Case Series

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Life-threatening perianaesthetic complications in five cats undergoing biliary tract surgery: case series and literature review

Paolo Monticelli, Thaleia Rengina Stathopoulou, Karla Lee and Chiara Adami

Abstract

Case series summary The aim of this case series was to describe the intra- and early postanaesthetic complications occurring in five cats undergoing major surgeries involving the gallbladder and the biliary tree. The five cases of this series were admitted to the Queen Mother Hospital for Animals between June and December 2015, and were all overseen by the same senior anaesthesist. Pre-existing pancreatitis was a common finding. Observed life-threatening events were persistent, unresponsive hypotension in the absence of major blood loss, which occurred mainly during surgical manipulation of the biliary tract, and postoperative renal failure.

Relevance and novel information Biliary surgery carries the potential for life-threatening complications in cats. The pathogenesis of such morbidities is likely to be multifactorial. The perianaesthetic use of haemoglobin-based oxygen-carrying solution may be considered as an alternative treatment option when hypotension is unresponsive to fluids and traditional positive inotropes and vasopressors.

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Case series description

Case 1

A 12-year-old male neutered Maine Coon weighing 7.4 kg was presented with a 1 day history of vomiting. Clinical examination revealed depressed demeanour, increased rectal body temperature (40.3°C), body condition score (BCS) of 7/9, increased respiratory rate (48 breaths per minute [brpm]), the presence of a IV/VI left-sided systolic heart murmur, and jaundice.

Blood tests showed decreased packed cell volume (PCV; 22%), and increased serum concentrations of alanine transaminase (ALT) (302 IU/l; reference interval [RI] 25–130 IU/l) and bilirubin (173 µmol/l; RI 0–3 µmol/l).

Abdominal ultrasonography revealed cholelithiasis and marked distension of the bile duct (20 mm), consistent with bile duct obstruction. The cat was scheduled for exploratory laparotomy.

After premedication with intravenous (IV) methadone (Physeptone 0.2 mg/kg; Martindale Pharmaceuticals), general anaesthesia was induced with alfaxalone (Alfaxan 2 mg/kg IV; Jurox) and maintained with isoflurane in oxygen (end-tidal 1.1–1.4%). Intraoperative analgesia was provided with a lumbosacral epidural injection of morphine (morphine sulfate 0.1 mg/kg; Martindale Pharmaceuticals), a subcostal transversus abdominis plane block with 1.5 mg/kg ropivacaine (Naropin; AstraZeneca) and a constant rate infusion (CRI) of fentanyl (0.4–0.5 µg/kg/min IV Fentadon; Eurovet). Hartmann's solution (Vetivex; Dechra) was administered intravenously at a rate of 5 ml/kg/h. The cat was instrumented with a multiparametric monitor during anaesthesia. Additionally, mean arterial pressure (MAP) was measured with a Doppler flow probe and an inflatable, occlusive cuff, placed proximally.

Royal Veterinary College, University of London, Hatfield, UK

Corresponding author:
Paolo Monticelli DVM, MRCVS, Department of Clinical Sciences and Services, Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, AL9 7TA, Hatfield, UK
Email: pmonticelli@rvc.ac.uk

During surgery – which consisted of duodenotomy followed by catheterisation of duodenal papilla and cholecystectomy – severe hypotension was detected on two occasions, in the presence of an unchanged heart rate (HR; 140–150 beats per minute [bpm]). The first time MAP transiently decreased to 45 mmHg but normalised (70 mmHg) after a bolus of tetrastarch (Voluven 6% 5 ml/kg IV; Fresenius Kabi). The second time, the decrease in MAP was more severe (25 mmHg) and prolonged (15 mins), and also unresponsive to tetrastarch (5 ml/kg IV), ephedrine (ephedrine hydrochloride 0.05 mg/kg IV, repeated after 10 mins; Martindale Pharmaceuticals) and dopamine infusion (dopamine hydrochloride 5–10 µg/kg/min IV; MercuryPharma). The surgeon reported minimal blood loss, which could not be verified owing to dilution of blood lost with saline used to lavage the abdomen; however, during the hypotensive period, haematology revealed a significant decrease in PCV (12%) and total solids (37 g/dl). Oxyglobin (Oxyglobin; Dechra) was infused at a rate of 2–5 ml/kg/h IV and within some minutes it resulted in normalisation of the MAP (100 mmHg), which then remained stable until the end of surgery. Oxyglobin administration was discontinued at recovery; the total volume infused was 5 ml/kg over 30 mins.

