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Case Report

Sudden bradycardia and impending cardiac arrest by intra-myometrial vasopressin in laparoscopic myomectomy: a case report and review of literature

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ABSTRACT

Vasopressin has long been used in myomectomy to decrease blood loss. Its efficacy is beyond doubt. But at the same time it is known to cause some of the serious cardiovascular side effects. We here report a case of severe bradycardia and impending cardiac arrest caused by intra-myometrial infiltration of 12 U of vasopressin and present a review of literature.

Keywords: Vasopressin, Myomectomy, Bradycardia, Cardiac arrest

INTRODUCTION

Vasopressin, a posterior pituitary hormone is used for reducing blood loss during myomectomy from more than 60 years. Although intra-myometrial vasopressin results in very good surgical hemostasis it may cause adverse cardiac events like bradycardia, arrhythmia, cardiac arrest and pulmonary oedema and lethal catastrophe if not diagnosed and managed soon.[1-4] We report a case of successful resuscitation following bradycardia and impending cardiac arrest by intra-myometrial injection of vasopressin in a case of laparoscopic myomectomy.

CASE REPORT

A 27 years old nulliparous woman, a case of primary infertility with posterior wall intra-myometrial fibroid was posted for operative hysterolaparoscopy. She had no past medical or surgical history. All her hematological, biochemical investigations and electrocardiography (ECG) was normal. The woman was ASA grade I and after thorough evaluation she was taken up for surgery after 6 hours of fasting. She was monitored by 5 lead ECG, pulse oximeter, ETCO2 and non-invasive blood pressure monitor. Baseline vitals were pulse- 82/minute, blood pressure (BP)-120/76 mmHg, O2 saturation 100% with normal sinus rhythm on ECG. She was preloaded with 1 liter ringer lactate and combined spinal epidural anesthesia was given in L3-4 space and level of T6 achieved. Dexmedetomidine infusion was started with a loading dose of 50 mcg in 10 min followed by infusion of 50 mcg/hr. She was supplemented with injection fentanyl 50 mcg intravenous (IV) and injection propofol 40 mg IV. Initially hysteroscopy was performed with 6 mm diagnostic rigid hysteroscope which showed normal uterine cavity and normal bilateral ostia. Afterwards laparoscopy was performed with supraumbilical primary port and three accessory 5 mm ports at intra-abdominal pressure of 15 mmHg, abdominal cavity visualized which showed a large bosselated subserosal fibroid of 7 by 7 cm arising from posterior wall of uterus at the level of isthmus. Bilateral tubes and ovaries were normal, and free spill of dye seen bilaterally on chromopertubation test. Till this time woman had normal vitals, SPO2 and ETCO2. For

reducing blood loss during myomectomy, 180 ml of intra-myometrial vasopressin injected in dilution of 20 U in 300 ml (12 U in total) slowly after negative aspiration. Within one minute of vasopressin infiltration patient developed sudden bradycardia with heart rate dropping to 25 bpm, hypotension as evidenced by systolic blood pressure of 70 mm Hg and signs of impending cardiac arrest. The patient had normal SPO2 and normal ETCO2 at this time also indicating adequate perfusion. There was intense facial pallor and peripheral pulses were not palpable. Pnemoperitoneum was deflated, injection atropine 0.6 mg was given intravenously and two more doses were given at interval of 30 seconds and 1 minute respectively. Intravenous crystalloids were given fast and patient was revived with heart rate picking upto 80-90 bpm and blood pressure values improving to 90/60 mm Hg. SPO2 and ETCO2 were normal throughout the surgery. Although the patient was in regional anesthesia we could not assess the consciousness level of the patient as she was given fentanyl, propofol and dexmedetomidine initially in view of laparoscopic surgery. We waited for around half an hour after resuscitation and proceeded with open myomectomy. Postoperatively patient was shifted in HDU in stable condition with normal vitals, SPO2 100% without O2 and normal findings of chest and CVS examination. The patient was discharged on 5th postoperative day in good condition.

DISCUSSION

Vasopressin is an anti-diuretic hormone and has a strong vasoconstrictive effect on smooth muscles. It is a direct vasoconstrictor and also acts by stimulating contraction of myometrial cells in the uterus via its action on V2 receptors. The half-life of vasopressin is 24 minutes as compared to very short life of other vasoconstrictors like epinephrine (2 minutes) and oxytocin (10 minutes), making it a superior agent for achieving hemostasis.[5-7]

Various studies have demonstrated proven efficacy of vasopressin in varied dosages in decreasing blood loss during myomectomy.

