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Case report

Risk of vasopressin use: a case of acute pulmonary oedema, post intramyometrial infiltration of vasopressin in laparoscopic myomectomy

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SUMMARY

A 34-year-old patient underwent a laparoscopic myomectomy, complicated by a profound episode of bradycardia and hypotension following intramyometrial infiltration of vasopressin (20 IU), promptly corrected with intravenous ephedrine (6 mg) and glycopyrrolate (200 µg). At extubation, pink frothy fluid was noted in the endotracheal tube; she was visibly distressed, desaturated to 89% in air and was coughing up pink stained fluid. Acute pulmonary oedema secondary to vasopressin was suspected. A tight-fitting oxygen mask (100%) with positive end expiratory pressure was applied and intravenous furosemide (20 mg) and diamorphine (4 mg, 1 mg increments) were administered to facilitate diuresis and oxygenation. Chest X-ray confirmed acute pulmonary oedema. Arterial blood gas demonstrated type 2 respiratory failure. Over 12 hours, the oxygen was weaned to 1 L/min. She demonstrated excellent diuresis. Troponin and brain-natriuretic peptide were elevated, but echocardiogram was normal. The cardiology diagnosis was vasopressin-induced coronary vasospasm, precipitating acute pulmonary oedema. She was discharged home on day 5.

BACKGROUND

This case demonstrated the risks associated with the routine intramyometrial use of vasopressin in myomectomy cases. The marked rate of onset of acute pulmonary oedema, requiring respiratory support and high dependency unit care in a patient with excellent premorbid function and in the absence of cardiac disease, raises the question, whether preoperative assessment of cardiac function should be considered prior to procedure.

Awareness of the risk of systemic vasopressin absorption and potential cardiac sequelae including bradycardia, hypotension and coronary artery vasospasm will facilitate the speed of recognition and initiation of treatment, to ensure prompt resolution.

On review of the literature regarding complications associated with intramyometrial vasopressin use, this is the first case demonstrating acute pulmonary oedema, requiring respiratory support. There are a number of cases, which have demonstrated significant haemodynamic instability, thought to be related to systemic absorption of vasopressin. This case highlighted the variation in dose and constitution of vasopressin in use worldwide and the absence of clear national guidance on safe vasopressin doses. The evidence supports efficacy at lower vasopressin doses than used in this case. This case highlights the need for clear national guidance on dosage and constitution, to ensure ongoing safe use of vasopressin.

CASE PRESENTATION

A 34-year-old female patient, with no significant past medical history (62 kg) underwent a routine laparoscopic myomectomy for a single, pedunculated fibroid. The main indication for surgery was significant pressure symptoms affecting her bladder. She had no previous surgical or medical history. She had never been pregnant. She took no regular medication and had no known allergies. She has been fasting from midnight the day prior to the procedure. She was counselled about the risks of surgery, including the potential to convert to an open procedure and proceeding to a hysterectomy, in the event of a complication. She was happy to proceed. She was assessed and consented by the anaesthetic consultant and was deemed to be American Society of Anaesthetists (ASA) grade 1. The anaesthetic consent also included any unexpected incidences related to other surgery or the anaesthetic and this was documented.

The patient had an uneventful awake, single-attempt spinal anaesthetic, with bupivacaine (2 mL, 0.5%) and diamorphine (750 µg). General anaesthetic was straight-forward, induction with intravenous propofol (200 mg) and atracurium (35 mg) and anaesthetic maintenance was with desflurane aimed at a minimum alveolar concentration (MAC) of 1.1. She was ventilated on synchronised intermittent mandatory ventilation–volume guarantee mode, with a respiratory rate of 12–15/min, positive end expiratory pressure (PEEP) of 7 cmH_2O, peak inspiratory pressure of 15 cmH_2O and a fraction of inspired oxygen (FiO_2) of 30%.

