Cardiopulmonary effects of diazepam-ketamine-isoflurane or xylazine-ketamine-isoflurane during abdominal surgery in foals

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Objective—To evaluate cardiopulmonary effects of anesthetic induction with diazepam and ketamine or xylazine and ketamine, with subsequent maintenance of anesthesia with isoflurane, in foals undergoing abdominal surgery.

Animals—17 pony foals.

Procedures—Foals underwent laparotomy at 7 to 15 days of age and laparoscopy 7 to 10 days later. Foals were randomly assigned to receive diazepam, ketamine, and isoflurane (D/K/Iso; n = 8) or xylazine, ketamine, and isoflurane (X/K/Iso; 9) for both procedures.

Results—During anesthesia for laparotomy, cardiac index, and mean arterial blood pressure ranged from 110 to 180 mL/kg/min and 57 to 81 mm Hg, respectively, in the D/K/Iso group and 98 to 171 mL/kg/min and 50 to 66 mm Hg, respectively, in the X/K/Iso group. Cardiac index, heart rate, and arterial blood pressures were significantly higher in the D/K/Iso group, compared with the X/K/Iso group. During anesthesia for laparoscopy, cardiac index and mean arterial blood pressure ranged from 85 to 165 mL/kg/min and 67 to 83 mm Hg, respectively, in the D/K/Iso group, and 98 to 171 mL/kg/min and 48 to 67 mm Hg, respectively, in the X/K/Iso group. Heart rates and arterial blood pressures were significantly higher in the D/K/Iso group, compared with the X/K/Iso group. There were no significant differences between groups during either experimental period for percentage end-tidal isoflurane, arterial blood gas partial pressures, or pH values.

Conclusions and Clinical Relevance—Anesthesia of foals for abdominal surgery with D/K/Iso was associated with less hemodynamic depression than with X/K/Iso. (*Am J Vet Res* 2009;70:574–580)

Foals may require general anesthesia in the first few weeks after birth to facilitate diagnostic procedures or emergency surgical interventions. Unfortunately, the anesthetic-related mortality rate is higher in foals < 1 month old, compared with that reported in adult horses.[1] To date, there are few comparative studies evaluating different anesthetic regimens in foals < 1 month old, and therefore, the optimal anesthetic protocol from a cardiopulmonary safety standpoint is unknown. At present, because of the lack of information regarding the effects of injectable anesthetic regimens in foals, induction and maintenance of anesthesia are often performed with an inhalant anesthetic alone. Advantages of this technique include a generally smooth induction and a rapid recovery, with the anesthetist being able to easily titrate the administration of the agent to effect. However, the superiority of using an inhalant anesthetic alone has been brought into question with the detection of a higher mortality rate with this technique versus techniques that use multiple agents.[1] A balanced anesthetic regimen that uses injectable and inhalant agents may therefore offer a safer alternative and warrants further evaluation in foals.

In adult horses, sedation with an α_2-adrenergic receptor agonist, such as xylazine, romifidine, or detomidine, followed by IV administration of ketamine is

Abbreviations

CI	Cardiac index
CO	Cardiac output
DAP	Diastolic arterial blood pressure
Et_{CO_2}	End-tidal carbon dioxide
EtIso	End-tidal isoflurane
HR	Heart rate
MAC	Minimum alveolar concentration
MAP	Mean arterial blood pressure
PIP	Peak inspiratory pressure
SAP	Systolic arterial blood pressure

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one of the most commonly used drug regimens for induction of anesthesia prior to maintenance of anesthesia with an inhalant agent.[2] The excellent quality and consistency of sedation resulting from administration of α_2-adrenergic receptor agonists are responsible for their popularity as preanesthetic agents in adult horses. However, IV administration of an α_2-adrenergic receptor agonist at sedative doses in horses is associated with bradycardia, a decrease in CO, and a transient increase in systemic arterial blood pressure.[3] The use of α_2-adrenergic receptor agonists in the perioperative period traditionally has not been recommended for neonatal horses because of the dependency of CO on HR in this age group[4]; however, objective comparisons with other premedication agents have not yet been performed. The potential excitement and muscle rigidity associated with the use of ketamine when not preceded with a sedative have also limited the use of this drug in neonatal horses. Although unreliable in adult horses, in foals < 2 weeks old, IV administration of diazepam induces excellent sedation.[2] Because diazepam has minimal adverse cardiovascular effects in adult horses,[5] diazepam may be a suitable alternative preanesthetic agent to an α_2-adrenergic receptor agonist in foals prior to induction of anesthesia with ketamine. To date, no studies have thoroughly evaluated the cardiopulmonary effects of the combination of xylazine or diazepam with ketamine when used to induce anesthesia in foals in this age group.

