Case Report Rapport de cas

Perianesthetic development of diaphragmatic hernia in a horse with equine pituitary pars intermedia dysfunction (PPID)

Molly K. Shepard, Wesley L. Lee, Randy B. Eggleston

Abstract — A 21-year-old Thoroughbred gelding with a history of equine pituitary pars intermedia dysfunction (PPID) presented with priapism of 2 days' duration. The horse received a caudal morphine epidural and then underwent corpus cavernosum lavage and phallectomy under general anesthesia. The patient's recovery featured multiple unsuccessful attempts to stand and his respiratory distress persisted for several hours until he acutely developed severe colic and was euthanized. Necropsy findings revealed a pituitary adenoma of the pars intermedia, bilateral adrenal cortical hyperplasia, and diaphragmatic herniation. This report suggests that horses with PPID may present a greater risk for diaphragmatic hernia under general anesthesia or during procedures placing stress on the diaphragm, including anesthetic recovery.

Résumé — Développement périanesthésique d'une hernie diaphragmatique chez un cheval atteint d'une dysfonction de l'hypophyse pituitaire (DHP). Un hongre Thoroughbred âgé de 21 ans avec une anamnèse de dysfonction de l'hypophyse pituitaire (DHP) a été présenté avec un priapisme présent depuis 2 jours. Le cheval a reçu une épidurale caudale de morphine et a ensuite subi un lavement du corps caverneux et une phallectomie sous anesthésie générale. Le rétablissement du patient a comporté de nombreuses tentatives infructueuses de se tenir debout et sa détresse respiratoire a persisté pendant plusieurs heures jusqu'à ce qu'il développe de graves coliques et soit euthanasié. Les constatations à la nécropsie ont révélé un adénome pituitaire de l'hypophyse, de l'hyperplasie corticale bilatérale et une herniation diaphragmatique. Ce rapport suggère que les chevaux atteints de DHP peuvent présenter un plus grand risque d'hernie diaphragmatique sous anesthésie générale ou durant des interventions exerçant un stress sur le diaphragme, y compris le réveil après l'anesthésie.

(Traduit par Isabelle Vallières)

Can Vet J 2015;56:48–52

Acquired diaphragmatic hernia is an uncommon cause for tachypnea, dyspnea, and colic in the horse (1–3). Conditions creating abrupt increases in intra-abdominal pressure, such as external trauma, parturition, and heavy exercise have been implicated in the development of acquired diaphragmatic hernias (4). To the authors' knowledge, there are no reports describing an association between perianesthetic events and development of a diaphragmatic hernia.

Equine pituitary pars intermedia dysfunction (PPID) is a common endocrine disease of older equids (5). Muscle wasting specifically affecting type 2 muscle fibers is a feature of PPID and is most notable in the gluteal and epaxial musculature (6). There are no reports describing muscular changes within the diaphragm of horses affected with PPID, which highlights the need for more precise histologic examination of diaphragmatic muscle in horses with this disease. The purpose of this case report is to describe the clinical case of an aged Thoroughbred gelding with PPID that was anesthetized for elective phallectomy and post-operatively was euthanized because of complications associated with an acquired diaphragmatic hernia.

Department of Large Animal Medicine, College of Veterinary Medicine, 501 DW Brooks Drive, University of Georgia, Athens, Georgia 30602, USA.

Address all correspondence to Dr. Molly Shepard; e-mail: mkshep@uga.edu

Case description

A 21-year-old Thoroughbred gelding with a history of PPID was presented to the University Teaching Hospital for evaluation of priapism of 2 days' duration. A previous history of laminitis and recurrent hoof abscesses was reported, as well as PPID managed with compounded oral pergolide mesylate.