Body temperature was 35.3ºC after extubation. Recovery was smooth and uneventful, and clinical parameters were stable in the early postoperative period. However, 5 h after recovery, the cat showed tachycardia (220 bpm), weak peripheral pulses and tachypnoea (40 brpm); arterial blood pressure could not be detected with either Doppler or oscillometry techniques. Oxyglobin infusion was reinitiated (2–5 ml/kg/h IV), which resulted in normalisation of cardiovascular and respiratory parameters. Early postoperative blood tests, performed at recovery from anaesthesia, showed a decrease in PCV (21%) and increased serum creatinine (393 µmol/l; RI 74.5–185.3 µmol/l) and lactate (10.0 mmol/l; RI 0–2.4 mmol/l) concentrations, which improved progressively during the following days.

The cat was discharged, in good clinical condition, from the intensive care unit (ICU) 4 days after surgery.

Case 2

A 2.5-year-old female neutered domestic longhair cat weighing 2.3 kg was presented with a 3 day history of anorexia and vomiting. On presentation, the cat was alert and responsive, and physical examination revealed an increased respiratory rate (44 brpm), a grade II/VI systolic apical heart murmur, discomfort upon abdominal palpation, and jaundice. Rectal body temperature was 39.2°C.

Blood tests revealed a marked increase in ALT (above the upper limit of test detection), lactate (7.0 mmol/l) and total bilirubin (317 IU/l) serum levels, a moderate increase in alkaline phosphatase (ALP; 132 IU/l) and neutrophilia (33.57 10^{-9}/l).

Ultrasonography demonstrated cholelithiasis, moderate distension of the gallbladder (10 mm) and also changes in pancreas echogenicity and texture, compatible with pancreatitis.

On the basis of these findings, an extrahepatic biliary obstruction was diagnosed and the cat was anaesthetised for exploratory laparotomy.

The cat was premedicated with methadone (0.2 mg/kg IV) and general anaesthesia was induced with propofol titrated to effect, and maintained with isoflurane in oxygen (end-tidal 0.5–1.4%). Intraoperative analgesia was provided as described for case 1, plus a CRI of ketamine (10 µg/kg/min IV). Fluid administration and monitoring were the same as for case 1; additionally, central venous pressure (CVP) was measured via a catheter placed in the cranial vena cava.

Surgical procedures were the same as described for case 1. During surgical manipulation of the gallbladder, MAP decreased on several occasions from 75 to 40–45 mmHg. The surgeon estimated a blood loss of approximately 7 ml, corresponding to 5% of blood volume. Hypotension initially resolved (MAP 75–100 mmHg) after treatment with boluses of IV crystalloid (six in total [3×5 ml/kg and 3×10 ml/kg]) and dopamine infusion (2.5–6.0 µg/kg/min). In order to treat further decreases in MAP to 50 mmHg, boluses of tetrastarch were also administered for a total volume of 10 ml/kg (IV). The latter resulted in a transient increase in MAP to 70 mmHg, which decreased again to remain below normal ranges (40–50 mmHg) for about 20 mins. During the administration of colloids, CVP increased from 2 to 5 mmHg but returned to baseline shortly thereafter. MAP normalised at the end of anaesthesia and the cat was transferred to the ICU for postoperative care. Body temperature was 35.4°C at recovery.

One hour after recovery, physical examination revealed pale mucous membranes, intermittent bradycardia (HR 60 bpm), which alternated with periods of normal heart rhythm (HR 150 bpm), a barely palpable femoral pulse and lethargy. MAP measured with the Doppler was 30 mmHg. Blood analysis revealed decreased PCV (7%) and total solids (TS) (27 g/l), and increased lactate levels (12 mmol/l). Because dopamine (5–10 µg/kg/min), colloids (20 ml/kg) and even noradrenaline (norepinephrine; noradrenaline hydrochloride 0.1–0.3 µg/kg/min; Martindale Pharmaceuticals) IV infusions failed to restore normal cardiovascular parameters, Oxyglobin infusion was started at a rate of 4 ml/kg/h and within a few minutes it resulted in normalisation of MAP (80 mmHg) and HR (140 bpm), and improvement of mentation. At this point, dopamine and noradrenaline were discontinued. One hour later, shortly after the discontinuation of

