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Prevalence of electrolyte disturbances and perianaesthetic death risk factors in 120 horses undergoing colic surgery

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Abstract
The objective of this study was to determine the prevalence of intraoperative electrolyte disturbances and risk factors associated with perianaesthetic death in horses undergoing colic surgery.
The files of 120 horses meeting the inclusion criteria were reviewed. Data retrieved from the medical records, including demographic data and the occurrence of electrolyte disturbances and other intraoperative complications, were analysed with a two step-approach by univariate and multivariate logistic regression models.
Hypocalcaemia was the most represented electrolyte disturbance (52.5%), followed by hypokalaemia (30.0%) that was associated with intraoperative administration of salbutamol (P = 0.045). Perianaesthetic death occurred in 46 horses, accounting for an overall mortality rate of 38.3%. Risk factors associated with death were anaesthetic duration (P = 0.001), body weight (P = 0.020), presence of gastric reflux before anaesthesia (P = 0.021), and intraoperative tachycardia (P = 0.043) and acidosis (P = 0.025).
The mortality in the study population was comparable to previously reported findings. Based on the study findings, it is advisable to optimise haemodynamics prior to anaesthesia, in order to prevent intraoperative tachycardia that is associated with increased risk of death. Heavier horses and those with gastric reflux may have higher risk of fatalities, and intraoperative salbutamol administration may contribute to hypokalaemia.

Keywords explorative laparotomy, equine, hypokalaemia, salbutamol, risk of perioperative death**.**

1. Introduction

Ventral midline laparotomy is indicated in approximately 10% of horses presented due to colic [1,2]. Colic horses undergoing emergency laparotomy may experience perianaesthetic complications, usually require pre- and postoperative intensive care, and their management is expensive in terms of costs and human resources [2]. Updated information about the actual risk of fatalities would enable both owners and veterinarians to make informed management decisions.

There is a body of published work pertaining to perianaesthetic mortality of equine patients and related risk factors. However, to the best of the authors' knowledge, the majority of these studies either included both emergency and elective cases [3,4], or focused on a specific gastro-intestinal condition [2,5-7], or they were published more than a decade ago or earlier [1,2,8-11].

Within the last decade, much progress has been made in veterinary anaesthesia, owing to the development of sophisticated and modern anaesthetic techniques and equipment, as well as to the increased number of board-certified specialists worldwide. Based on this, it would be reasonable to update the current knowledge regarding equine perianaesthetic mortality with particular focus on critically ill horses undergoing surgical treatment of colic.

With respect to electrolyte disturbances, there is a number of publications focusing on their occurrence in horses with colic. Of these, some included horses undergoing medical management of colic [12-14], and one focused on the postoperative period after surgical treatment [15]. Several studies including horses undergoing emergency laparotomy specifically investigated the alteration of calcium and magnesium homeostasis during the anaesthetic [16-17].

Potassium serum concentration may also be affected by the anaesthetic, owing to starving and/or to the administration of catecholamines [18]. Moreover, salbutamol, a selective beta 2-adrenoreceptor agonist that is often used, in aerosolised form, in equine anaesthesia to improve the respiratory function [19], is known to decrease serum potassium in dogs [20] and may cause hypokalaemia in colic horses as well. Sodium homeostasis may be affected during the anaesthetic of colic horses due to dehydration, administration of hypertonic saline solution, or both. To the best of the authors' knowledge, these aspects have never been extensively investigated in colic horses undergoing anaesthesia and surgery.

The main objectives of this retrospective investigation were:

- To determine the mortality risk and to identify the risk factors for perianaesthetic death in a population of 120 horses undergoing surgical treatment of colic in a large referral hospital;
- To define the prevalence of the intraoperative electrolyte imbalances – including calcium, potassium and sodium - in the study population, and
- To determine whether the intraoperative administration of aerosolised salbutamol was associated with changes in blood potassium concentration in the study population.

2. Materials and methods

The study was conducted under approval of the Social Science Ethical Review Board (SSERB) of the Royal Veterinary College (license number: URN SR: 2017-1030).

2.1. Case selection criteria and medical records review

The patient files of horses with colic admitted to the Equine Referral Hospital of the Royal Veterinary College between October 2012 and June 2018 were reviewed. The case-specific key word-combinations entered in the database were "horse + colic", "horse + colic + anaesthesia/anaesthetic", and "horse + colic + abdominal surgery/laparotomy/celiotomy". The search was manually refined in order to include only patients that underwent surgery, and whose anaesthetic record was complete. Donkeys, mules and horses undergoing relaparotomy were excluded from the study.