Initial physical examination revealed a thin body condition score (4/9) with marked gluteal and epaxial muscle atrophy as well as an edematous, flaccid penis progressing to priapism within 8 h of hospitalization. The priapism failed to improve with medical therapies, so phallectomy was elected. The patient was fasted 12 h prior to surgery and was allowed free-choice access to water. Preanesthetic blood work revealed a mild lymphopenia [1.056×10^3, reference interval (RI): 1.16 to

Table 1. Results of arterial blood gas analysis

Parameter (unit) (reference interval)	81 minutes after start of anesthesia (15:39)	166 minutes after start of anesthesia (17:10)	41 minutes after standing (22:11)
F_iO_2	1.0	1.0	0.21
pH (7.35–7.45)	7.52	7.45	7.5
PaO_2 (mmHg) (80.3–99.8)	162.8	60.8	84.0
$PaCO_2$ (mmHg) (34.5–45.0)	31.5	40.5	31.5
HCO_3 (mmol/L) (22–26)	26.0	28.2	24.7
BE (−2 to +2)	2.9	4.0	
Lactate (mmol/L) (1–2)	2.0	2.7	6.0
BUN (mmol/L) (3.7–8.9)	5.7	5.7	5.7
Creatinine (mmol/L) (79.6–176.8)	97.2	114.9	141.4
Glucose (mmol/L) (3.7–6.8)	17.9	23.6	19.5
iCa (mmol/L) (1.55–1.61)	1.26	1.18	1.34
Hct (%) (32–48)	22	27	47
$ETCO_2$ (mmHg) (30.0–39.8)	30.7	33.8	n/a

FiO_2 — inspired fraction of oxygen; PaO_2 — partial pressure of oxygen in arterial blood; $PaCO_2$ — partial pressure of CO_2 in aterial blood; BUN — blood urea nitrogen; iCa — ionized calcium; Hct — hematocrit; $ETCO_2$ — partial pressure of CO_2 in an exhaled breath.
n/a — not available.

$5.1 \times 10^3/\mu L$], and mildly elevated gammaglutamyl transaminase (GGT) (31, RI: 3 to 22 U/L).

In the morning before the procedure, potassium penicillin, (Pfizerpen, Pfizer, New York, New York, USA) 22 000 IU/kg body weight (BW), gentamicin sulfate, (Gentafuse, Butler Schein, Dublin, Ohio, USA) 6.6 mg/kg BW, and flunixin meglumine, (Banamine, Intervet, Millsboro, Delaware, USA) 1.1 mg/kg BW, were administered intravenously (IV). The horse received IV premedication with xylazine (AnaSed, Lloyd, Shenandoah, Iowa, USA), 0.31 mg/kg BW, which resulted in a moderate level of sedation. A caudal epidural was administered using morphine sulfate (Hospira, Lake Forest, Illinois, USA), 0.1 mg/kg BW, diluted to a total volume of 10 mL with sterile 0.9% NaCl via the hanging drop technique (7). Xylazine, 0.36 mg/kg BW, was given IV for premedication in the induction stall, and anesthesia was smoothly induced with ketamine (Ketaset, Boeringer Ingelheim Vetmedica, St. Joseph, Missouri, USA), 2.2 mg/kg BW and diazepam (Hospira), 0.05 mg/kg BW. The patient was placed in lateral recumbency, intubated, and ventilated via demand valve for 2 to 3 min, with a 2-second inspiratory time. He was hoisted from the induction stall to dorsal recumbency on the surgery table, with hind legs in a frog-legged posture.