Laparoscopic entry with veres needle was uncomplicated with an opening pressure of 6 mm Hg and a pneumoperitoneum to 20 mm Hg. Primary trochar entry with a 10 mm port was routine; two further lateral ports (5 and 10 mm) were inserted under direct vision. Intramyometrial vasopressin (20 IU) into the stalk of the fibroid was used routinely to facilitate vasoconstriction and reduce blood loss. An episode of sinus bradycardia (heart rate 30) associated with significant hypotension (systolic blood pressure (SBP) 45 mm Hg) immediately followed

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vasopressin infiltration. The bradycardia was treated promptly with ephedrine (6 mg), followed by glycopyrrolate (200 μg) and a 500 mL bolus of intravenous crystalloid (plasmalyte). The desflurane rate was reduced and the oxygen concentration was turned up. Non-invasive blood pressure measurements were taken every minute and central pulse was monitored until blood pressure normalised. The patient was in the head down position, under the operative drapes, with the forced air warming device maintaining her temperature. Intraoperatively she also received intravenous paracetamol (1 g), ondansetron (4 mg), amoxicillin (1.2 g), tranexamic acid (1 g) and 2 L of crystalloid fluid (Plasmalyte) in total. The myomectomy procedure was performed routinely using monopolar diathermy. The myometrium was closed with interrupted Vicryl-1 sutures. The fibroid was morcellated within a bag and removed via a port. Blood loss was estimated to be 100 mL, operating time was 1 hour 15 min. Endo-close was used to close the 10 mm ports and Monocryl for the 5 mm lateral ports.

At extubation, the patient was sat up, train of four monitoring was checked, to ensure reversal of neuromuscular blockade, desflurane was turned off and the oxygen flow was increased to inspired FIO_2 100% to wash out the desflurane in anticipation of extubating the patient awake. A positive end expiratory pressure of 7 cmH_2O was maintained until the time of extubation. At that time, a volume of pink fluid was noted in the heat and moisture exchanger, the connector and endotracheal tube were changed. The patient suddenly regained consciousness and virtually self-extubated due to the rapid offset of the desflurane. The cuff of the endotracheal tune was let down and the patient pulled out the endotracheal tube herself. Attempts at suctioning her mouth were made but she was not cooperative. At no point did the patient have any airway obstruction or bite down on the endotracheal tube. Following extubation, she desaturated to 89%, started coughing up pink fluid and was visibly distressed. It was difficult to keep the anaesthetic face mask on the patient without restraining her. On examination, the patient looked slightly grey and continued to cough up pink froth. Bi-basal crepitations were audible, but no wheeze. The differential diagnosis at this point was negative pressure pulmonary oedema but this did not fit with the sequence of events during extubation as the endotracheal tube had fluid in it prior to extubation, suggesting an event had occurred before she was extubated.

The decision was made to transfer the patient to a level two recovery area to facilitate access to invasive monitoring and treatment as appropriate. She was promptly transferred and Optiflow (a respiratory support system delivered via nasal cannula) was commenced in recovery. The intensive care unit outreach team were called to review.

INVESTIGATIONS

As per the initial observations in recovery, she was hypoxic (SpO_2 94%) and hypotensive (blood pressure (BP) 83/54 mm Hg). She was afebrile (temperature 36.7°C) with a normal respiratory rate (RR 11) and heart rate (HR 87).

A chest X-ray demonstrated patchy, diffuse pulmonary airspace infiltrate and interstitial lines, but no pleural effusion. Findings were suggestive of acute pulmonary oedema or acute respiratory distress syndrome.

The initial arterial blood gas, taken on 60% oxygen in recovery, demonstrated type 2 respiratory failure and a respiratory acidosis (PO_2 10.6 Kpa, PCO_2 7.1 Kpa, pH 7.30, BE −3.0, lactate 0.9). The blood gas was repeated 2 hours later on 15 L/min of oxygen and showed the respiratory acidosis had been corrected, but she remained hypoxic (PO_2 21.8 Kpa, PCO_2 5.8 Kpa, pH 7.38, lactate 1.2). She significantly improved and the oxygen was slowly weaned. Eight hours later, the blood gas was repeated on 1 litre/min, which demonstrated adequate oxygenation (PO_2 18.9 Kpa, PCO_2 4.9 Kpa, pH 7.44, lactate 0.6); she was stepped down to ward-based level of care.

An ECG, taken in recovery, demonstrated sinus tachycardia with nil ischaemic change. An echocardiogram was arranged by cardiologists, which showed normal left and right ventricle size with no significant valve disease.

Bloods taken on day 1 showed a normal haemoglobin (11.4 mg/dL) and platelet count (381×10^9/L), mildly elevated white cell count (17.5×10^9/L). To consider the differential diagnosis and precipitant for pulmonary oedema, B-type natriuretic protein (BNP) and troponin I were done, both of which were found to be elevated at 130 pg/mL and 477 ng/L respectively. The troponin I and BNP were repeated on day 4 and demonstrated a significant reduction (BNP 19 pg/mL and troponin 83 ng/L). She had normal renal function and electrolytes (sodium 136 mmol/L, potassium 3.7 mmol/L, creatinine 60 μmol/L and urea 3.4 mmol/L).