Demographic variables, namely sex, age, breed, body weight (BW) and Body Condition Score (BCS; 0-9) [21] were collected and used for statistical analysis. Aspiration of stomach contents through a nasogastric tube prior to anaesthesia, reported either in the anaesthetic record or elsewhere in the medical file of the horse, was annotated as "gastric reflux". The occurrence of intra-operative complications, namely hypotension, hypoxaemia, cardiac arrhythmias, metabolic acidosis, metabolic alkalosis and electrolyte imbalances, was extrapolated from the anaesthetic record. Intra-operative complications were defined as follows:

- Hypotension: mean arterial pressure, measured invasively, lower than 70 mmHg for at least three consecutive 5 minute-interval readings [22];
- Hypoxaemia: PaO_2 lower than 60 mmHg in at least half of the measurements [22];
- Cardiac arrhythmias: any disturbance of the cardiac rhythm, as detected with electrocardiography, among ventricular premature contraction, atrial fibrillation, second degree atrio-ventricular (A-V) blocks, third degree A-V blocks, bradycardia (heart rate < 24 bt/min, either supraventricular or ventricular) and tachycardia (heart rate > 55 bt/min, either supraventricular or ventricular) [23-24];
- Metabolic acidosis: pH < 7.34 and HCO_3^- < 22 mmol/L in at least half of the measurements [25-26];
- Metabolic alkalosis: pH > 7.43 and HCO_3^- > 32 mmol/L in at least half of the measurements [25-26];
- Hypokalemia: K^+ blood concentration < 2.7 mmol/L in at least half of the measurements [12-27];
- Hyperkalemia: K^+ blood concentration > 5 mmol/L in at least half of the measurements [12];
- Hypocalcemia: iCa^{2+} blood concentration < 1.4 mmol/L in at least half of the measurements [12];
- Hypercalcemia: iCa^{2+} blood concentration > 1.7 mmol/L in at least half of the measurements [12];
- Hyponatremia: Na^+ blood concentration < 132 mmol/L in at least half of the measurements [12];
- Hypernatremia: Na^+ concentration > 146 mmol/L in at least half of the measurements [12].

All the aforementioned variables were measured during the anaesthetics, from whole arterial blood, with two different point-of-care analysers: a radiometer (IRMA Trupoint blood analysis system, Lifehealth MN USA) and a portable device with disposable cartridges (i-STAT blood analyser and cartridges CG8+, Abbott NJ USA), on a number of samples ranging from 3 to 7 per case. Electrolyte supplementation during surgery was noted. Other information extrapolated from the anaesthetic record included the American Society of Anaesthesiologists (ASA) risk classification (1-5E), the intra-operative administration of dobutamine, of noradrenaline and of beta 2-agonists (inhalational salbutamol), the indication for laparotomy, time to standing (defined as the minutes elapsed from arrival of the horse in the recovery box to standing), and the recovery score. Recovery scores were assigned by the anaesthesist in charge, based on a simple descriptive scale ranging from 1 (excellent) to 5 (very poor) [28].

Indications for laparotomy were sub-categorised in ischaemic (large colon volvulus, small and large intestine volvuli, inguinal hernias, mesenteric hernias, and pedunculated lipomas causing strangulating obstruction) and non-ischaemic (obstructive: large colon impaction/displacement, ileal impaction, nephro-splenic entrapment, large colon enterolithiasis) conditions.

Perianaesthetic death was defined as a binary variable with two possible outcomes: survival or death, including euthanasia, from anaesthetic induction to 72 hours after the end of the anaesthetic.

2.2. Statistical analysis

The Kolmorgov-Smirnov and the Skewness and Kurtosis tests for normality were used to assess the distribution of discrete and continuous variables, respectively. Descriptive statistics was used to quantitatively describe the basic features of the data.

Univariate binary logistic regression, with perianaesthetic death set as dependent variable, was run separately for each of the following independent variables: sex, breed, BCS, ASA risk classification, indication for surgery, gastric reflux, hypotension, hypoxaemia, arrhythmias, metabolic acidosis, metabolic alkalosis, hypo- and hyperkalaemia, hypo and hypercalcaemia, hypo- and hypernatraemia, coexistence of more than one type of electrolyte imbalance, intraoperative calcium or potassium supplementation, ischaemic condition, intraoperative use of dobutamine, noradrenaline and/or salbutamol, duration of anaesthesia, time to standing and recovery score. Univariate binary logistic regression was further used to determine whether there was an association between hypokalaemia and the intraoperative administration of salbutamol.

