patna, Bihar, India,

The study was conducted on 150 patients with uterine fibroid and American Society of Anesthesiologists (ASA) physical status I and II, undergoing elective laparoscopic myomectomy for 1 year.

The exclusion criteria were patients with ischaemic heart disease, cardiac valvular disease, hypertension, severe respiratory disease, obese patients, abnormal preoperative coagulation profiles, anti-inflammatory medications through two weeks preoperatively, severe hepatic or renal disease.

The patients were randomly allocated (the concealment of allocation was done by using random numbers generated through excel) into two equal groups ( $n = 75$  each). Patients were divided into two groups. 75 patients received intramyometrial injection of vasopressin during myomectomy whereas myomectomy was also performed in 75 patients without using vasopressin.

For all patients, an 18 gauge peripheral venous line was inserted and 500 ml of intravenous crystalloids was administered before surgery. Premedication with intravenous midazolam 2 mg was given 10-20 minutes before induction. After attaching the monitors [electrocardiogram (ECG), pulse oximeter, and non-invasive arterial blood pressure], the induction of anaesthesia was done for all patients by

preoxygenation with 100% oxygen, intravenous fentanyl (1-2 µg/kg), etomidate (0.3 mg/kg), and atracurium (0.5 mg/kg).

After tracheal intubation, anaesthesia was maintained with oxygen: air (50:50%), and sevoflurane (2-3%). An additional dose of intravenous atracurium (0.08-0.1 mg/kg) was given guided by the peripheral nerve stimulator to provide a train-of-four count zero. The ventilation was adjusted to maintain the end-tidal PaCO<sub>2</sub> (30-35 mmHg). Sevoflurane concentration was adjusted to maintain the mean arterial blood pressure and heart rate within ±20% of the pre-induction values. Intraoperative tachycardia (heart rate >100 bpm), and systemic hypertension (systolic arterial blood pressure >20% above baseline), was managed by increasing the concentration of sevoflurane by increments of 1.0% and bolus doses of fentanyl (0.5-1 µg/kg). Intraoperative hypotension (systolic arterial blood pressure <20% below baseline) was managed by bolus doses of ephedrine (5-10 mg) and fluid administration. Bradycardia (heart rate <60 bpm) was managed by a bolus dose of atropine (0.02 mg/kg). At the end of the

surgery, the sevoflurane was discontinued, and controlled ventilation with 100% oxygen was maintained until the end-tidal sevoflurane concentration was <0.1%. Intravenous lidocaine (1 mg/kg) was given for all patients 2 min before the removal of the endotracheal tube to provide smooth extubation. Residual neuromuscular blockade was reversed with a combination of neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg) intravenously.

Data were statistically described in terms of mean ± standard deviation (±SD), or frequencies (number of cases) and percentages when appropriate. A comparison of numerical variables between the study groups was done using the Student's t-test for independent samples. For comparing categorical data, a Chi-square test was performed. The exact test was used instead when the expected frequency was less than 5. P values less than 0.05 were considered statistically significant. All statistical calculations were done using computer program Statistical Package for the Social Science; (SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

## Results

**Table 1: Baseline characteristics of patients**

<b>Baseline characteristics</b>	<b>Group I (With vasopressin)</b>	<b>Group II (Without vasopressin)</b>
Mean age (in years)	35.50	34.60
Mean Parity	1.70	1.80
<b>No of fibroid</b>		
Single	40	45
Multiple	35	30
<b>Mean HB %</b>		
Pre-operative	12 (SD 1.150)	10.8 (SD 1.600)
Post-operative	11 (SD 1.450)	9 (SD 1.590)

Baseline characteristics of patients of both groups were comparable and are summarized in Table 1. The two groups were almost similar in respect to their past surgical and medical history. The two study groups were comparable with respect to the number of uterine fibroids.

There was no significant difference in the pre-operative haemoglobin level in the two study groups. There is no statistical significance in the two groups with a 'p' value of > 0.05. The mean pre-operative Hb and mean post-operative haemoglobin in patients of group A was 11 (SD 1.124)

and 10.4 (SD 1.485) respectively with a ‘p’ value of 0.06.