Oxyglobin infusion, the cat showed again intermittent bradycardia (HR 40 bpm), which was successfully treated (HR 120 bpm) with atropine (0.02 mg/kg IV). Arterial blood pressure was undetectable. Echocardiography ruled out fluid overload and cardiac function impairment. A further bolus of Oxyglobin (2 ml/kg IV) was administered over 10 mins but failed to restore normal arterial pressure. Oxyglobin and noradrenaline infusions were started (1 ml/kg/h and 0.2 µg/kg/h, respectively), but MAP remained unmeasurable. Three hours after recovery the cat had a cardiopulmonary arrest and cardiopulmonary–cerebral resuscitation (CPCR) was attempted. However, during CPCR the owner requested euthanasia.

Case 3

A 12-year-old male neutered domestic shorthair cat weighing 3.8 kg presented with a 1 week history of vomiting and inappetence. On presentation, the cat was alert and mentation was normal. Physical examination was unremarkable and BCS was 4/9.

While haematology was unremarkable, biochemistry revealed marked elevation in liver enzymes (ALT 895 IU/l [RI 25–130 IU/l]; ALP 173 IU/l [RI 11–58 IU/l]; gamma-glutamyl transferase 4 IU/l [RI 11–58 IU/l]; and hyperbilirubinaemia 43.7 nmol/l).

Abdominal ultrasonography showed cholelithiasis with common bile duct obstruction, and pancreatitis with evidence of focal peritonitis.

The cat was anaesthetised for exploratory laparotomy.

After premedication with methadone (0.2 mg/kg IV), general anaesthesia was induced with IV alfaxalone and ketamine (1 mg/kg each IV) and maintained with sevoflurane in oxygen (end-tidal 1.2–2.2 %). Intraoperative fluid rate, analgesia, and monitoring were the same as described for case 1.

Duodenotomy, followed by choledocotomy and cholecystectomy, was performed to access the major duodenal papilla and allow flushing of the common bile duct and stent placement. During surgery, MAP dropped intermittently, several times, from normal values to 60 mmHg. On each occasion, hypotension responded to treatment with boluses of Hartmann's solution (5–10 ml/kg each for a total volume of 23 ml/kg IV) and noradrenaline infusion (0.05–0.15 µg/kg/min IV), started after the second hypotensive episode. At the end of the anaesthetic the cat was transferred to the ICU.

Postoperatively, MAP was measured using the Doppler technique at 2 h intervals and ranged from 90–136 mmHg. Basic physical and haematological parameters were also regularly monitored and found to be stable and within normal ranges for the species. The cat was discharged, in good clinical condition, from the ICU after 4 days.

Case 4

A 17-year-old female neutered Burmese cat weighing 3.1 kg was presented with a 4 day history of vomiting. On presentation, the cat was alert and responsive. Rectal body temperature was 39.4°C and HR was slightly elevated (220 bpm); other physiological variables were within normal ranges for the species. Clinical examination revealed marked cranial abdominal discomfort.

Blood biochemistry showed mild ionised hypocalcaemia (0.99 mmol/l; RI 1.15–1.37 mmol/l) and a marginal elevation in serum creatinine concentrations (143 µmol/l). Haematology was unremarkable, and PCV and TS were 35% and 80 g/l (RI 61–80 g/l), respectively.

Abdominal ultrasonography revealed chronic bilateral renal changes, hyperechoic sludge within the gallbladder lumen, dilation of the common bile duct and cholelithiasis. The cat was scheduled for exploratory laparotomy and cholecystectomy.

The anaesthetic protocol was the same as described for case 2, including monitoring, plus a CRI of dexmedetomidine (Dexdomitor 1.5 µg/kg/h IV; Vètoquinol). Hartmann's solution was administered at a rate of 4 ml/kg/h during the anaesthetic.