Variables showing significant association with the dependent variable ($P < 0.05$) were carried forward to be evaluated in a multiple logistic regression model, built using manual forward selection procedures. Odd ratios (OR) and associated 95% confidence intervals (CI) were estimated from the final logistic regression model and used as a measure to assess the quality of model fit, together with the goodness-of-fit test.

The Spearman correlation coefficient was used to investigate correlations between numerical discrete variables (recovery score versus time to standing, body weight and age, and time to standing versus body weight and age). Finally, in order to determine whether heavier, obese or older horses had a higher risk for perianaesthetic death, body weight, BCS and age were subcategorised (<500 and ≥500 kg, <6 and ≥6, and <120 and ≥ 120 months, respectively) and analysed with either Chi-square or Fisher Exact test where appropriate.

Commercially available software was used for statistical analysis (Sigma Stat 4.0 and Sigma Plot 14.0, Systat Software Inc., NV USA; IBM SPSS Statistics 24, UK). The level of significance was always defined as $P < 0.05$.

3. Results

3.1 Demographic data

Data are presented as either mean ± SD or medians and ranges [min - max], depending on data distribution.

One hundred and twenty horses of various breeds were included in the study (Table 1). Of these, 35.0% (n = 42) were intact female, 40.8 % geldings (n = 49), and the remaining 24.2% (n = 29) intact males. Body weight, age and BCS were 510 [53-803] kg, 161 ± 75 months and 5 [3-9], respectively. The ASA risk classification assigned to the horses was 4[3-5], with 17.5% (n = 21), 54.2 % (n = 65) and 28.3% (n = 34) of the horses classified as ASA 3E, 4E and 5E, respectively; all cases were classified as emergencies (E).

3.2 Anaesthesia and perioperative period

Preoperatively, stomach content was aspirated via nasogastric tube in 35% of the horses (n = 42). The indications for surgery, 30.0% of which (n = 36) were defined as ischaemic conditions, are listed in Table 2.

A team composed of one resident and one of four Diplomates of the European College of Veterinary Surgery (large animals) performed the surgeries. The anaesthetics were provided by a resident in Veterinary Anaesthesia, supervised by one of eight Diplomates of the European or American Colleges of Veterinary Anaesthesia and Analgesia.

Premedication was provided with an intravenous (IV) alpha 2 adrenoreceptor-agonist - either xylazine (Chanazine, Chanelle UK; dose: 1 [0.05 - 1.1] mg/kg) or romifidine (Sedivet, Boehringer Ingelheim UK; dose: 0.08 [0.05 - 0.08] mg/kg). Anaesthetic induction was achieved with IV ketamine (Ketamidor, Chanelle UK; dose: 2.2 [2.2 - 2.5] mg/kg) with either diazepam (Valium, Roche UK; dose: 0.05 [0.05 - 0.1] mg/kg) or midazolam (Dormicum, Roche UK; dose: 0.05 [0.05 - 0.1] mg/kg), IV. Isoflurane (IsoFlo, Abbott UK) in either 100% oxygen or a mixture of air/oxygen, with or without an IV lidocaine infusion (Lidocaine Hydrochloride 0.2%, Fresenius Kabi UK; dose: 0.03 [0.02-0.05] mg/kg/min), was used for maintenance of anaesthesia. Intraoperatively, IV dobutamine (Dobutamine Concentrate, Hameln Pharmaceutical Germany; dose: 1 [0.5 - 2] µg/kg/min) and inhalational salbutamol (Ventolin, GlaxoSmithKline UK dose: 2 [0.5 - 2] µg/kg) were administered to 99.2 % (n = 119) and to 41.7% (n = 50) of the horses, respectively, while noradrenaline (Noradrenaline, Hospira UK; dose: 0.2 [0.1 – 0.4] µg/kg/min) to 40.0% (n = 48) of the horses. Analgesia was provided with either IV butorphanol (Alvegesic, Dechra UK; dose: 0.05 [0.04-0.05] mg/kg or IM morphine (Morphine Sulphate, Mercury Pharmaceuticals Ireland; dose: 0.1 [0.1-0.15] mg/kg, both given at 2 hour-intervals, starting from the beginning of surgery until standing. Intra-operative fluids were administered to each horse, with fluid types and volumes decided at the anaesthesists' discretion based on the patient requirement. The proportions and numbers of horses that experienced intraoperative complications are presented in Table 3.