The purpose of the study reported here was to evaluate the cardiopulmonary effects of anesthetic induction with diazepam and ketamine or xylazine and ketamine, with subsequent maintenance of anesthesia with isoflurane, in foals undergoing laparotomy and laparoscopy.

Materials and Methods

Animals—The University of Guelph Animal Care Committee approved the experimental protocol, and the guidelines of the Canadian Council on Animal Care were followed throughout the study. Seventeen pony foals, weighing from 29 to 51 kg (mean ± SD, 33.4 ± 6.7 kg), that were being used for a concurrent surgical investigation[6,7] were used in the present study. All foals were determined to be healthy on the basis of results of a physical examination, CBC, serum biochemical profile, and serum IgG measurement.[a] Throughout the study period, the foals were housed with their dams in a box stall and were allowed ad libitum access to hay and fresh water. Food was not withheld prior to the experimental periods. Each foal underwent 2 surgical procedures; a laparotomy was performed when the foals were 7 to 15 days of age, and a laparoscopy followed 7 to 10 days later. The surgical interventions are described in detail in previous publications.[6,7] In brief, both surgical procedures were performed with the foals in dorsal recumbency. For the first surgical intervention, abdominal exploration was performed via a routine ventral midline laparotomy. Following exposure and manipulation of the small intestine, a routine 3-layer closure of the abdomen was performed. The second surgery involved laparoscopic exploration of the abdomen performed through 3 portal sites by use of an automatic high-flow carbon dioxide insufflator[b] to insufflate the abdomen to a pressure of 12 mm Hg. During the laparoscopic procedure, the operating table was tilted to a 10° head-down position. At the completion of the laparoscopic procedure, the surgical table was repositioned into a horizontal position, and the abdominal cavity was manually decompressed.

Experimental groups—Foals were randomly assigned to receive either diazepam[c] (0.2 mg/kg), ketamine[d] (2.0 mg/kg), and isoflurane[e] (D/K/Iso; n = 8) or xylazine[f] (0.8 mg/kg), ketamine (2.0 mg/kg), and isoflurane (X/K/Iso; 9) for induction and maintenance of anesthesia for both anesthetic periods. In both groups, isoflurane was delivered in oxygen with the inspired percentage adjusted to achieve an adequate depth of anesthesia as assessed by an individual unaware of the treatments. Eye position, degree of muscle relaxation, and presence-absence of movement were used to determine depth of anesthesia.

Experimental protocol—Prior to each anesthetic episode, foals were weighed, an IV catheter[g] was placed in a jugular vein, and a venous blood sample was obtained for electrolyte[h] and hemoglobin measurement.[i] Ceftiofur[j] (2.2 mg/kg) and flunixin meglumine[k] (1.0 mg/kg) were administered IV. Following a 20-minute stabilization period, either diazepam or xylazine was administered IV according to the assigned experimental group. Ketamine was administered IV 5 minutes later, and foals were gently restrained during the induction of anesthesia. Foals were positioned in lateral recumbency, orotracheally intubated, and connected to a circle anesthetic circuit with an out-of-circuit isoflurane-specific vaporizer. A side-stream infrared gas analyzer[l] was used to continuously monitor the EtIso and Et_{CO_2} concentrations. Prior to each experimental day, the gas monitor was calibrated with a commercial reference gas.[m] The oxygen flow rate was set at 40 mL/kg/min, and the vaporizer setting was adjusted to achieve an adequate depth of anesthesia as assessed by evaluation of eye position, palpebral eye reflexes, and muscle relaxation. Intermittent positive-pressure ventilation[n] was provided during anesthesia with a tidal volume of 12 to 15 mL/kg with the frequency adjusted to maintain Et_{CO_2} from 35 to 45 mm Hg. Peak inspiratory pressure was recorded from an aneroid pressure manometer mounted within the circle breathing circuit. A 1-inch, 20-gauge catheter[o] was placed in the facial artery, and a lithium-sensitive sensor[p] and pressure transducer[q] were connected to the catheter by use of a 3-way valve, and the lithium sensor was connected to a CO computer.[r] Leads for the ECG were connected in a base-apex configuration, and the ECG leads and pressure transducer were connected to a physiologic monitor.[s] The point of the shoulder was used as the zero pressure reference point. The pressure transducer was calibrated before each experimental day with a mercury column. Heart rate, SAP, DAP, and MAP were recorded from the physiologic monitor, and CO was determined by use of the lithium dilution technique as described.[8,9] The foal's most recent hemoglobin concentration, the serum sodium concentration, and the injection dose of LiCl[t] were entered into the CO computer prior to each determination. The dose of LiCl used to measure CO was 0.005 mmol/kg of a

