Original Research Article

Study of effectiveness of vasopressin as hemostatic agent in laparoscopic myomectomy at tertiary health care center

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Abstract

Background: Myomectomy is an invasive surgical procedure and surgical removal is necessary when the myoma is symptomatic and resistant to medical management or interferes with reproduction. Present study was aimed to A study of effectiveness of vasopressin for the patients undergoing Laparoscopic Myomectomy at tertiary health care center. **Material and Methods:** Present study was hospital based, comparative, parallel-group study, conducted in patients with uterine fibroid, ASA physical status I/II, posted for elective laparoscopic myomectomy. 60 patients were randomly allocated by sealed envelope method into two equal groups (n = 30 each), into Group V and Group NS. **Results:** 60 patients were randomly divided into two groups (n=30) each. General Characteristics such as Mean age in years, ASA grade I/II, BMI, Mean maximum diameter of the largest myoma in cm, number of myomas and position of myomas were comparable in both groups and difference was not statistically significant. In operative characteristics, we noted longer duration of surgery, more amount of blood loss, more Intraoperative Blood transfusions and increased Hemoglobin difference between preop and at 3rd day in NS group as compared to Group V and difference was statistically significant ($p<0.05$). We monitored Vital parameters and Side effects of all patients. Bradycardia (HR of 41-60 bpm) and. Hypertension (SAP ≥20% above baseline) was more in group V as compared to group NS and difference was statistically significant ($p<0.05$). All side effects were effectively managed medically and no incidence of myocardial infarction, pulmonary oedema, congestive heart failure, cardiac arrest, mortality was noted in present study. **Conclusion:** Vasopressin is effective for the patients undergoing Laparoscopic Myomectomy in terms of blood loss, duration of surgery, though few side effects are noted for which caution is needed during surgical procedure.

Keywords: Vasopressin, Laparoscopic Myomectomy, hemorrhage, blood transfusion

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INTRODUCTION

Uterine myomas are the most frequent tumours of the female genital tract affecting 20–50% of all women, with an increased incidence in the later years of a woman's reproductive life.[1] Myomectomy is necessary when the myoma is symptomatic and resistant to medical management or interferes with reproduction. Over the 2-3 decades the laparoscopic approach became very popular amongst gynecologic surgeons and patients for the reasons of faster recovery, shorter hospitalization, better cosmetic results and excellent long-term results both in terms of resolution of symptoms and reproductive outcomes.[2,3] 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

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therefore it reduces the blood loss during surgery.[4] 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.[5] 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.[6] However, vasopressin was reported to be associated with severe complications such as bradycardia, arrhythmias, pulmonary edema, and cardiac arrest.[7] Present study was aimed to A study of effectiveness vasopressin for the patients undergoing Laparoscopic Myomectomy at tertiary health care centre.

MATERIAL AND METHODS

Present study was hospital based, comparative, parallel-group study, conducted in Department of Anaesthesiology, Bhaskar Medical College & General Hospital, Yenkapally, India. Present study was conducted over 2 years period (January 2019 to December 2020). Study was approved by institutional ethical committee.

Inclusion criteria: Patients with uterine fibroid, ASA physical status I/II, posted for elective laparoscopic myomectomy, willing to participate in study.

Exclusion criteria: Patients with ischaemic heart disease, cardiac valvular disease, hypertension, severe respiratory disease, severe hepatic or renal disease. Patients with BMI > 30 kg/m^2

Study was explained to patients and a written informed consent was taken for participation. 60 patients were randomly allocated by sealed envelope method into two equal groups (n = 30 each), into Group V (Vasopressin group) and Group NS (Normal saline group: Patients received 15 ml of normal saline, for each myoma).

The vasopressin was prepared by dilution of 20 units vasopressin in 200 ml normal saline as 0.1 unit/ml, then 15 ml was injected by the surgeon slowly after negative aspiration of blood in the plane between the myometrium and the myoma. A single injection of 15 ml was made for each myoma.

In operation theatre, electrocardiogram (ECG), pulse oximeter, and non-invasive arterial blood pressure, were monitored. All patients were operated under general anaesthesia with atracurium (0.5 mg/kg) and sevoflurane (2-3%). Intraoperatively, parameters such as amount of blood loss, blood transfusion (the transfusion trigger was the amount of blood loss >20% of the estimated blood volume), heart rate, mean arterial blood pressure, a continuous ECG with automatic ST-segment analysis (leads II and V), arterial oxygen saturation (SPO2) and the end-tidal carbon dioxide (ETCO2). The values were collected at preoperatively, just before intramyometrial vasopressin administration, at 15, 30, 45, 60 minute and at the end of surgery.