The first of these studies have been reported by Dillon et al almost sixty years ago on 20 patients in whom vasopressin was used to decrease blood loss associated with gynecologic surgery.[8] They used 4 U as the total maximum dose diluted in 20 ml of saline (0.2 U/ml). They injected 5-10 ml (1 to 2 U) at the beginning of the surgery, repeated the injections as needed, but did not exceed a total cutoff of 4 U. The authors monitored the ECG and vital signs and found no evidence of abnormalities or untoward events while still noting a marked decrease in blood loss. A recent study has shown the efficacy of vasopressin in reducing blood loss during my-omectomy.[9] The mean EBL was 321.8±246.0 ml in control group as compared with 147.8±171.8 mL in the group using vasopressin ($p<0.001$). A randomized controlled trial (RCT) by Frederick et al showed that vasopressin use during laparoscopic myomectomy (20 U in 20 ml normal saline) was associated with a significant reduction in mean blood loss (225 versus 675 ml, $p<0.001$), and mean hemoglobin (Hb) (1.7 versus 5.3 g/dL, $p<0.001$) and hematocrit (HCT) drop (5% versus 13%, $p<0.001$) as compared with placebo.[10] The latest Cochrane database review showed that vasopressin use is associated with a reduction in blood loss of between 392.51 and 507.49 ml during abdominal myomectomy and between 121.73 ml and 172.17 ml during laparo-scopic myomectomy.[11]

Although vasopressin is a very good hemostatic agent but at same time there are published case reports of ad-verse cardiac effects by vasopressin like bradycardia, hypotension, arrhythmias, atrioventricular block, pulmonary edema, and even cardiac arrest. In Greece, France and Italy for example, vasopressin has been withdrawn long ago in response to safety concerns.

We performed a search on PubMed and Google scholar using terms vasopressin, myomectomy, cardiac complications, bradycardia and hypotension.

Table 1 shows the various case reports with their complications, dosages of vasopressin used and the final outcome.

Barcroft et al reported a case of acute pulmonary edema which developed in a case of laparoscopic myomectomy after infiltration of 20 U of vasopressin.[1] This case initially developed bradycardia and hypotension which was managed with glycopyrrolate, ephedrine and crystalloids. The patient settled down but at extubation was found to have pink frothy sputum and desaturated to 89% suggesting that she developed acute pulmonary edema. She was managed with IV furosemide and diamorphine and recovered after stay in intensive care unit (ICU).

Hobo et al reported a case of bradycardia and cardiac arrest caused by infiltration of 56 ml of 20 U of vasopressin diluted in 200 ml saline (0.2 U/ml).[2] The patient was managed with ephedrine, atropine and cardiac massage and had uneventful recovery.

Hung et al described two cases of bradycardia followed by cardiac arrest and pulmonary edema after local infiltration of 6-10 ml of dilute vasopressin (2 U/ml) during an open myomectomy.[3]

Lee et al reported a case of severe bradycardia and cardiac arrest during robotic assisted myomectomy after infiltration of vasopressin in doses of 20 IU (20 IU diluted in 40 ml of normal saline).[4] The patient was success-fully revived with atropine 0.5 mg, reversal of Trendelenburg position and supportive care. They attributed bradycardia to physiologic effects of vasopressin, pneumoperitoneum in steep Trendelenburg position for laparoscopy, shoulder braces for robotic surgery which add to carotid sinus compression and lowered sympathetic activity leading to bradycardia.

Table 1: Case reports showing complications with different vasopressin doses and outcome.

Case report	Vasopressin dose	Route of surgery	Complication	Final outcome
Barcroft et al[1]	20 U	Laparoscopic	Bradycardia, hypotension, pulmonary edema	Recovered
Hobo et al[2]	18 U (0.5U/ml)	Laparoscopic	Bradycardia, cardiac arrest	Recovered
Hung et al[3]	12 to 20 U (in two cases)	Abdominal	Bradycardia, cardiac arrest, pulmonary edema	Recovered
Lee et al[4]	20 U	Robotic	Bradycardia, cardiac arrest	Recovered
Nezhat et al[15]	4-5U (0.6 U/ml)	Laparoscopic	Bradycardia, hypotension, pulmonary edema	Recovered
DeschampS et al[16]	3 U (0.5 U/ml)	Abdominal	Bradycardia, absent radial pulse, AV block with bigemini	Recovered.
Muthukumar et al[17]	4 U (0.13 U/ml)	Abdominal	Bradycardia, hypotension, absent peripheral pulses	Recovered
Jayaram et al[18]	20 U (0.1 U/ml)	Laparoscopic	Vasospasm, absent radial pulse, stable ECG, stable ETCO2	Recovered
Tulandi et al[19]	5 U (0.5 U/ml)	Laparoscopic	Bradycardia, hypotension, AV block, pulmonary edema	Recovered
Butala et al[20]	20 U (1 U/ml)	Abdominal	Bradycardia, hypertension	Recovered
Kabade et al[21]	8 U (0.2 U/ml)	Abdominal	Bradycardia, hypotension, ST segment depression, pulmonary edema	Died
Reiss et al[12]	60 U	Abdominal	Absent peripheral pulses, severe vasospasm, hypotension	Recovered