0.15 mmol/mL LiCl solution. Cardiac index was subsequently calculated as CO (mL/min)/body weight (kg).

Foals were positioned in dorsal recumbency, and data, including HR, SAP, MAP, DAP, CO, EtIso, and PIP, were recorded 5, 10, 20, and 30 minutes after administration of ketamine. Subsequent measurements were obtained 10 and 20 minutes after surgical access to the abdomen was obtained via laparotomy or following abdominal insufflation with carbon dioxide and again 5 and 10 minutes after the abdominal wall was closed after either procedure. Of note, foals were in dorsal recumbency for all recordings, but they were positioned in a 10° head-down position for recordings taken during laparoscopy. Arterial blood samples were obtained from the facial artery catheter for blood gas,[u] electrolyte, and hemoglobin analysis 20 minutes after ketamine administration, 10 minutes after the abdominal wall was opened via laparotomy or the abdominal insufflation was complete during laparoscopy, and 5 minutes after the abdominal incisions were closed.

Following the termination of surgery, the arterial catheter was removed and butorphanol[v] (0.04 mg/kg, IV) was administered. Isoflurane administration was discontinued, and when foals resumed spontaneous ventilation, they were moved to a recovery stall, where they recovered with assistance.

Statistical analysis—Statistical analysis was performed with a statistical software program.[w] A Shapiro-Wilk test was done to check for normality of the data. Cardiopulmonary variables were analyzed with a repeated-measures ANOVA. For those variables in which a significant ($P < 0.05$) difference was detected between treatment groups within an anesthetic period or between anesthetic periods within a treatment group, time was coded into 3 blocks as presurgery, surgery, and postsurgery. The least squares means were calculated for all variables during each time block, and they were used to test for significant ($P < 0.05$) differences between treatment groups during each of the experimental periods, between experimental periods within a treatment group, and within a group at the surgery and postsurgery time block, relative to the presurgery time block, during each of the experimental periods.

Results

During both anesthetic periods, all foals in both treatment groups achieved recumbency and sufficient anesthetic depth to permit orotracheal intubation following administration of ketamine. At the end of anesthesia, foals all stood on the first attempt and had minimal ataxia once standing.

Effect of anesthetic regimen during laparotomy—During the first experimental period, in which foals underwent a laparotomy, HR, SAP, MAP, DAP, and CI were significantly lower in the X/K/Iso group in the presurgery, surgery, and postsurgery blocks, compared with the D/K/Iso group (**Tables 1 and 2**). There were no significant differences in this experimental period between the treatment groups in EtIso, arterial blood gas variables, or PIP.

In the X/K/Iso group, HR and CI values were significantly lower during the surgery period, compared with the presurgery values. In this group, the EtIso and DAP values were significantly higher during surgery, relative to the values recorded during the presurgery period. In the postsurgery period, HR and CI values remained significantly lower than presurgery values, whereas MAP and DAP values were significantly higher than presurgery values.