Isoflurane was delivered in 100% oxygen for maintenance, with a target end-tidal isoflurane concentration between 1.1% and 1.6%. Intermittent positive pressure ventilation (Mallard, Rachel model 2800; Mallard Medical, Redding, California, USA) was instituted using the following parameters: 10 breaths/min, tidal volume 6 L, and peak inspiratory pressure (PIP) 2.4 kPa (24 cm H_2O). Plasma-lyte A (Baxter, Deerfield, Illinois, USA) was administered IV at an average rate of 12 mL/kg BW/h. The facial artery was cannulated for direct blood pressure monitoring, and ECG leads were attached in a standard lead I orientation. A bolus (1 mg/kg BW) and constant rate infusion of 2% lidocaine hydrochloride (Hospira) was given (0.05 mg/kg BW/min). The following parameters were monitored at 5-minute intervals: pulse, respiratory rate, palpebral reflex, eye position, neck muscle tone, direct arterial blood pressure, ECG, pulse oximetry, capnography, and inhalant agent concentration. Body temperature, IV fluid totals, tidal volume, and PIP were recorded every 15 min. Arterial gas analysis was performed at 81 and 166 min after the start of inhalant anesthesia. All parameters were within normal limits for the first 36 min of anesthesia, with the exception of pulse oximetry, which would not generate a pulse waveform — a problem initially attributed to recent technical difficulties observed in this particular device.

Thirty-six minutes after the start of anesthesia, the heart rate increased from 40 to 55 beats/min (bpm) and the mean arterial blood pressure (MAP) increased from 75 to 90 mmHg. These changes were attributed to pain from the surgical procedure and were treated with morphine sulfate (Hospira), 0.1 mg/kg BW, IV. Within 22 min of the morphine injection, the pulse decreased to 42 bpm and MAP to 75 to 80 mmHg, and remained in this range for the remainder of surgery. Morphine was selected instead of butorphanol in order to avoid reversal of the morphine epidural. At this time, an arterial blood gas chemistry analysis and hematocrit (Stat Profile Critical Care Xpress; Nova Biomedical, Waltham, Massachusetts, USA; Table 1) revealed a mixed acid-base disorder characterized by a mild respiratory alkalosis unaccompanied by the expected compensatory decrease in HCO_3^-, hyperglycemia, and moderate anemia. The hyperglycemia was attributed to the horse's endocrine disease, and the anemia was considered spurious, based on a normal pre-operative hematocrit (36%) and the minimal hemorrhage or fluid dilution that could have occurred by that point in the procedure. Arterial oxygenation was decreased (PaO_2 163.1 mmHg) relative to the inspired fraction of oxygen (F_iO_2 = 0.98). Given the normal blood pressure and pulse rate, low-normal $PaCO_2$ and high tidal volume at this time (9 L, 16 mL/kg BW, PIP 24 cm H_2O), it was decided to reduce the tidal volume to 6 L.

Eighty-five minutes after the first blood gas analysis, another arterial sample was drawn and analyzed, revealing a mixed acid-base disorder characterized by a slightly elevated HCO_3^- with pH and $PaCO_2$ within normal range (Table 1). The PaO_2 had decreased further (61.0 mmHg), which was attributed at

the time to ventilation/perfusion mismatch associated with the horse's prolonged recumbency in a dorsal position (166 min). The following therapies were initiated: 15 puffs albuterol sulfate (Ventolin; GlaxoSmithKline, Research Triangle Park, North Carolina, USA) (total 1.35 mg) were administered into the breathing circuit, the operating room table was tilted 5 degrees with the head upward, and minute ventilation was increased. Tidal volume was increased from 6.0 to 10 L per breath (23 cm H_2O PIP), then decreased to 8 L per breath (30 cm H_2O PIP) according to subjective evaluation of chest excursions. It was unclear at the time why a decrease in tidal volume was accompanied by an increase in PIP. A continuous-rate infusion (CRI) of dobutamine (Hospira), 0.15 μg/kg BW/min, was initiated to improve alveolar perfusion but was shortly discontinued when the MAP increased from 73 mmHg to 90 to 95 mmHg.