Anaesthesia lasted 146 ± 63 minutes, and time to standing was 41 [10 – 185] minutes. The quality of recovery was scored and recorded in 76 of 120 horses only; recovery score was 1, 2, 3 and 4 in 22.4% (n = 17), 36.8% (n = 28), 28.9% (n = 22) and 10.5% (n = 8) of the cases, respectively. Overall, recovery score from all horses was 2 [1-5]. There were statistically significant correlations between time to standing and recovery score (Spearman correlation coefficient = 0.47; $P< 0.001$), and between age and recovery score (Spearman correlation coefficient = -0.24; $P = 0.039$).

3.3 Electrolyte disturbances

The 79.2% (n = 95) of the horses experienced single (29.2%; n = 35) or multiple (50.8%; n = 61) electrolyte imbalances during surgery. Electrolytes were supplemented IV in 20.8% of the cases (n = 25); of these, 19 horses out of 25 received calcium gluconate (Calcium Gluconate 10%, Hameln Pharmaceutical Germany; dose: 0.5 mL/kg, IV) and the remaining 6 potassium chloride (Potassium Chloride 7.45%, Braun UK). The horses that received electrolyte supplementation during the anaesthetics had their iCa^{2+} and K^+ blood concentrations below 0.9 and 2.7 mmol/L, respectively. Blood electrolytes were measured with the radiometer in 55% of the horses, and with the portable device and disposable cartridges in the remaining 45%. Hypocalcaemia (52.5%; n = 63) and hypokalaemia (30.0%; n = 36) were the most represented electrolyte imbalances. There was a significant association between the use of salbutamol during surgery and the development of intraoperative hypokalaemia (P = 0.045).

3.4 Perianaesthetic death and risk factors

Perianaesthetic death occurred in 46 horses, of which the 54.3% (n = 25) were euthanised during surgery, 10.9% (n = 5) died/ were euthanised during recovery and the remaining 34.8% (n = 16) were euthanised during the following 72 hours. This accounted for an overall mortality rate of 38.3%. Except for three horses that experienced a cardiopulmonary arrest in the recovery box and died spontaneously, all the study horses that died were euthanised. Euthanasia was performed when either the patient demanded further surgical intervention that was declined by the owner, or its clinical condition was so severe that the clinician in charge had no reasonable hope for a successful outcome.

Horses weighing ≥ 500 kg or aged ≥ 120 months had a higher risk of perianaesthetic death (P = 0.014 and P = 0.02, respectively). The univariate logistic regression indicated the following variables as significant risk factors for perianaesthetic death: duration of anaesthesia (P = 0.006), gastric reflux (P = 0.011), acidosis (P = 0.014), intraoperative tachycardia (P = 0.033) and body weight (P = 0.037). The multivariate model confirmed these significances (Table 4).

3.5 Suitability of the statistical model

The confidence intervals were narrow for most variables, suggesting that the logistic regression model was overall accurate and fitted the data satisfactorily. The coefficient of determination R^2 obtained with the goodness-of-fit test was equal to 0.8.

Table 1
Breeds of 120 colic horses undergoing laparotomy under general anaesthesia.

Breed	**Number of horses**	**% of total**
Crossbreed	44/120	36.7
Irish Sport	13/120	10.8
Thoroughbred	12/120	10.0
Welsh	10/120	8.3
Irish Cob	9/120	7.5
Shetland Pony	8/120	6.7
British Warmblood	6/120	5.0
Dutch Warmblood	3/120	2.5
Arabian	3/120	2.5
Hanoverian	3/120	2.5
Andalusian	3/120	2.5
New Forest Pony	2/120	1.7
Hackney	1/120	0.8
Oldenburg	1/120	0.8
Trakehner	1/120	0.8
Holstein	1/120	0.8

Table 2
Indication for surgery for 120 colic horses undergoing laparotomy under general anaesthesia.

Indication for surgery	**Number of horses**	**% of total**
Strangulation	39/120	32.5
• Pedunculated lipoma (n = 37)		
• Foreign body (n = 2)		
Small intestine entrapment	20/120	17.0
• Nephrosplenic space (n = 6)		
• Epiploic foramen (n = 11)		
• Inguinal hernia (n = 1)		
• Diaphragmatic hernia (n = 1)		
• Gastrosplenic ligament (n = 1)		
Large colon impaction	18/120	15.0
Dorsal colon displacement	17/120	14.2
• Right (n = 12)		
• Left (n = 5)		
Large colon volvulus	10/120	8.3
Ileus/inflammation	8/120	6.7
Intestinal lymphoma	2/120	1.7
Intestinal rupture	3/120	2.5
Gastric ulceration	1/120	0.8
Ileocaecal intussusception	1/120	0.8
Intra-abdominal mass	1/120	0.8

Table 3
Intraoperative complications occurring in 120 colic horses undergoing laparotomy under general anaesthesia.