After extubation patients were monitored in postoperative anaesthesia care unit for next 12 hours and heart rate, mean arterial blood pressure, a continuous ECG with automatic ST-segment analysis (leads II and V), arterial oxygen saturation (SPO2) were monitored every 30 minutes. Later patients were shifted to respective wards. Patients were interviewed during discharge for any complaints.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

60 patients were randomly divided into two groups (n=30) each. General Characteristics such as Mean age in years, ASA grade I/II, BMI, Mean maximum diameter of the largest myoma in cm, number of myomas and position of myomas were comparable in both groups and difference was not statistically significant. In majority of cases mean maximum diameter of the largest myoma was 5-7 cm, 2-3 myomas and intramural position of myomas was noted.

Table 1: General Characteristics

Patient Characteristics	Group V (Mean ± SD)/ No. of cases (%)	Group NS (Mean ± SD)/ No. of cases (%)	p value
Mean age in years	36.91 ± 5.70	36.68 ± 6.13	0.42
ASA grade I/II	22/8	21/9	0.64
BMI in kg/m2 (SD)	24.01 ± 3.1	23.82 ± 3.13	0.66
Mean maximum diameter of the largest myoma in cm			0.46
<5 cm	7 (23.33 %)	9 (30 %)	
5-7 cm	15 (50 %)	14 (46.67 %)	
>7 cm	8 (26.67 %)	7 (23.33 %)	
Number of myomas			0.81
1 myoma	9 (30 %)	11 (36.67 %)	

2-3 myomas	15 (50 %)	14 (46.67 %)	
≥ 4 myomas	6 (20 %)	5 (16.67 %)	
Position of myomas			0.75
Intramural	16 (53.33 %)	14 (46.67 %)	
Submucosal	2 (6.67 %)	1 (3.33 %)	
Subserosal	6 (20 %)	8 (26.67 %)	
Mixed	6 (20 %)	7 (23.33 %)	

In operative characteristics, we noted longer duration of surgery, longer duration of anaesthesia, more amount of blood loss, more Intraoperative Blood transfusions and increased Haemoglobin difference between preop and at 3rd day in NS group as compared to Group V and difference was statistically significant (p<0.05).

Table 2: Operative characteristics

Patient Characteristics	Group V (Mean ± SD)/ No. of cases (%)	Group NS (Mean ± SD)/ No. of cases (%)	p value
Duration of surgery (min)	102.62 ± 23.38	129.92 ± 32.14	0.025
Duration of anesthesia (min)	107.23 ± 20.52	134.35 ± 31.72	0.035
Amount of blood loss (ml) Intraoperative	411.11 ± 89.70	545.44 ± 72.23	0.001
Number of patients received Blood transfusion	5 (16.67 %)	11 (36.67 %)	0.021
Haemoglobin difference between preop and at 3rd day (g/dl)	1.98 ± 1.25	2.51 ± 1.57	0.045

we monitored Vital parameters and Side effects of all patients. Bradycardia (HR of 41-60 bpm) and. Hypertension (SAP ≥20% above baseline) was more in group V as compared to group NS and difference was statistically significant (p<0.05). other side effects such as Severe bradycardia (HR <40-30 bpm), Tachycardia (HR >100 bpm), Atrial extrasystole and Hypotension (SAP ≤20% below baseline) were more in group V as compared to group NS and difference was not statistically significant (p>0.05). All side effects were effectively managed medically and no incidence of myocardial infarction, pulmonary oedema, congestive heart failure, cardiac arrest, mortality was noted in present study.

Table 3: Vital parameters and Side effects

Patient Characteristics	Group V (Mean ± SD)/ No. of cases (%)	Group NS (Mean ± SD)/ No. of cases (%)	p value
Bradycardia (HR of 41-60 bpm)	6 (20 %)	2 (6.67 %)	0.023
Severe bradycardia (HR <40-30 bpm)	1 (3.33 %)	-	--
Tachycardia (HR >100 bpm)	3 (10 %)	1 (3.33 %)	0.52
Atrial extrasystole	4 (13.33 %)	1 (3.33 %)	0.63
Hypertension (SAP ≥20% above baseline)	6 (20 %)	2 (6.67 %)	0.023
Hypotension (SAP ≤20% below baseline)	4 (13.33 %)	2 (6.67 %)	0.13
Arterial oxygen saturation (SPO2) (%)	99.20 ± 021	99.18 ± 0.22	0.92
Partial pressure of carbon dioxide (PaCO2)(mmHg)	35.73 ± 3.25	35.54 ± 3.42	0.92

SAP: Systolic arterial blood pressure; HR: Heart rate

DISCUSSION

Myomectomy is a fairly hemorrhagic operation. Several measures have been tried to achieve a reduction of blood loss during open and laparoscopic myomectomy, including the use of bipolar energy, application of a variety of vasoconstrictive and uterotonic agents, use of tourniquets, temporary clipping of the uterine arteries, and use of barbed sutures.[8,9,10,11] Myomectomy is associated with intraoperative and postoperative complications including excessive haemorrhage, pyrexia, visceral damage, thrombo-embolism, conversion to hysterectomy, blood transfusions, scar dehiscence in future pregnancy and many others.[12]