Hyperlactatemia (2.7 mmol/L), hyperglycemia (23.6 mmol/L), and hypocalcemia (1.18 mmol/L) were present. Given the stability of the horse's blood pressure (MAP between 73 and 80 mmHg) prior to this reading and over the following 20 min, no calcium supplementation was administered. Meanwhile, in anticipation of the end of surgery, inhalant concentrations were decreased from end-tidal 1.6% to 1.4%. Approximately 30 min after the second blood gas analysis, a different pulse oximetry device was used, yielding values of 97% to 100%. Considering this new information and the impending end of the procedure, a third blood gas was not performed. Total surgery time was 2 h and 52 min. Total anesthesia time was 3 h and 56 min and total IV fluids administered over the course of general anesthesia were 27 L.

Inhalant anesthesia and the lidocaine CRI were discontinued, and the horse was hoisted into a padded recovery stall and placed in lateral recumbency. Xylazine, 0.2 mg/kg BW was administered IV 7 min after the end of anesthesia. Manual breaths (10 breaths/min, 2-second inspiratory time) were given by demand valve until the horse resumed spontaneous ventilation. Flow-by oxygen was then administered (15 L/min). After extubation (25 min after gas off), bilateral nasopharyngeal tubes were placed due to nasal edema, and nasal oxygen supplementation was continued at the same rate. A head and tail rope were used for assisted recovery.

The horse achieved sternal recumbency 55 min after the end of anesthesia, and made several unsuccessful attempts to stand. He appeared exhausted, with bilateral hind limb weakness and transiently increased respiratory effort after each attempt. Flunixin meglumine, 1.1 mg/kg BW, IV, was given at this time, followed by approximately 5 g of calcium gluconate (Cal-Nate 1069, Butler Schein) (250 mL of 23% calcium gluconate) diluted in 3 L of Normosol-R (Hospira) over 20 min. Approximately 2.5 h after the end of anesthesia, the horse was put into a sling in the recovery stall, which required no additional sedation. He was lifted to a standing position with sling assistance 3 h and 5 min after the end of anesthesia; moderate overexertion (5 to 10 s of weak bucking) was exhibited during the lifting. After standing, the horse supported his weight, but still required stability from the sling. He was offered hay in an attempt to ease his anxiety and help him maintain position under the hoist rail supporting the sling; he ate the hay readily. There was no apparent musculoskeletal injury, but his respiratory effort and rate were significantly increased and mucous membranes were cyanotic. His body temperature was 37.8°C. Thoracic auscultation of the left side revealed a heart rate of 80 bpm, a grade III-IV/VI holosystolic murmur, moderately increased bronchovesicular sounds, and increased borborygmi, presumed to be referred from the abdomen. The right side could not be safely auscultated at that time. Oxygen was administered, 15 L/min, through a unilateral nasal oxygen cannula, but did not improve mucous membrane color. Forty-one minutes after standing, the horse was allowed to breathe room air for 5 min, then a blood gas analysis was performed on a sample drawn from the facial artery (Table 1), showing normoxemia (PaO_2 84.2 mmHg), an elevated pH, slightly decreased $PaCO_2$ with normal HCO_3 (Table 1). The hyperlactatemia (6.0 mmol/L) was more severe than it had been intraoperatively, creatinine was slightly more elevated (141.4 mmol/L, RI: 79.6 to 176.8 mmol/L), as was ionized calcium (1.34 mmol/L).