Intraoperative complication	Number of horses	% of total
Hypotension	106/120	88.3
Tachycardia	63/120	52.5
Hyponatraemia	2/120	1.7
Hypernatraemia	7/120	5.8
Hypokalaemia	36/120	30
Hyperkalaemia	6/120	5
Hypocalcaemia	63/120	52.5
Hypercalcaemia	1/120	0.8
Acidosis	12/120	10
Alkalosis	55/120	45.8

Table 4
Details of multiple logistic regression and significant risk factors associated with perioperative death in 120 colic horses undergoing laparotomy under general anaesthesia.

Variable	Coefficient	Standard Error	P value	OR (95% CI)
Body weight (kg)	0.004	0.004	0.020	1.00 (1.00 - 1.01)
Tachycardia (y/n)	0.908	0.452	0.043	2.48 (1.03 - 5.96)
Acidosis (y/n)	1.925	0.857	0.025	6.86 (1.28 - 36.76)
Gastric reflux (y/n)	1.048	0.525	0.021	2.85 (1.03 - 7.87)
Duration of anaesthesia (min)	-0.012	> 0.001	0.001	0.99 (0.98 - 0.99)

4. Discussion

The main findings of this retrospective study were that in the study population hypocalcaemia and hypokalaemia were the most common electrolyte disorders, and that perianaesthetic mortality was comparable to what has been reported previously in horses undergoing colic surgery [4,10], with heavier horses, presence of gastric reflux, longer anaesthetics and the occurrence of intraoperative tachycardia and acidosis being significant risk factors.

Similarly as found by other studies [12,17], in the study population hypocalcaemia and hypokalaemia were the most common intraoperative electrolyte imbalances.

Possible causes of hypocalcaemia are endotoxaemia, sepsis and diarrhoea, although the use of volatile anaesthetics has also been associated with a decrease in calcium serum concentrations [16,29,30].

Regarding hypokalaemia, its origin in horses with colic may be multifactorial, with altered intake and absorption and excess loss from the gastrointestinal tract due to diarrhoea being the most common causes [31].

Beta-adrenergic stimulation is known to increase the uptake of potassium into cells [32]. Interestingly, a significant association was found in the study population between the intraoperative use of a beta-2 agonist, salbutamol, and the occurrence of hypokalaemia. This finding should be critically interpreted, considering that two different point-of-care analysers were used to measure blood potassium concentration. The reference ranges for blood potassium concentration provided by the manufacturer of the i-Stat (1.9-4.1 mmol/L) [33] are considerably lower than those reported in the literature [12,27]. This represents a drawback which might limit the validity of our findings. Nevertheless, one study comparing the i-Stat with a radiometer whose measuring principles are similar to the one used in the current study found very good agreement between the two devices with respect to blood potassium concentration in horses, with excellent correlation of the measured values [27]. Moreover, the min-max i-Stat values for equine blood potassium concentrations reported in this study were 2.7-5.9 mmol/L, suggesting that horses with concentrations lower than 2.7 mmol/L, as measured by the i-Stat, are likely to suffer from actual hypokalaemia [27]. Overall, these aspects seem to indicate that our findings are relevant, and that the intraoperative administration of salbutamol may contribute to the development of hypokalaemia. Whether such hypokalaemia would be clinically relevant, however, remains debatable. Although both hypokalaemia and hypocalcaemia may potentially increase perioperative morbidity by causing muscle weakness, ileus and tachycardia [13-14], we failed to demonstrate their association with mortality in the study population. This could be because, in the sample population, in many cases the anaesthesist in charge chose to supplement the electrolytes whenever they felt this was indicated, an action that could have prevented the complication from worsening the outcome.

The current study identified a mortality rate of 38.3%, which also included horses euthanised intraoperatively. These results are comparable to those of two studies that included large numbers of equine patients. Johnston and colleagues found that perioperative fatalities, including euthanasia, occurred in 1843 out of 5330 horses undergoing colic operation, which represents the 35% of all cases [4]. Similarly, in 792 horses anaesthetised for surgical colic the risk of death or euthanasia was 35.5% [10]. Another study that included 300 horses identified a short-term mortality rate to discharge, following a single laparotomy, of 29.3% [2]. Proudman and colleagues reported a lower mortality rate and found that 88 out of 774 horses [11], equal to 13% of the total, died or were euthanised intraoperatively. However, this number did not include the postoperative deaths. The results of the current investigation might indicate that the quality of anaesthesia delivered to equine patients has not improved over the last decade. Alternatively, they could also reflect a tendency to offer to the horse owners more advanced treatment options than in the past, and therefore to be more prone to attempt surgery in patients that are critically ill.