In the D/K/Iso group, HR and CI values were significantly lower during the surgery period than the presurgery period; however, there were no significant differences in systemic blood pressures between these 2 time periods. End-tidal isoflurane was also significantly higher in this group during the surgery period, compared with the presurgery period. Relative to the presurgery period, HR and CI were significantly lower, whereas SAP, DAP, and MAP were significantly higher during the postsurgery period.

Effect of anesthetic regime during laparoscopy—During the second experimental period, in which foals underwent laparoscopic abdominal exploration, HR, SAP, MAP, and DAP were significantly lower in the X/K/Iso group in the presurgery, surgery, and postsurgery periods, compared with the D/K/Iso group (**Tables 3 and 4**). There were no significant differences, how-

Table 1—Cardiovascular determined variables during isoflurane anesthesia for laparotomy in foals following induction of anesthesia with D/K/Iso (n = 8) or X/K/Iso (9).

		Anesthesia time							
		Presurgery period				Surgery period		Postsurgery period	
Variable	Group	5 minutes	10 minutes	20 minutes	30 minutes	10 minutes	20 minutes	5 minutes	15 minutes
HR (beats/min)	D/K/Iso	105 ± 12	97 ± 10	98 ± 11	96 ± 14	92 ± 19*	86 ± 15*	84 ± 12*	91 ± 15*
	X/K/Iso	91 ± 6†	88 ± 7†	83 ± 8†	79 ± 9†	77 ± 8*†	73 ± 8*†	76 ±8*†	79 ± 8*†
SAP (mm Hg)	D/K/Iso	92 ± 8	94 ± 21	89 ± 17	80 ± 13	96 ± 15	82 ± 9	102 ± 21*	111 ± 28*
	X/K/Iso	85 ± 17†	82 ± 13†	76 ± 7†	73 ± 9†	78 ± 14†	67 ± 20†	82 ± 11†	88 ± 10†
MAP (mm Hg)	D/K/Iso	67 ± 9	67 ± 20	62 ± 11	58 ± 9	73 ± 11	57 ± 6	74 ± 17*	81 ± 21*
	X/K/Iso	65 ± 9†	55 ± 6†	48 ± 6†	48 ± 8†	59 ± 10†	50 ± 12†	61 ± 9*†	66 ± 8*†
DAP (mm Hg)	D/K/Iso	48 ± 9	50 ± 18	47 ± 10	43 ± 7	57 ± 9	44 ± 4	59 ± 14*	62 ± 16*
	X/K/Iso	45 ± 7†	38 ± 5†	37 ± 7†	37 ± 7†	48 ± 9*†	41 ± 9*†	49 ± 7*†	52 ± 7*†
CI (mL/kg/min)	D/K/Iso	ND	180 ± 20	194 ± 38	175 ± 37	111 ± 23*	124 ± 49*	124 ± 17*	139 ± 27*
	X/K/Iso	ND	171± 28†	154± 15†	143± 18†	104 ± 22†	98 ± 19†	107 ± 20*†	117 ± 18*†

Data are reported as mean ± SD.
*Significant ($P < 0.05$) difference from presurgery value. †Significant ($P < 0.05$) difference from the D/K/Iso group at this time interval.
ND = Not determined.

ever, in CI between treatment groups during any time period. There were also no significant differences between the treatment groups in the EtIso, arterial blood gas variables, or PIP.

In the X/K/Iso group, HR and CI were significantly lower, whereas MAP and DAP were significantly higher in the surgery and postsurgery periods, relative to the presurgery period (Tables 3 and 4). There were no significant changes over time in SAP in this group. The EtIso and the PIP were significantly higher in the surgery and postsurgery periods, compared with the presurgery values, in the X/K/Iso group.

In the D/K/Iso group, HR and CI were significantly lower during the surgery and postsurgery periods, relative to the presurgery period (Tables 3 and 4). The SAP, MAP, and DAP were significantly higher during the surgery period, compared with the presurgery period, for this latter treatment group. The EtIso and PIP were significantly higher during the surgery and postsurgery periods, relative to the presurgery period.

Experimental period effect—Comparison between experimental periods (laparotomy vs laparoscopy) in foals revealed that during the surgery period, the foals

Table 2—Arterial blood gas and respiratory variables determined in the same foals as in Table 1.