DIFFERENTIAL DIAGNOSIS

The working diagnosis following extubation was in keeping with acute pulmonary oedema, given the presentation of hypoxia, associated with significant coughing, productive of frothy fluid and the presence of pink fluid within the endotracheal tube at extubation. The pattern of onset of symptoms immediately following extubation and removal of the positive end expiratory pressure is likely to have precipitated the acute deterioation and be in keeping with a presentation of acute pulmonary oedema.

Other differentials to consider in the presentation of acute hypoxia post-operatively, included cardiac (coronary vasospasm or cardiomyopathy) and respiratory (pneumothorax, ventilation-induced lung injury (VILI), pulmonary embolism, significant atelectasis, aspiration lung injury) causes. The presence of good air entry bilaterally reduced the likelihood of pneumothorax. The absence of significant comorbidities, no limitation in activities preoperatively made the likelihood of a significant cardiomyopathy less likely, but important to exclude as a possible cause. Ventilation induced lung injury was unlikely due to the short period of ventilation and low tidal volumes/pressures used. While venous thromboembolism (VTE) is always a risk in any surgical patient, our patient had no significant risk factors (young age, no personal history of VTE/thrombophilia and excellent mobility prior to the procedure). Intraoperatively mechanical pneumatic calf compression was used to reduce the risk of venous thromboembolism. The procedure was straight forward, with an operative time of less than 2 hours and blood loss was not significant (100 mL), such to precipitate a coagulopathy. Significant atelectasis or aspiration-related lung injury is a possible differential to consider in view of laparoscopic approach to procedure and use of trendelenberg position intraoperatively.

The working diagnosis of acute pulmonary oedema, precipitated by systemic absorption of vasopressin, given the acute onset of systemic manifestations (bradycardia and hypotension) immediately following vasopressin injection.

Vasopressin acts as a vasoconstrictor and stimulates myometrial contractility through its action on V1 receptors within the uterus. In the collecting tubules vasopressin acts on V2 receptors, causing water retention; the 2 L of fluid given intraoperatively may have precipitated significant fluid overload.

Vasopressin has been shown to cause both systemic and coronary artery vasoconstriction in an animal model, through its action on the V1 receptor.[1] It has been suggested that vasopressin may also cause transient suppression of the autonomic nervous system, which may explain the transient bradycardic and hypotensive response.[2] The elevated BNP and troponin in this case would suggest some form of cardiac insult. Improvement in symptoms and oxygen saturations with administration of high flow oxygen with positive end expiratory pressure, upright position and intravenous furosemide helped secure the working diagnosis of acute pulmonary oedema, likely caused by vasopressin.

TREATMENT

Initial treatment included positioning the patient in an upright position, application of high flow oxygen via a tight-fitting anaesthetic mask, held on the anaesthetist with a water circuit applying positive end expiratory pressure. With a suspected diagnosis of pulmonary oedema, intravenous furosemide (20 mg) was administered along with diamorphine to alleviate distress (at 1 mg increments—total dose of 4 mg). The patient already had a catheter in situ.

In recovery, Optiflow, a respiratory support system with supplementary oxygen (60%) was commenced, oxygen saturations improved from 89% to 94%. A radial arterial line (20 G abbocath) was sited for monitoring and to optimise oxygen replacement. Chest X-ray was performed, which confirmed acute respiratory distress syndrome/acute pulmonary oedema. She had excellent diuresis, passing 500 mL of urine within the first hour. Twelve lead ECG demonstrated sinus tachycardia and nil acute ischaemia. The intensive care unit registrar reviewed and recommended a further 20 mg of intravenous furosemide to optimise diuresis. The oxygen flow rate was gradually reduced to 1 L/min over a period of 10 hours. She was stepped down to ward-based care, maintaining her saturations above 94% via nasal prongs. She had excellent diuresis, with a urine output more than 200 mL/hour. She was gradually weaned off oxygen and was able to maintain her oxygen saturations in room air.