The current study found that heavier horses are at higher risk for perianaesthetic mortality. This is in agreement with the findings of previous investigations. Proudman and others found that heavier breeds carried a higher risk of postoperative fatalities and hypothesised that the size may be a more likely risk factor than any specific breed susceptibility [11]. Besides the specific problems of colic horses, heavier horses may be predisposed to various complications, namely post-anaesthetic myopathies and neuropathies. Interestingly, correlation statistics found an association between older age and mortality; however, this finding was not confirmed by regression, which questions its actual significance.

In contrast with another study [11], which found no association between nasogastric reflux and the outcome, in the current study population horses with nasogastric reflux were at higher risk of death. It is challenging to provide a reasonable explanation for this finding. The presence of nasogastric reflux may reflect an increased intragastric pressure that could potentially account for impaired cardiovascular function during dorsal recumbency. However, possibly owing to stomach decompression and IV fluids administration prior to anaesthesia, in the current study no significant association was found between the presence of reflux and intraoperative tachycardia or hypotension. As an alternative explanation, nasogastric reflux might predispose to aspiration of gastric content during induction or recovery of anaesthesia, with consequent impairment of the respiratory function [34]. Although none of the horses experienced post-operative respiratory distress, undetected aspiration of gastric content may have accounted for some intraoperative deaths by causing hypoxaemia, hypercapnia and potentially adrenergic response.

With respect to the duration of anaesthesia, the current work confirms the findings of previously published work, which identified this variable as a risk factor for death of both colic and non-colic horses, and found that the longer the duration of the anaesthetic or of the operation, the higher the risk for perioperative fatalities [4,9,10].

The occurrence of intraoperative tachycardia was identified as another significant risk factor for perianaesthetic death in the current investigation. Whilst other types of arrhythmias, namely sinus bradyarrhythmias and A-V blocks, may be interpreted as a more benign alteration of the equine dromotropism [23], in this species tachycardia is more likely to reflect a certain degree of cardiovascular instability – although during surgery it may also result from inadequate analgesia or dobutamine overdose. Increased heart rate has been interpreted by various authors as a sign of cardiovascular compromise in colic horses, possibly resulting from endotoxaemia and/or hypovolaemia [35-36] and has been reported to increase the risk of death in horses undergoing colic operation [11]. Tachycardia may be blunted in the awake colic horses under the effect of previously administered alpha 2-agonists and become evident only during general anaesthesia. Moreover, mechanical ventilation and dorsal recumbency are likely to worsen the venous return to the heart and hence further decrease the cardiac output. In this scenario, optimizing the cardiovascular function before anaesthesia with adequate fluid therapy may help to improve the outcome and decrease the risk of mortality.

In colic horses, acidosis may impair cardiac function by altering the inotropism, and worsen the vasodilation caused by endotoxaemia. The occurrence of metabolic acidosis during anaesthesia was found a significant risk factor for mortality in the horses of this study. However, this finding should be interpreted cautiously, owing to both the intrinsic limitations of the variable and its associated large CI obtained from the multivariate regression model –which indicates a low accuracy of the model with respect to this specific variable. Serum bicarbonate concentrations and pH were both evaluated with the purpose of identifying all the cases of metabolic acidosis. Nevertheless, without a full electrolyte panel, which would have allowed a more comprehensive evaluation of the acid-base status, the presence of mixed electrolyte disorders could not be completely ruled out. Therefore, there could have been cases with a normal blood pH and yet undetected acidosis, or alkalosis, or even both.

In the horses of this study, recovery score was negatively correlated to age and positively correlated to time to standing. In other words, the younger the horses and the more time they took to stand, the worse was the quality of their recovery. Whilst the association between duration and quality of recovery was somewhat expected, geriatric horses would be expected to have a worse recovery than younger ones, as they may more easily develop muscular weakness and fatigue. However, recovery from anaesthesia is a process that is likely to be affected by learning behaviour, and it is reasonable to assume that older horses, owing to a quieter temperament and possibly previous experience of anaesthesia, may cope better with the situation [37].