		Anesthesia time							
		Presurgery period				Surgery period		Postsurgery period	
Variable	Group	5 minutes	10 minutes	20 minutes	30 minutes	10 minutes	20 minutes	5 minutes	15 minutes
Pa_{O_2} (mm Hg)	D/K/Iso	ND	ND	464 ± 81	ND	450 ± 63	ND	460 ± 90	ND
	X/K/Iso	ND	ND	438 ± 105	ND	410 ± 71	ND	417 ± 200	ND
$Paco_2$ (mm Hg)	D/K/Iso	ND	ND	49 ± 3	ND	50 ± 0.8	ND	53 ± 2.4	ND
	X/K/Iso	ND	ND	47 ± 5	ND	48 ± 3	ND	49 ± 8	ND
pHa	D/K/Iso	ND	ND	7.38 ± 0.07	ND	7.36 ± 0.03	ND	7.32 ± 0.02	ND
	X/K/Iso	ND	ND	7.38 ± 0.03	ND	7.38 ± 0.02	ND	7.36 ± 0.03	ND
PIP (cm H_2O)	D/K/Iso	20 ± 4	20 ± 3	21 ± 3	22 ± 3	23 ± 6	23 ± 6	23 ± 3	23 ± 2
	X/K/Iso	19 ± 4	19 ± 4	19 ± 4	19 ± 4	19 ± 4	19 ± 4	19 ± 4	19 ± 4
EtIso (%)	D/K/Iso	1.08 ± 0.10	1.11 ± 0.20	1.32 ± 0.33	1.22 ± 0.22	1.59 ± 0.24*	1.53 ± 0.33*	1.35 ± 0.23	1.43 ± 0.22
	X/K/Iso	0.93 ± 0.15	1.10 ± 0.23	1.26 ± 0.20	1.11 ± 0.22	1.56 ± 0.25*	1.47± 0.24*	1.23 ± 0.12	1.23 ± 0.15

pHa =Arterial pH. *See* Table 1 for remainder of key.

Table 3—Cardiovascular variables during isoflurane anesthesia for laparoscopy in the same foals as in Table 1.

		Anesthesia time							
		Presurgery period				Surgery period		Postsurgery period	
Variable	Group	5 minutes	10 minutes	20 minutes	30 minutes	10 minutes	20 minutes	5 minutes	15 minutes
HR (beats/min)	D/K/Iso	103 ± 7	101 ± 8	100 ± 12	105 ± 17	93 ± 13*	86 ± 12*	86 ± 14*	81 ± 10*
	X/K/Iso	89 ± 9†	90 ± 8†	86 ± 8†	84 ± 10†	76 ± 13*†	75 ± 14*†	77 ± 14*†	76 ± 15*†
SAP (mm Hg)	D/K/Iso	99 ± 12	99 ± 11	100 ± 10	89 ± 6	108 ± 24*‡	105 ± 15*‡	99 ± 6	103 ± 5
	X/K/Iso	90 ± 11†	84 ± 11†	78 ± 10†	78 ± 8†	86 ± 12†‡	84 ± 9†‡	83 ± 16†	84 ± 10†
MAP (mm Hg)	D/K/Iso	72 ± 10	70 ± 13	67 ± 11	67 ± 12	83 ± 20*	78 ± 14*	73 ± 6	64 ± 4
	X/K/Iso	60 ± 5†	55 ± 6†	50 ± 6†	50 ± 6†	66 ± 11*†‡	64 ± 7*†‡	64 ± 10*†	62 ± 7*†
DAP (mm Hg)	D/K/Iso	53 ± 9	55 ± 17	50 ± 11	51 ± 14	67 ± 20*	65 ± 17*	59 ± 6	60 ± 5
	X/K/Iso	44 ± 4†	41 ± 5†	37 ± 5†	36 ± 4†	55 ± 12*†‡	54 ± 6*†‡	52 ± 8*†	51 ± 7*†
CI (mL/kg/min)	D/K/Iso	ND	165 ± 31‡	159 ± 45‡	167 ± 54‡	88 ± 13*‡	85 ± 16*‡	93 ± 27*‡	94 ± 25*‡
	X/K/Iso	ND	152 ± 36	160 ± 21	148 ± 23	87 ± 22*	83 ± 25*	89 ± 25*	98 ± 32*

‡Significant ($P < 0.05$) difference from the same treatment group during laparotomy.
See Table 1 for remainder of key.