Intramyometrial infusion of vasopressin causes vasoconstriction, stimulates the uterine contractions and therefore it reduces the blood loss during surgery.[4] However, vasopressin was reported to be associated with severe complications such as bradycardia, arrhythmias, pulmonary edema, and cardiac arrest.[6] The variations in heart rate (HR) and blood pressure after intramyometrial vasopressin injection might be correlated to the systemic absorption of vasopressin especially during the surgical excisions of the fibroid and not linked to the direct intravascular injection.[10]

Frishman recommended intramyometrial dose of 4–6 U at a concentration 0.2 U/ml to be safe, based on assumption that low dose and low concentration are equally effective in achieving hemostasis without cardiac complications.[13] Moda, N *et al.*,[14] found that 20 units intramyometrial vasopressin used dogmatically by surgeons drops blood loss but it is connected with cardiovascular impediments. Hence, 10 units of intramyometrial vasopressin as

compared to 20 units is associated with similar blood loss and lesser side effects such as bradycardia, pulmonary edema, hypotension, blood loss, and increased airway pressure.[14] In a study conducted by H. Fletcher *et al.*[15] there was <800ml blood loss in vasopressin group compared to 1000ml in tourniquet group. Protopapas A *et al.*,[16] studied 150 patients undergoing laparoscopic myomectomy; 50 were treated without the use of any vasoconstrictivec agent (group 1), and 100 were treated with intraoperative intramyometrial injection of dilute vasopressin (20 IU/100 mL normal saline) (group 2). Overall, the mean estimated blood loss was 321.8 ± 246.0 mL in group 1 compared with 147.8 ± 171.8 mL in group 2, respectively (p <.001). The risk factors for hypercapnea and subcutaneous emphysema included the size and intramural position of the largest myoma. Vasopressin was not associated with serious cardiovascular adverse events. Soliman R *et al.*,[17] studied 194 patients divided into two groups as Vasopressin group (vasopressin 0.1 unit/ml, 15 ml) and Control group (equal amount of normal saline). The heart rate decreased significantly in both groups, but the decrease was lower with vasopressin than the control group through the time points T3 to T5 (P < 0.05) The mean arterial blood pressure increased significantly in both groups, but the increase was higher with vasopressin than the control group through T3 to T5 (P < 0.05). The amount of blood loss decreased significantly with vasopressin than the control groups (P = 0.001). The number of transfused packed red blood cells was lower with vasopressin than the control group (P = 0.001). The incidence of hypertension, bradycardia and atrial extrasystole was higher with vasopressin than the control group (P = 0.005, P = 0.012, P = 0.033, respectively). Similar findings were noted in present study. Saha MM *et al.*,[18] compared intraoperative blood loss following abdominal myomectomy after receiving intramyometrial vasopressin or tourniquet application, blood loss in the tourniquet group was significantly higher (p=<0.001). Postoperative haemoglobin and haematocrit were lower in tourniquet group than vasopressin group. There was significant fall in haemoglobin and haematocrit in postoperative period in both group (p=<0.001) but it was more in tourniquet group. Total five patients (three in tourniquet group and two in vasopressin group) had received one unit whole blood transfusion.

The safety of vasopressin has been challenged in the past as a result mainly of case reports of serious and potentially lethal cardiovascular complications associated with its use as a vasoconstrictive agent, including bradycardia, hypotension, arrhythmias, atrioventricular block, pulmonary edema, and even cardiac arrest.[19,20,21]

Low concentrations of vasopressin has been considered to be safe, but sometimes it can lead to undesirable effects such as bradycardia with loss of peripheral pulse, non recordable blood pressure further leading to cardiac arrest. Nikhilesh B *et al.*, reported a case of acute onset bradycardia and dyspnea along with loss of peripheral pulse after local infiltration of 5 unit of vasopressin (20units diluted in 100ml NS), patient was revived by successful resuscitation.[22]

Severe adverse reactions, such as myocardial infarction and cardiac arrest, have also been reported even after local intramyometrial infiltration of AVP during gynecological surgery under general anesthesia.[23]

Bradycardia induced by vasopressin infiltration so, the dose used should range from 0.05-0.3 units/ml and the total administered dose should be as small as possible. In addition, close communication between the anesthesiologist and the gynecologist is also important to identify and treat such rare complications, which can sometimes be induced by the local infiltration of vasopressin.[21]

CONCLUSION

Vasopressin is effective for the patients undergoing Laparoscopic Myomectomy in terms of blood loss, duration of surgery, though few side effects are noted for which caution is needed during surgical procedure. An effective communication between the anesthesiologist and gynaecologist is very important for early identification and appropriate treatment of rare complications associated with local vasopressin.

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