The horse was kept in the sling in the recovery stall, and treated over the following few hours with IV fluid therapy and nasal oxygen supplementation. Approximately 2.5 h after standing, the horse was bright, alert and responsive, with a pulse rate of 90 bpm, respiratory rate of 66 breaths/min, dark pink/purple mucous membrane color, and normal gut sounds. The sling was removed at this time. Approximately 30 min later, the horse displayed colic signs (flank-watching), with a heart rate of 92 bpm, and respiratory rate of 80 breaths/min. Xylazine, 0.27 mg/kg BW, was administered IV and the horse was briefly left unobserved while preparing for nasogastric intubation. During this time the horse went into lateral recumbency, heart rate of 80 bpm, cyanotic mucous membranes, and was found paddling his front legs, but still apparently aware of his surroundings. Nasogastric intubation was not attempted due to the horse's positioning and personnel safety concerns. The horse's IV fluids and nasal oxygen were continued, and he was administered 2 doses of 500 mg furosemide (Salix; Intervet, Millsboro, Delaware, USA) IV, 20 min apart. Furosemide therapy was initiated as an emergency empirical treatment for possible pulmonary edema, based on clinical signs. The horse's clinical signs progressed to severe colic, characterized by thrashing and rolling in the stall. Neither a cursory abdominal ultrasound nor thoracic ultrasound revealed abnormal findings. Butorphanol and xylazine (dosages unknown) were given IV thrice over the course of 30 min in an attempt to manage pain while discussion with the owner took place. The owner elected euthanasia and the horse was humanely euthanized with 100 mL of a phenobarbital-based euthanasia solution (Beuthanasia-D Special; Schering-Plough Animal Health, Summit, New Jersey, USA).

Necropsy revealed a pituitary adenoma of the pars intermedia, bilateral adrenal cortical hyperplasia, and diaphragmatic herniation with small intestinal entrapment. Marked cavernous congestion of the remaining penile tissue following surgery was noted, but the source of the priapism remained undetermined. Microscopically, the diaphragm at the herniated site had been replaced by a thick rim of fibrous connective tissue with areas of fibrin deposition and hemorrhage. The presence of fibrous tissue at the site of herniation indicates chronicity and the presence

of hemorrhage suggests that the herniation likely occurred antemortem. Thus, it is possible that the herniation occurred at a site of muscle weakening with atrophy and fibrosis resulting in acute intestinal herniation possibly associated with trauma or movement.

Discussion

This case represents the first documented example of an acquired diaphragmatic hernia in a horse with PPID, and presents histological evidence that the hernia may have been associated with this patient's endocrine disease and anesthetic factors which increased intra-abdominal pressure. The shortage of this clinical presentation in the literature may be due to under-reporting of affected animals, failure to identify affected animals, increased risk that is too small to be readily identified, or a lack of increased risk among horses with PPID.

Body wall hernia as a probable sequela of hyperadrenocorticism has been rarely reported in animals (8,9). The effects of prolonged excessive cortisol on muscle and connective tissue, however, have been well-described in animals (10,11). The herniation of viscera through defects in connective tissue layers has been reported in humans with hyperadrenocorticism, most commonly following adrenalectomy (12). More recently, visceral herniation reportedly occurred spontaneously in 1 woman with iatrogenic hyperadrenocorticism (13). Given the preexistence of hyperadrenocorticism in this horse and the histologic description of his diaphragm on necropsy, it is plausible that his endocrine disease increased his risk for perianesthetic diaphragmatic hernia.

The timing of this patient's hernia rupture is unclear. While the necropsy findings prove that herniation occurred antemortem, histological data cannot rule out the presence of a diaphragmatic hernia prior to anesthesia. Significant preanesthetic rupture was unlikely, given the absence of respiratory or gastrointestinal signs and largely normal physical examination before surgery. Intra-anesthetic or post-anesthetic rupture is more likely, given the multiple events after induction (for example, hoisting, mechanical ventilation, recovery and sling-lifting into standing position) that likely increased intra-abdominal pressure, and exacerbated a preexisting hernia, or caused the chronically weakened diaphragm to tear.

The complication most suggestive of intra-anesthetic hernia rupture was severe hypoxemia. While some degree of intraoperative hypoxemia was expected in a geriatric horse kept dorsally recumbent for 4 h, the degree of hypoxemia he developed was inappropriate for a horse with no other significant morbidities. Given the necropsy findings, the significant V/Q mismatch we observed during surgery likely resulted from abdominal viscera herniation. Another feature of anesthetic maintenance suggesting rupture while under anesthesia is the changing, incongruent relationship observed between peak airway pressure and tidal volume. Tidal volume was increased from 6.3 to 10 L per breath with no accompanying change in PIP (23 cm H_2O), which may have been due to an increased thoracic compliance provided by the hernia. A few minutes later, tidal volume was decreased to 8 L, at which time, PIP increased to 30 cm H_2O, perhaps due to herniation of abdominal viscera through the diaphragm, effectively decreasing thoracic compliance.