OUTCOME AND FOLLOW-UP

Following appropriate diuresis and relative fluid restriction, oxygen saturations were maintained on room air. Cardiology reviewed with the echocardiogram results, BNP and troponin, and felt the likely diagnosis in the absence of an underlying cardiac issue to explain such a deterioration was vasopressin-induced coronary vasospasm, precipitating acute pulmonary oedema. Both the gynaecology team and anaesthetic team apologised for the unexpected complication, as part of the duty of candour process. The patient was discharged home on day 5 with follow-up in gynaecology outpatient clinic for an appropriate de-brief.

DISCUSSION

Intramyometrial injection of vasopressin is used routinely in myomectomies to reduce the blood loss. Vasopressin is a profound vasoconstrictor. Systemic absorption is known to cause profound bradycardia, loss of peripheral pulses, hypotension and significant cardiac complications, including cardiac arrest.[3]

There have been a number of case reports demonstrating the systemic impact of vasopressin use.

Reiss *et al* described a case of severe peripheral arterial vasospasm with use of vasopressin (60 IU diluted in 33 mL of 0.9% normal saline) resulting in haemodynamic instability and non-measurable blood pressures.[4]

Butula *et al* demonstrated severe bradycardia during open myomectomy in a 43-year-old patient following administration of 20 IU (diluted in 20 mL of 0.9% saline). The bradycardia was corrected intraoperatively with nitroglycerine, the procedure was completed and she made an uneventful recovery.[5]

Hobo *et al* reported a case of cardiac arrest following intramyometrial injection of vasopressin (11 IU, 0.2 IU per mL), in a young woman with multiple uterine fibroids.[3]

The dose of vasopressin used varies among clinicians. The standard vasopressin preparation comes as 20 IU in 1 mL vials; the volume of dilution is based on the preference of the clinician. In this case, 20 IU was diluted in 20 mL of normal (0.9%) saline, giving a concentration of 1 IU/mL. Despite careful intramyometrial administration, it may also result in a relatively large dose being injected intravenously.

Vasopressin is an effective method of reducing intraoperative blood loss in various gynaecological surgeries, including myomectomy and hysterectomy. Given the significant cardiac morbidity associated with doses as low as 11 units.[3] we need to identify a safe, but effective vasopressin dose range to use.

Reduction of blood loss with the use of vasopressin at a concentration of 0.01 IU and 0.5 IU per mL (administering a volume of 17 mL, total dose: 1–2 IU) was demonstrated in comparison to a placebo in vaginal surgery by Neilson and Valentin.[6]

A recent randomised controlled trial compared the efficacy of dilute (10 IU in 200 mL) vs concentrated (10 IU in 30 mL) vasopressin use in laparoscopic myomectomy. No difference in intraoperative blood loss was demonstrated between the two groups. No vasopressin-related complications were identified in either group.[7]

An up-to-date Cochrane review demonstrated a reduction in intraoperative blood loss by 121–172 mL in laparoscopic and 392–507 mL in open myomectomies with intramyometrial injection of 5 IU (diluted in 100 mL 0.9% saline),[8] and 6 IU (diluted with 20 mL 0.9% saline) of vasopressin.[9 10]

Given the significant cardiac morbidity and adverse effects that has been demonstrated with the use of intramyometrial vasopressin in our case (20 IU) and other cases in the literature, there needs to be significant caution with its use. The efficacy of vasopressin has been demonstrated at more dilute concentrations and in lower doses (5–6 IU) without any clear adverse effects, which leads us to question our current practice. In the absence of clear guidance about the recommended, safe dose of intramyometrial vasopressin, the 5–6 IU dose used in the Cochrane review seems a logical limit to ensure efficacy without compromising patient safety.[10] The use of more dilute constitution may also limit the potential systemic impact of incidental intra-vascular injection.

Learning points

- Review the dose and constitution of vasopressin—20 units is over the recommended limit, more dilute preparation will reduce systemic absorption.
- Discuss complications associated with vasopressin in the preoperative consent.
- Consider relative fluid restriction if using vasopressin.
- Carefully review cardiac history preoperatively to determine if further cardiac investigations are required.

Unexpected outcome (positive or negative) including adverse drug reactions

This case has highlighted a requirement for clear objective guidance on vasopressin use (dose/constitution) in laparoscopic myomectomy, which we plan to develop at a trust level to ensure we limit potential adverse effects. It has also raised awareness of the importance of preoperative assessment, particularly of a patient's cardiac function, given the potential for cardiac complications associated with vasopressin use.

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