Table 4—Arterial blood gas and respiratory variables determined during isoflurane anesthesia for laparoscopy in the same foals as in Table 1.

		Anesthesia time							
		Presurgery period				Surgery period		Postsurgery period	
Variable	Group	5 minutes	10 minutes	20 minutes	30 minutes	10 minutes	20 minutes	5 minutes	15 minutes
Pa_{O_2} (mm Hg)	D/K/Iso	ND	ND	466 ± 58	ND	452 ± 37	ND	357 ± 114	ND
	X/K/Iso	ND	ND	462 ± 70	ND	458 ± 40	ND	363 ± 208	ND
$Paco_2$ (mm Hg)	D/K/Iso	ND	ND	46 ± 6	ND	51 ± 4	ND	54 ± 2	ND
	X/K/Iso	ND	ND	47 ± 5	ND	44 ± 2	ND	46 ± 4	ND
pHa	D/K/Iso	ND	ND	7.39 ± 0.05	ND	7.35 ± 0.02	ND	7.31± 0.03	ND
	X/K/Iso	ND	ND	7.37 ± 0.06	ND	7.44 ± 0.03	ND	7.30 ± 0.02	ND
PIP (Cm H_2O)	D/K/Iso	21 ± 4	22 ± 4	22 ± 4	22 ± 4	33 ± 6*	34 ± 6*	26 ± 5*	25 ± 5*
	X/K/Iso	20 ± 5	21 ± 6	21 ± 6	21 ± 6	32 ± 5*	32 ± 5*	24 ± 5*	24 ± 5*
EtIso (%)	D/K/Iso	1.02 ± 0.20	1.12 ± 0.15	1.25 ± 0.18	1.34 ± 0.21	1.63 ± 0.23*‡	1.81 ± 0.21*‡	1.50 ± 0.26*	1.53 ± 0.10*
	X/K/Iso	0.95 ± 0.14	1.09 ± 0.14	1.12 ± 0.13	1.24 ± 0.08	1.65 ± 0.13*‡	1.63 ± 0.07*‡	1.43 ± 0.02*‡	1.45 ± 0.23*‡

See Tables 2 and 3 for key.

that received X/K/Iso had a significantly greater SAP, MAP, and DAP during the second anesthetic period when undergoing laparoscopy, compared with laparotomy. In addition, in these foals, EtIso concentrations were significantly higher during both the surgery and postsurgery periods when foals were undergoing laparoscopy, compared with laparotomy. Similarly, higher systemic arterial pressures were detected in foals receiving D/K/Iso during laparoscopy, compared with laparotomy. In the foals receiving D/K/Iso, CI was significantly lower at all times points during laparoscopy, compared with laparotomy. End-tidal isoflurane concentrations were significantly higher only during the surgery period during laparoscopy, compared with laparotomy, in this treatment group.

Discussion

Administration of diazepam or xylazine followed by ketamine resulted in a controlled anesthetic induction in all foals in this investigation, no doubt in part because of the manual restraint provided from the time of ketamine administration until the foals were in lateral recumbency. In the younger foals (< 15 days of age) undergoing laparotomy, premedication with diazepam prior to induction of anesthesia with ketamine and maintenance of anesthesia with isoflurane resulted in significantly less hemodynamic depression than that observed when xylazine was used. Although the differences in cardiopulmonary effects were less marked in older foals during a second anesthetic period in which laparoscopy was performed, premedication with diazepam continued to offer hemodynamic advantages over xylazine prior to induction of anesthesia with ketamine and maintenance of anesthesia with isoflurane. In this study, the use of diazepam in place of xylazine in the older foals did not have a detectable negative effect on anesthetic induction or recovery characteristics.