Features of the anesthetic recovery that suggest post-operative rupture include the horse's marked clinical deterioration after sling-lifting. His arterial blood gas results in recovery, specifically his normoxemia, were unexpected, given the cyanotic appearance of his mucous membranes and his increased respiratory effort. Although care was taken to allow enough equilibration time on room air, residual high alveolar oxygen concentration may have artificially increased P_aO_2.

At the time of recovery, diaphragmatic hernia was not considered as a cause for the patient's dyspnea. Other differentials included pain, stress, or hypoxemia due to pulmonary or pleural space disease. Pulmonary thromboembolism was considered, given the possible hypercoagulative effect of this horse's concurrent endocrine disease (14). Rupture of the chordae tendinae was considered, after discovery of the new heart murmur in this cyanotic, dyspneic patient, but he lacked external (e.g., foamy nasal discharge) or auscultable findings suggestive of pulmonary edema.

The other significant feature of this horse's recovery was difficulty in rising due to apparent hind limb weakness. Probable contributing factors included age and underconditioned muscle mass associated with his endocrine disease (PPID), subclinical degenerative joint disease, the frog-legged positioning during his 4-hour anesthetic episode, or myopathy or neuropathy resulting from prolonged recumbency (although arterial blood pressure was normal throughout anesthesia). It is possible, but not likely, that the epidural injection contributed to the patient's hind limb weakness. While the use of local anesthetics in epidurals has been documented to cause hind limb weakness and ataxia in horses (15–17), opioid epidurals have not been associated with similar side effects (18).

Residual lidocaine from his intraoperative CRI may have also caused hind limb ataxia. One study by Valverde et al (19) showed that horses under isoflurane anesthesia that received lidocaine infusions through the end of their anesthetic procedure were significantly more ataxic in recovery than those whose lidocaine infusions were discontinued 30 min prior to the end of anesthesia, although no significant correlation was established between recovery score and treatment *versus* control groups. Another study describes lidocaine's terminal half-life as 54 min in horses that received a 1.3 mg/kg BW bolus followed by a constant infusion of 50 μg/kg BW/min for 105 min, while anesthetized with sevoflurane and with vaporizer settings kept between 2.88% and 3.88% (20). Plasma lidocaine concentration in this horse was likely very low by the time he attempted to stand, but we cannot definitively rule it out as a potential cause of his ataxia in recovery.

While this patient's progressive increase in lactate and creatinine most likely resulted from systemic hypoperfusion or shock, his consistently normal intra-anesthetic blood pressure, minimal intraoperative hemorrhage, adequate IV fluid rates, and normal mucous membrane color during surgery do not support this explanation. The horse's progressive hyperlactatemia may also have been due to anoxic hypoxia related to a reduction in lung compliance caused by the diaphragmatic hernia.

This case represents the first report of a horse with previously diagnosed pituitary pars intermedia dysfunction that developed

a perianesthetic diaphragmatic hernia. The complications he developed were significant, and likely resulted from standard anesthetic management procedures (e.g., hoisting, mechanical ventilation) and unanticipated events in recovery (e.g., repeated unsuccessful attempts to stand and sling-lifting to a standing position). This case report may serve to alert practitioners to an increased risk for diaphragmatic hernia in Cushingoid equine patients undergoing general anesthesia. CVJ