The mean Hb in pre-operative and post-operative period of group B were found to be 12(SD 1.150) and 11(SD 1.600) respectively with a ‘p’ value of <0.0001 which is considered extremely significant.

The post-operative mean haemoglobin comparision between Group A and B was statistically significant (‘p’ value is 0.0056). The mean post-operative haemoglobin in Group A and B was 10.8(SD1.450) and 9(SD 1.590) respectively.

**Table 2: Comparison between Group A & B**

Group	Blood loss (in ml)	Duration of surgery (in min)	Number of blood transfusion
A	210 SD (106.55)	71.60 SD (5.650)	3
B	495.15 SD (91.06)	72.50 SD (5.600)	4

The mean blood loss in ml in Group A was 210 (SD 106.55) and Group B was 495.15 (SD 91.06) with ‘p’ value being <0.0001 which is considered extremely significant (table 2). The mean duration of surgery in Group A was 71.60 minutes SD (5.650) and Group B was 72.50 minutes SD (5.600), with ‘p’ value >0.05 (0.6851). Both the groups were comparable in regard to the duration of surgery.

## Discussion

The mean age in this study was  $30 \pm 3.3$  years. Shozo Matsuoka et al. reported mean age of myomectomy at  $37.3 \pm 4.2$  years. [11] Similar results were seen in two studies conducted by Hyo Jin et al. [12] and YashusiKotani et al. 2009. [13] Studies by Parazzini F, Negri E, La Vecchia et al. showed a decreased in the incidence and number of clinically apparent fibroids with increasing parity. [14] Similar result was obtained in a study conducted by Baird DD, Dunson DB et al. [15]

Vasopressin, a hormone naturally secreted by the posterior pituitary, acts on V1 and V2 receptors present in blood vessels and the kidney. Anaesthesiologists use vasopressin in cardiopulmonary resuscitation, diabetes insipidus and as a vasopressor in septic shock.

In gynaecological practice, vasopressin, a potent vasoconstrictor, is often used intramyometrially to reduce blood loss during myomectomy. [16] Vasopressin acts by constricting the smooth muscles in the walls of the capillaries, small arterioles and venules. The vasoconstrictive effects of intramyometrial vasopressin manifest within seconds with a half-life of 10–20 min and a duration of action of 2–8 h. [17]

In this study, the mean fall in Hb was not significant with the use of vasopressin. Fletcher H et al. in 1996 reported similar observation that there was no significant fall in post-operative Hb with the use of vasopressin. [18] HirotoShimanuki et al. in 2005 reported the same. [19] A randomised placebo controlled trial by Frederick J, Fletcher J, Hardie M, Simeon D, Mulling S. in 1994 with the use of vasopressin as a haemostatic showed a lower fall in haemoglobin level and haematocrit compared with the controls.

The mean fall in Hb without intervention was significantly more compared to vasopressin group in the present study. Seracchioliet al. 2000 [20], Landi et al. 2001 [21] and Lee et al. 2004 [12] made similar observations. It is thus observed that there is more amount of blood loss and a significant fall in Hb level without the use of haemostatic as shown by our study and several other studies. In the

present study the incidence of intra-operative or post-operative blood transfusion was significantly lesser with the use of vasopressin. Ginsberg in 1993 [22] and A. Taylor et al. 2005 reported that the need for blood transfusion during myomectomy is reduced with the use of vasopressin. [23]

There was no significant difference in the incidence of post-operative complications & febrile morbidity in the two study group. Similar observation was made by IverChelmow & co-workers and Celik et al. 2003. [24,25]

### Conclusion

Vasopressin, a synthetic derivative of anti-diuretic hormone has been tried in several studies for reducing blood loss during myomectomy. Technically, the use of vasopressin is a safe and simple procedure. Vasopressin being cheap and easily available can be used routinely while doing myomectomy whether laparoscopic or abdominal. The effectiveness of vasopressin has been shown beyond doubts by several studies including the present study. However, there is need for more well designed studies to shed more light on the effectiveness of different interventions to reduce blood loss during myomectomy. Therefore, anaesthesiologists and gynaecologists must follow the precautions to avoid and minimise the incidence of cardiovascular complications associated with intramyometrial vasopressin.

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