During cholecystectomy, MAP significantly decreased and remained below normal ranges (55–25 mmHg) for approximately 1 h. Attempts to treat hypotension consisted of a decrease in isoflurane end-tidal concentration (0.60–0.25%), Hartmann's solution boluses (5–10 ml each, for a total volume of 26 ml/kg IV), ephedrine (0.05 mg/kg IV, repeated after 20 mins) and, eventually, dopamine infusion (10 vg/kg/min IV). Except for a transient (one recording) increase of MAP to 70 mmHg after the second ephedrine administration, all these treatments failed in restoring normal MAP values. Although the intraoperative blood loss could not be precisely quantified, the surgeon reported that it was minimal. At the end of the anaesthetic the cat was transferred to the ICU. Body temperature was 35.6ºC. Postoperative blood tests performed 1 h after recovery revealed a marked decrease in PCV (22%) and TS (55 g/l), and a further increase in creatinine serum levels (198 µmol/l) compared with preoperative values.

Ninety minutes after admission to ICU, the cat had a cardiorespiratory arrest. Despite the fact that CPCR was initiated promptly, CPCR failed to restore adequate cardiac and respiratory function and, at the request of the owner, it was discontinued after 25 mins owing to a poor prognosis.

Case 5

A 9-year-old female neutered British Blue cat weighing 5.2 kg was presented with a history of postoperative anorexia after duodenal mass removal, performed 5 days earlier by the referring veterinarian. On presentation, mentation was normal and physiological

parameters were within normal ranges for the species. Clinical examination revealed enlargement of the stomach and pain upon palpation of the cranial abdomen, which appeared distended.

Blood tests showed decreased PCV (22%), TS (43 g/l) and serum albumin (19 g/l; RI 28–42 g/l) concentrations, hyperkalaemia (5.6 mmol/l; RI 3.8–5.5 mmol/l). Ultrasonographical examination of the abdomen revealed mild peritoneal effusion, thickening of the left lobe of the pancreas, which appeared hypoechoic, and enlargement of the cystic and biliary ducts, which appeared tortuous. On the basis of these findings, acute pancreatitis and pyloric outflow obstruction were diagnosed.

The cat was anaesthetised for exploratory laparotomy.

The anaesthetic protocol was the same as described for case 2, including analgesia, intraoperative fluid type and rates, and monitoring. Hypotension was detected shortly after the beginning of anaesthesia (MAP 50–60 mmHg), and treated with a bolus of crystalloid (5 ml/kg IV) and dopamine infusion (5 µg/kg/min, IV), which resulted in mild increase in MAP (65 mmHg). However, during surgical manipulation of the gallbladder, without evidence of appreciable blood loss, an episode of more severe, unresponsive hypotension (unmeasurable MAP and inaudible Doppler sounds) occurred and lasted approximately 30 mins, until the end of anaesthesia. Increases in dopamine rate of infusion to 7.5 µg/kg/min and further administration of crystalloids (total volume 30 ml/kg IV) did not result in appreciable improvement of the MAP values. Intraoperative blood work revealed a further increase in potassium serum levels (7.9 nmol/l), which was treated with 10% calcium gluconate (0.5 ml/kg IV, over 15 mins), as well as increases in phosphates (2.78 mmol/l; RI 0.92–2.16 mmol/l), creatinine (376 mmol/l) and blood urea nitrogen serum concentrations (17 mmol/l; RI 6.1–12.0 mmol/l). During surgery, a ligature located within the path of the common bile duct was found cut, resulting in bile leak in the peritoneum. Owing to the poor prognosis, the cat was euthansed at request of the owner.

Discussion

This case series describes the intra- and early postoperative complications occurring in five cats after major surgeries involving the gallbladder and the biliary tree.

The common denominators in the five cases presented in this work were the presence of underlying pancreatitis and the occurrence of intraoperative hypotension, which, in most cases, was unresponsive to treatment, in the absence of clinically relevant blood loss. The most common postoperative complication was renal injury, as demonstrated by the increase in creatinine and phosphate serum levels occurring in 3/5 cases during and after surgical manipulation of the biliary tract. These findings are in agreement with those of previous studies, which reported a high risk of perianaesthetic pancreatitis and intraoperative hypotension in cats,[1] and, in human patients, an incidence of complications of 27.8%,[2] and an increased risk of renal failure,[3] following biliary surgery.