In the current study, the ASA classification was not found a significant risk factor for perianaesthetic death. One reason for this finding may be that data distribution affected the statistical modelling process for this specific variable; since only colic horses were included in the study, an ASA grade 4 was assigned to most patients while ASA grades 1 and 2 were not represented in the study population.

This study has two important limitations. Each referral centre represents a unique set-up and, since this study was not designed as multicentric, the study sample may not represent well the entire equine population. However, it is worth considering that the Royal Veterinary College is a referral centre with an international background and generational diversity, including specialists who come from all over the world and were trained in either Europe or the US.

Another study limitation is that this study included a considerably smaller number of horses compared to previous studies that investigated equine perianaesthetic mortality. However, the suitability of the statistical model, together with the selection of a specific, presumably relatively small sub-population (colic horses undergoing surgery), suggest that our findings may be useful to implement the scientific knowledge pertaining to equine perianaesthetic mortality.

5. Conclusions

To date, there is no evidence that the mortality rate of colic horses undergoing surgery may be lower than in the past years, despite the increased number of anaesthesia specialists. Heavier horses and those with preoperative gastric reflux may carry a higher risk of fatalities. In the attempt to prevent intraoperative tachycardia, which was associated with increased risk of death in the study horses, the cardiovascular function should be optimised prior to anaesthetic induction and during anaesthetic maintenance. During anaesthesia, hypokalaemia may develop – or worsen - as a result of aerosolised salbutamol administration.

References

[1] Mair TS, Smith LJ. Survival and complication rates in 300 horses undergoing surgical treatment of colic. Part 4: Early (acute) relaparotomy. Equine Vet J 2005a;37:315-8.
[2] Mair TS, Smith LJ. Survival and complication rates in 300 horses undergoing surgical treatment of colic. Part 1: Short-term survival following a single laparotomy. Equine Vet J 2005b;37:296-302.
[3] Dugdale AH, Obhrai J, Cripps PJ. Twenty years later: a single-centre, repeat retrospective analysis of equine perioperative mortality and investigation of recovery quality. Vet Anaesth Analg 2016;43:171-8.
[4] Johnston GM, Eastment JK, Wood J, Taylor PM. The confidential enquiry into perioperative equine fatalities (CEPEF): mortality results of Phases 1 and 2. Vet Anaesth Analg 2002;29:159-70.
[5] Lawless SP, Werner LA, Baker WT, Hunt RJ, Cohen ND. Duodenojejunal mesenteric rents: Survival and complications after surgical correction in 38 broodmares (2006-2014). Vet Surg 2017;46:367-75.
[6] Lindegaard C, Ekstrøm CT, Wulf SB, Vendelbo JMB, Anderson PH. Nephrosplenic entrapment of the large colon in 142 horses (2000-2009): analysis of factors associated with decision of treatment and short-term survival. Equine Vet J Suppl 2011;39:63-8.
[7] Suthers JM, Pinchbeck GL, Proudman CJ, Archer DC. Survival of horses following strangulating large colon volvulus. Equine Vet J 2013;45:219-23.
[8] Johnston GM, Taylor PM, Holmes MA, Wood JLN. Confidential enquiry of perioperative equine fatalities (CEPEF-1): preliminary results. Equine Vet J 1995a;27:193-200.
[9] Johnston GM, Steffey E. Confidential enquiry into perioperative equine fatalities (CEPEF) Vet Surg 1995b;24:518-9.
[10] Mee AM, Cripps PJ, Jones RS. A retrospective study of mortality associated with general anaesthesia in horses: emergency procedures. Vet Rec 1998;142:307-9.
[11] Proudman CJ, Dugdale AH, Senior JM, Edwards GB, Smith JE, Leuwer ML, et al. Pre-operative and anaesthesia-related risk factors for mortality in equine colic cases. Vet J 2006;171:89-97.
[12] Hesselkilde EZ, Almind ME, Petersen J. Cardiac arrhythmias and electrolyte disturbances in colic horses. Acta Vet Scand 2014;56-8.
[13] Borer KE, Corley KTT. Electrolyte disorders in horses with colic. Part 1: potassium and magnesium. Equine Vet Educ 2006a;18:266-71.
[14] Borer KE, Corley KTT. Electrolyte disorders in horses with colic. Part 2: calcium, sodium, chloride and phosphate. Equine Vet Educ 2006b;18:320-5.
[15] Protopapas K. Studies on metabolic disturbances and other postoperative complications following equine surgery. DVetMed Thesis 2000; Royal Veterinary College, University of London.
[16] Dart AJ, Snyder JR, Spier SJ, Suvillan KE. Ionized calcium concentration in horses with surgically managed gastrointestinal disease: 147 cases (1988-1990). J Am Vet Med Assoc 1992;201:1244-8.
[17] Garcia-Lopez JM, Provost PJ, Rush JE, Zicker SC, Burmaster H, Freeman LM. Prevalence and prognostic importance of hypomagnesemia and hypocalcemia in horses that have colic surgery. Am J Vet Res 2001;62:7-12.
[18] Kaltofen A, Lindner KH, Ensinger H, Ahnefeld FW. The modification of the potassium concentration in blood by catecholamines. A literature review. Anasth Intensivther Notfallmed 1990;25:405-10.