References

1. Hart SK, Brown JA. Diaphragmatic hernia in horses: 44 cases (1986–2006). J Vet Emerg Crit Care 2009;19:357–362.
2. Santschi EM, Juzwiak JS, Moll HD, Slone DE. Diaphragmatic hernia repair in three young horses. Vet Surg 1997;26:242–245.
3. Kelmer G, Kramer J, Wilson DA. Diaphragmatic hernia: Etiology, clinical presentation, and diagnosis. Compend Equine 2008;Jan/Feb:28–44.
4. Bristol DG. Diaphragmatic hernias in horses and cattle. Compend Contin Educ Pract Vet 1986;8:S407–S412.
5. Brosnahan MM, Paradis MR. Assessment of clinical characteristics, management practices, and activities of geriatric horses. J Am Vet Med Assoc 2003;223:99–103.
6. Aleman M, Nieto JE. Gene expression of proteolytic systems and growth regulators of skeletal muscle in horses with myopathy associated with pituitary pars intermedia dysfunction. Am J Vet Res. 2010;71:664–670.
7. Skarda RT, Tranquilli WJ. Local and regional anesthetic and analgesic techniques: Horses. In: Tranquilli WJ, Thurmon JC, Grimm KA, eds. Lumb and Jones' Veterinary Anesthesia and Analgesia. 4th ed. Ames, Iowa: Blackwell Publishing 2007:620.
8. Starkey SR, Morrisey JK, Stewart JE, Buckles EL. Pituitary-dependent hyperadrenocorticism in a cockatoo. J Am Vet Med Assoc 2008;232:394–398.
9. Smeak DD. Abdominal hernia. In: Slatter D, ed. Textbook of Small Animal Surgery. Philadelphia, Pennsylvania: WB Saunders, 1993:433–454.
10. Capen CC. Endocrine glands. In: Maxie MG, ed. Jubb, Kennedy and Palmer's Pathology of Domestic Animals. 3rd ed. Edinburgh, UK: Elsevier Saunders, 2007:415–418.
11. La Perle KMD. Endocrine system. In: Zachary J, McGavin MD, eds. Pathologic Basis of Veterinary Disease. St. Louis, Missouri: Elsevier 2012:675–676.
12. Walmsley D, McIntyre R, Sawers HA, et al. Laparoscopic transperitoneal adrenalectomy: A preliminary report of 14 adrenalectomies. Clin Endocrinol (Oxf) 1996;45:141–145.
13. Lee CY, Wang WK, Lin YH, Wang CB, Tseng CJ. Transvaginal evisceration in a case with iatrogenic Cushing's syndrome and no previous gynecologic surgery. Taiwan J Obstet Gynecol 2009;48:196–199.
14. Jacoby RC, Owings JT, Ortega T, Gosselin R, Feldman EC. Biochemical basis for the hypercoagulable state seen in Cushing syndrome; discussion 1006-7. Arch Surg 2001;136:1003–1006.
15. Olbrich VH, Mosing M. A comparison of the analgesic effects of caudal epidural methadone and lidocaine in the horse. Vet Anaesth Analg 2003;30:156–164.
16. LeBlanc PH. Regional anesthesia. Vet Clin North Am Equine Pract 1990;6:693–704.
17. LeBlanc PH, Caron JP, Patterson JS, Brown M, Matta MA. Epidural injection of xylazine for perineal analgesia in horses. J Am Vet Med Assoc 1988;193:1405–1408.
18. Natalini CC, Robinson EP. Effects of epidural opioid analgesics on heart rate, arterial blood pressure, respiratory rate, body temperature, and behavior in horses. Vet Ther 2003;4:364–375.
19. Valverde A, Gunkelt C, Doherty TJ, Giguere S, Pollak AS. Effect of a constant rate infusion of lidocaine on the quality of recovery from sevoflurane or isoflurane general anaesthesia in horses. Equine Vet J 2005;37:559–564.
20. Feary DJ, Mama KR, Wagner AE, Thomasy S. Influence of general anesthesia on pharmacokinetics of intravenous lidocaine infusion in horses. Am J Vet Res 2005;66:574–580.