Unlike dogs, underlying pancreatitis is a common finding in cats affected by extrahepatic biliary obstruction, owing to anatomical differences between the two species. While in dogs the pancreatic duct empties in the duodenum at the minor duodenal papilla, in the cat, similar to humans, the major pancreatic duct enters the duodenum at the level of the major duodenal papilla along with the common bile duct.[4–6] The main result of this ductal fusion is that pancreatic and biliary diseases are often concomitant.[1,7] Additionally, because biliary culture is positive for bacterial growth in 35% of cats, the risk of bacteraemia and mortality as sequelae of hepatobiliary surgery is higher in this species than in dogs.[8]

Hypotension is a common sequela of anaesthesia, the treatment of which usually requires fluids, positive inotropes and/or vasopressors. An experimental trial demonstrated that in dogs the critical level of MAP below which the risk of cardiovascular arrest is imminent is 30–40 mmHg,[9] which seems to confirm that the degree of hypotension observed in the cats of this report was to be regarded as a life-threatening condition. Although unresponsive hypotension is a common complication in patients with obstructive jaundice, the mechanisms by which bilirubinaemia may affect the vascular tone are not completely understood. However, on the basis of the existing literature, some hypotheses can be proposed.

One possibility is that the endotoxaemia associated with bilirubinaemia and possibly biliary tract infection would cause a reduction in responsiveness and functional activity of alpha$_1$-adrenoreceptors, owing to either a direct effect on the receptors,[10] or an indirect action on the sympathetic nervous system.[11] In support of this hypothesis, it has been demonstrated that the experimental ligation of the canine bile duct and the consequent hyperbilirubinaemia result in decreased vascular reactivity to circulating noradrenaline and 5-hydroxytryptophan hydroxyltryptamine.[12] Another experimental study conducted in rats showed that the presence of high concentrations of bile salts in the bloodstream can significantly decrease the noradrenaline plasma levels by affecting its pulmonary metabolism.[13] These results would explain why noradrenaline infusion failed to restore normotension in one of the cats included in this report.

As an alternative explanation, it has been demonstrated that experimentally induced obstructive jaundice is associated with an increased release of nitric oxide (NO), one of the most potent endogenous vasodilators, from the canine endothelium.[12] Furthermore, there is good evidence that this also occurs in species other than dogs,[14] and that the renal vasculature is significantly affected.[15] In the light of these findings, it is reasonable to

assume that the mechanism by which Oxyglobin, but not other vasopressors, effectively improved blood pressure in two cats of this series was its scavenger effect on endothelial NO,[13,16] rather than volume replacement, plasma expansion and oxygen carrying.[14] The minimal intraoperative blood loss experienced by the aforementioned companion animals corroborates this hypothesis. The use of Oxyglobin in cats is supported by the current literature,[17–19] and owing to the paucity of suitable blood donors it is regarded as a valid alternative to blood transfusion in feline patients.

The occurrence of unresponsive hypotension in patients undergoing biliary and liver surgery may also be the result of an incompetent renin–angiotensin–aldosterone system (RAAS). Indeed, it has been demonstrated that liver angiotensinogen is the primary source of angiotensin II.[20] As a result, patients in which the biliary condition is accompanied by a clinically relevant liver failure might also have decreased angiotensinogen production, and, consequently, failure of the RAAS to maintain circulatory homeostasis. However, this explanation is the least likely as none of the cats in this investigation showed signs of significant liver dysfunction prior to anaesthesia.

Four out of five cats, only one of which had a pre-existing renal condition, showed signs of kidney damage after or during surgery.

Renal dysfunction is a well-recognised complication of biliary disease in humans. One study found that the incidence of pre-existing renal compromise in patients affected by biliary obstruction was 15%,[6] while postoperative renal impairment has been regarded as the most significant sequela of biliary surgery associated with morbidity and mortality.[3,21] Suggested pathogeneses are a direct effect of bile salts and bilirubin on renal tubules,[21] and/or hypoperfusion of renal parenchyma as a sequela of unresponsive hypotension.[12] Among the cats that experienced renal impairment, those with the most severe intraoperative hypotension also had the highest postoperative values for serum creatinine. This seems to suggest that the maintenance of adequate parenchyma perfusion during biliary surgery plays a crucial role in preventing further kidney damage.

Conclusions

The prognosis for cats undergoing biliary surgery should be regarded as guarded, owing to the potential for fatal perioperative complications, namely unresponsiveness and persistent hypotension during anaesthesia, and postoperative renal failure.

In cases in which hypotension is severe, and volume replacement and vasopressors fail to restore normal blood pressure values, alternative treatments such as Oxyglobin, which acts as an NO scavenger, might be considered as an option.

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