[19] Casoni D, Spadavecchia C, Adami C. Cardiovascular changes after administration of aerosolized salbutamol in horses: five cases. Acta Vet Scand 2014;56:49.
[20] Hohnloser SH, Verrier RL, Lown B. Influence of beta 2-adrenoceptor stimulation and blockade on cardiac electrophysiologic properties and serum potassium concentration in the anesthetized dog. Am Heart J 1987;113:1066-70.
[21] Henneke DR, Potter GD, Krieder JL, Yeates BF. Relationship between condition score, physical measurements and body fat percentage in mares. Equine Vet J 1983;15:371-2.
[22] Trim CM, Shepard MK. Horse with Colic. In: Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, editors. Veterinary Anesthesia and Analgesia, 5th Ed. Lumb and Jones, Ames: 2015, p. 867-886.
[23] McGuirk SM, Muir WW. Diagnosis and treatment of cardiac arrhythmias. Vet Clin North Am Equine Pract 1985;1:353-70.
[24] Barton MH. A guide to differential diagnosis of arrhythmias in horses. Veterinarynews.dvm.360.com, DVM360 MAGAZINE Feb 01, 2008.
[25] www.vetlab.com – Equine normal values; last accessed on 8.04.2019.
[26] www.ahdc.vet.cornell.edu - New York State Veterinary Diagnostic Laboratory – Venous blood gas and electrolyte reference interval; last accessed on 8.04.2019.
[27] Peiró JR, Borges AS, Gonçalves RC, Mendes LC. Evaluation of a portable clinical analyser for the determination of blood gas partial pressures, electrolyte concentrations, and haematocrit in venous blood samples collected from cattle, horses, and sheep. Am J Vet Res 2010;71:515-21.
[28] Young SS, Taylor PM. Factors influencing the outcome of equine anaesthesia: a review of 1314 cases. Equine Vet J 1993;25:147-51.
[29] Grubb TL, Foreman JH, Benson GJ, Thurmon JC, Tranquilli WJ, Constable PD, et al. Hemodynamic effects of calcium gluconate administered to conscious horses. J Vet Intern Med 1996;10:401-4.
[30] Grubb TL, Benson GJ, Foreman JH, Constable PD, Thurmon JC, Olson WO, et al. Hemodynamic effects of ionized calcium in horses anesthetized with halothane or isoflurane. Am J Vet Res 1999;60:1430-5.
[31] Nappert G, Johnson PJ. Determination of the acid-base status in 50 horses admitted with colic between December 1998 and May 1999. Can Vet J 2018;42:703-7.
[32] Gennari FJ. Hypokalaemia. New Eng J Med 1998;339:451-8.
[33] https://www.abaxis.com/sites/default/files/resource-brochures/887-0307%20Rev.%20A%20VetScan%20i-STAT%20Reference%20Range%20Chart.pdfArcher DC, Pinchbeck GL, last accessed on 8.04.2019.
[34] Monticelli P, Adami C. Aspiration pneumonitis (Mendelson's syndrome) as perianaesthetic complication occurring in two horses: A case report. Equine vet Educ 2017; DOI:10.1111/eve.12781.
[35] Freeman DE, Hammock P, Baker GJ, Goetz T, Foreman JH, Schaeffer et al. Short- and long-term survival and prevalence of postoperative ileus after small intestinal surgery in the horse. Equine Vet J Suppl 2000;32:42-51.
[36] Puotunen-Reinert A. Study of variables commonly used in examination of equine colic cases to assess prognostic value. Equine Vet J 1986;18:275-7.
[37] Platt JP, Simon BT, Coleman M, Martinez EA, Lepiz MA, Watts AE. The effects of multiple anaesthetic episodes on equine recovery. Equine Vet J 2018;50:111-6.