General anesthesia and recumbency in horses are associated with dramatic changes in cardiovascular and respiratory function. In general, the goals of the anesthetist include maintaining a patient's CO, oxygenation, and arterial blood pressure at values sufficient to maintain oxygen delivery and perfusion of vital organs. In this study, to minimize the stress of handling on both mares and foals, we did not collect hemodynamic measurements in the foals prior to induction of anesthesia. It is therefore not possible from this study to make specific conclusions regarding the effects of either of the anesthetic regimens evaluated on the cardiovascular system, relative to awake values. However, despite all of the foals receiving similar doses of ketamine and isoflurane, greater hemodynamic depression throughout the entire anesthetic period was evident in foals sedated with xylazine, compared with diazepam, prior to induction of anesthesia. Although α_2-adrenergic receptor agonists are undoubtedly the most popular preanesthetic agents available for use in horses, they are not without adverse cardiovascular effects, unfortunately. Typical cardiovascular alterations associated with IV administration of xylazine have been well characterized in adult horses and include a decrease in HR secondary to a peripherally mediated increase in vagal tone and a centrally mediated reduction in sympathetic tone, a decrease in CO, and a transient increase followed by a decrease in systemic blood pressure.[2] When administration of xylazine is followed with administration of ketamine, the sympathomimetic effects of the latter agent generally result in an increase in HR.

In the present study, although ketamine likely caused in an increase in HR, relative to postsedation values, HR values remained significantly lower in the foals receiving xylazine, compared with those receiving diazepam, throughout both experimental periods. Although the HR values observed in both groups of foals were still within clinically acceptable ranges, the lower HR in the foals receiving xylazine likely contributed to the lower CI values and may have contributed to the low systemic arterial blood pressures observed. Mean arterial blood pressure is routinely monitored during equine anesthesia, and values > 60 to 65 mm Hg are considered the minimum values required to result in adequate skeletal muscle, coronary, renal, and cerebral perfusion. During both experimental periods, most foals that received xylazine had values < 60 to 65 mm Hg. In adult horses, MAP values in this range are associated with an increased risk of postanesthetic myopathy, and although this is not a common postanesthetic complication in foals, it has been reported.[10] In healthy conscious foals in the age range used in this study, arterial blood pressure is reported to be similar to that of adult horses, and it is reasonable to assume that maintaining values in the reference range during anesthesia would be ideal.[11]

Although foals receiving either premedication agent had a similar pattern of cardiovascular changes throughout both experimental periods, it is interesting that differences in variables between groups persisted for a period of time beyond that associated with xylazine when it is administered alone in adult horses. Specifically, Wagner et al[3] reported horses' HR and CO values to be significantly less than baseline values for 30 and 45 minutes, respectively, following administration of 1.1 mg of xylazine/kg in adult horses. In the present study, the differences in several variables, including HR and CI, were evident until the end of the study period, which exceeded approximately 90 minutes. A similar duration of effect was reported by Carter et al,[12] who found a significant decrease in HR over a 120-minute recording period in 10- and 28-day-old foals following administration of 1.1 mg of xylazine/kg, IV. Unfortunately, in that study,[12] CO was not measured. The longer period of hemodynamic depression associated with administration of xylazine in foals is of concern, particularly when used in combination with other potent cardiodepressant agents such as the inhalant anesthetics.

The doses of the injectable agents used in the present study were selected on the basis of recommended doses in the literature and clinical experience.[2,4] Although the xylazine dose was higher than is generally used clinically in sick foals < 1 week old, the dose used in the present study was, in our experience, the minimum effective dose for healthy pony foals > 1 week old. The delivery of isoflurane was subsequently adjusted by use of subjective clinical signs that are used clinically. Both diazepam and xylazine reduce the MAC of inhal-

ant anesthetics in adult horses, which may explain the lack of differences in the isoflurane requirements between groups throughout the experimental periods.[13,14] Although xylazine is considered to have more analgesic properties than diazepam, no differences in the EtIso were evident between the 2 groups at the time of surgery. Unlike the cardiovascular effects, it is possible that the effect of xylazine on the inhalant requirements was largely gone by the time surgery started and that any potential benefits of its analgesic properties, relative to diazepam, would have been minimal. Alternatively, the methods used to determine depth of anesthesia may not have been adequate to detect differences in anesthetic requirements, resulting in excessive administration of isoflurane in the foals in the X/K/Iso group.