There are three kind of vasopressin receptors V1, V2 and V3. V1 and V2 receptors are located in the periphery whereas V3 receptors are found in central nervous system (CNS). Vasopressin produces generalized constriction of most blood vessels including coronary vessels resulting in increase in blood pressure. This sudden hypertension induces sympatho-inhibitory reflex by activating baroreceptors in aortic arch and carotid sinus resulting in lowering of cardiac contractility and heart rate. In the collecting tubules vasopressin acts on V2 receptors, causing water retention and it also acts on area postrema of brain to decrease cardiac output. Thus, there is decrease in heart rate and cardiac output as a result of coronary vasoconstriction, decreased blood flow, altered sympathetic tone and potentiated baroreflex in response to generalized vasoconstriction, which results in bradycardia, global hypotension and in severe cases cardiac arrest.

There are further risk factors associated with laparoscopy. Pneumoperitoneum with CO2 stretches the peritoneum which induces the vagal-mediated cardiovascular reflex leading to bradycardia. Trendelenburg position leads to increased venous return resulting in increase in stroke volume, and cardiac output thereby activating baroreceptors further which may lower the heart rate by diminishing sympathetic activity.

Our patient exhibited similar manifestations as pallor, sudden bradycardia and hypotension just after intra-myometrial injection of vasopressin. Pale conjunctiva may be due to cutaneous vasoconstriction while brady-cardia is due to potentiated baroreflex and altered sympathetic tone. Hypotension may be due to decrease cardiac output, heart rate, altered sympathetic tone or because of peripheral vasopressin mimicking hypotension.

Treatment includes identification of this situation and cardiac life support measures oxygenation and atropine for bradycardia. Vasopressin has short half-life so early recognition and correct resuscitation results in successful outcome. Failure to identify this will lead to treatment with vasopressors which will worsen cardiac complications.

There are some previous case reports of vasopressin overdose resulting in bradycardia and apparent hypotension that was treated with anticholinergic, inotropic, and vasoconstrictor drugs. Many of these cases subsequently developed pulmonary edema and acute ST-segment changes suggestive of myocardial injury. These complications point to the fact that caution is required when using vasopressors in the treatment of vasopressin-induced vasospasm. Treatment of bradycardia or hypotension after high-dose vasopressin with additional vasopressors and inotropes may be deleterious. Vasodilators such as nitroglycerine, atropine or increasing depth of anesthesia may theoretically have benefits in these situations. Noninvasive blood pressure measurement based on oscillometric waveform of blood flow may not be truly applicable in the setting of peripheral vasospasm and can lead to administration of additional inotropic drugs that can contribute to iatrogenic cardiovascular morbidity. It has also been proposed to measure central blood pressure using preoperative placement of central arterial catheter as peripheral vasospasm with central hypertension may give misleading clinical signs.[12]

In case invasive cardiac monitoring is not performed, palpable carotid pulses and normal value of positron emission tomography (PET) CO2 can help in differentiating peripheral vasospasm from global hypotension.

Contrary to all the above case reports, a study of the effects of vasopressin during laparoscopic myomectomyhas shown that it has less effect on larger and more central vessels. Although the study was conducted on nine patients, the concentration of vasopressin used was 4 IU (20 IU diluted in 100 ml saline) and uterine blood flow was measured using transvaginal ultrasound evaluating arcuate artery and ascending branch of uterine artery while systemic blood flow was measured using transesophageal doppler evaluating aorta and measuring urine output.[13]

Another RCT by Cohen et al comparing different dilutions of vasopressin- 200 ml of diluted vasopressin solution (20 U in 400 ml saline), and 30 ml of concentrated vasopressin solution (20 U in 60 ml normal saline) found no significant difference in blood loss or change in HCT levels in both the groups.[14]

CONCLUSION

To summarize, vasopressin is cost effective agent in reducing blood loss during myomectomy the efficacy of which has been proven in well-designed RCT. But cardiovascular complications may occur with vasopressin use in varied dosages. The safe dose and concentration of vasopressin still needs to be determined. The amount of blood loss saved during myomectomy using vasopressin and the rare but potentially serious cardiovascular complications caused by its use needs to be weighed using risk benefit analysis in larger well randomized con-trolled trials. Whether we may consider invasive monitoring using central arterial line in women undergoing myomectomy with vasopressin use also needs to be addressed in future.

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