The foals' cardiovascular responses to surgical manipulation in this study were similar to those reported in adult horses and dogs.[15,16] Specifically, systemic arterial pressures were higher, despite an increase in the EtIso, and HR and CI were lower during surgery, compared with presurgery values. As is known from previous investigations, the MAP was not a good predictor of CI in foals in this study in either experimental group. Unfortunately, monitoring CO in the clinical setting is not routinely performed, although newer, less invasive techniques such as the lithium dilution technique used in this study may facilitate monitoring CO in the future.

Comparisons within a treatment group between experimental periods (laparotomy vs laparoscopy) revealed several differences. We were not able to conclude whether those differences were the result of the age of the foals or the surgical procedure. In general, the inhalant requirements were higher during the second period, in which foals underwent a laparoscopy versus a laparotomy. Although it is possible that the MAC of isoflurane may have changed in the foals as they aged, abdominal insufflation is a strong noxious stimulus and likely resulted in the increased isoflurane requirements during the laparoscopy, compared with the laparotomy. Despite the delivery of increased inhalant concentrations, the systemic arterial pressures were greater during laparoscopy than during laparotomy. Similar findings have been reported in mechanically ventilated, dorsally recumbent adult horses undergoing laparoscopy.[17] An increase in systemic vascular resistance because of either vasoconstriction or venous compression during the laparoscopic procedure was likely responsible for these changes because CI was either unchanged or lower during the laparoscopic procedure versus during the laparotomy. The lower CI in the D/K/Iso group during the laparoscopic procedure, compared with the laparotomy, was likely a result of the increased isoflurane concentrations; however, the CI values remained higher than in foals in the X/K/Iso group.

Overall, in this study, we determined that diazepam use prior to induction and maintenance of general anesthesia with ketamine and isoflurane resulted in improved hemodynamic stability in foals, compared with the use of xylazine, at the doses selected. When diazepam was used, improved cardiovascular function was not accompanied by any detectable adverse effects, regarding the quality of anesthetic induction, maintenance, or recovery.

a. Gamma-Check-C, Veterinary Dynamics Inc, San Luis Obispo, Calif.
b. Laparoflator, Stryker Corp, Santa Clara, Calif.
c. Sabex Inc, Boucherville, QC, Canada.
d. Ketalean, Bimeda-NTC, Cambridge, ON, Canada.
e. Isoflurane USP, Abbott Laboratories Ltd, St-Laurent, QC, Canada.
f. Rompun, Bayer Inc, Toronto, ON, Canada.
g. Long-term catheter (guidewire style), Mila International Inc, Florence, Ky.
h. NOVA 5 CRT, Nova Biomedical, Waltham, Mass.
i. OSM 3 hemoximeter, Radiometer, Copenhagen, Denmark.
j. Excenel, Pharmacia and Upjohn Inc, Orangeville, ON, Canada.
k. Cronyxin, Vetrepharm, London, ON, Canada.
l. Criticare 1100, Criticare Systems Inc, Waukesha, Wis.
m. Anesthesia calibration gas, Criticare Systems Inc, Waukesha, Wis.
n. Hallowell EMC Model 2000, Hallowell Engineering and Manufacturing Corp, Pittsfield, Mass.
o. Insyte-W, Becton-Dickinson, Sandy, Utah.
p. Lithium sensor, flow-through-cell electrode assembly, LiDCO Ltd, London, England.
q. DTX Plus DT-36 single pressure transducer, Becton-Dickinson, Sandy, Utah.
r. Cardiac 31-01 computer, LiDCO Ltd, London, England.
s. Criticare 1100, Criticare Systems Inc, Waukesha, Wis.
t. Lithium chloride injection, 0.15 mmol/mL, LiDCO Ltd, London, England.
u. ABL 500 blood gas analyzer, Radiometer A/S, Copenhagen, Denmark.
v. Torbugesic, Ayerst Laboratories, Montreal, QC, Canada.
w. SAS, SAS Institute Inc, Cary, NC.

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