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Article *in* American Journal of Veterinary Research · December 2017

DOI: 10.2460/ajvr.78.12.1359

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Effects of intravenous administration of lidocaine and buprenorphine on gastrointestinal tract motility and signs of pain in New Zealand White rabbits after ovariohysterectomy

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Received July 27, 2016.
Accepted February 16, 2017.

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OBJECTIVE
To compare analgesic and gastrointestinal effects of lidocaine and buprenorphine administered to rabbits undergoing ovariohysterectomy.

ANIMALS
Fourteen 12-month-old female New Zealand White rabbits.

PROCEDURES
Rabbits were assigned to 2 treatment groups (7 rabbits/group). One group received buprenorphine (0.06 mg/kg, IV, q 8 h for 2 days), and the other received lidocaine (continuous rate infusion [CRI] at 100 μg/kg/min for 2 days). Variables, including food and water consumption, fecal output, glucose and cortisol concentrations, and behaviors while in exercise pens, were recorded.

RESULTS
Rabbits receiving a lidocaine CRI had significantly higher gastrointestinal motility, food intake, and fecal output and significantly lower glucose concentrations, compared with results for rabbits receiving buprenorphine. Rabbits receiving lidocaine also had a higher number of normal behaviors (eg, sprawling, traveling, and frolicking) after surgery, compared with behaviors such as crouching and sitting that were seen more commonly in rabbits receiving buprenorphine. Both groups had significant weight loss after surgery. Pain scores did not differ significantly between treatment groups. Significant decreases in heart rate and respiratory rate were observed on the day of surgery, compared with values before and after surgery. Rabbits in the lidocaine group had significantly overall lower heart rates than did rabbits in the buprenorphine group.

CONCLUSIONS AND CLINICAL RELEVANCE
A CRI of lidocaine to rabbits provided better postoperative outcomes with respect to fecal output, food intake, and glucose concentrations. Thus, lidocaine appeared to be a suitable alternative to buprenorphine for alleviating postoperative pain with minimal risk of anorexia and gastrointestinal ileus. (*Am J Vet Res* 2017;78:1359–1371)

Because of a variety of physiologic, anatomic, and behavioral differences, it is challenging to select an appropriate analgesic protocol that does not cause systemic complications and adverse effects in lagomorphs.[1] Effective surgical analgesia in lagomorphs has been poorly investigated, which has forced veterinarians and researchers to rely on extrapolation of analgesic protocols used in domestic mammals. Pain assessment in rabbits is challenging because responses to noxious stimuli are often subtle and assessment of abnormal behaviors can be extremely difficult in prey species.[1] Only a few studies[2–4] on postoperative pain control in rabbits have been reported. Meloxicam, buprenorphine, fentanyl patches, and ketoprofen have been used in rabbits for postoperative analgesia after ovariohysterectomy, but with unsatisfactory results.[2–6] Additional research in the areas of pain assessment and analgesic efficacy in rabbits is needed.

Systemic administration of lidocaine has been used in both human and veterinary medicine to reduce the requirement of volatile inhalation agents, reduce intraoperative and postoperative pain, promote gastrointestinal tract motility, and reduce the release of endotoxin and inflammatory mediators.[7–10] Lidocaine provides analgesia in part by blocking sodium channels in sensory nerve fibers, thereby inhibiting the activity, amplitude, and conduction of electrical impulses.[7,8] Effects are dose dependent and occur rapidly in the fibers (unmyelinated C nerve fibers and small thinly myelinated A and δ fibers) responsible

ABBREVIATIONS
CRI Continuous rate infusion

for transmitting pain sensations.[7] It also causes suppression of spinal cord sensitization and inhibition of spinal visceromotor neurons.[7] Lidocaine also interacts with muscarinic, dopaminergic, potassium, nicotinic, and *N*-methyl-D-aspartate channels, which results in decreased postoperative pain.[11] Furthermore, lidocaine has substantial anti-inflammatory and free-radical scavenging properties that may reduce postoperative pain, and it has a direct excitatory effect on intestinal smooth muscles, which is thought to result from inhibition of the myenteric plexus.[12]

Studies[7,9,10] on the effects of lidocaine on postoperative pain in humans, rodents, canids, and equids have found decreases in recovery time and aberrant behaviors as well as hormonal changes. In humans, lidocaine decreases the sympathetic pain response to surgery. Patients who were administered lidocaine intraoperatively had a 90% decrease in postoperative pain.[13] In another study[14] of men undergoing prostatectomy, IV administration of lidocaine during and after surgery significantly decreased pain, hastened the return of intestinal motility, and decreased the hospital stay. Furthermore, in horses undergoing castration, CRI of lidocaine (100 µg/kg/min) decreased the bispectral index or level of consciousness by 95%, as determined by analysis of an electroencephalogram.[15] A study[16] of rabbits revealed that a CRI of lidocaine at 50 and 100 µg/kg/min reduced the minimum alveolar concentration of isoflurane by 12% and 21.7%, respectively. Given the relatively high LD_{50} in rabbits of 20 mg/kg as well as the potential benefits, IV administration of lidocaine might be a useful tool for alleviating postoperative pain and ileus.[17]

Buprenorphine, an oripavine derivative, acts as a partial receptor agonist with high affinity at µ-opioid receptors.[11] Buprenorphine has gained widespread popularity in laboratory animal medicine and is often used as a first-choice analgesic drug.[18] It is an analgesic commonly used to alleviate postoperative pain in rabbits because of its ease of transmucosal administration and its long half-life.[1] The dose-response curve indicates that buprenorphine has a lower ceiling effect and thus does not provide better analgesia than full µ-opioid receptor agonists and is only suitable for the treatment of mild to moderate pain.[4] A study[18] of rabbits receiving doses from 0.0075 to 0.3 mg/kg revealed that the higher doses appeared to have little effect on maximum analgesia but did increase the duration of action. Some pharmacokinetic analyses for lagomorphs have found that buprenorphine is effective for 8 to 10 hours.[18] Adverse effects of buprenorphine may include pica in rodents or gastrointestinal tract stasis, depending on the dosage.[19] In contrast to other opioids that may cause sedation, buprenorphine at analgesic dosages does not cause obvious sedation in healthy rabbits.[18] Buprenorphine has been associated with a reduction of food consumption and fecal pellet production for 24 hours after administration to rabbits undergoing ovariohysterectomy.[4] In a study[20] of rabbits with experimentally induced myoma viral infections, behavioral signs associated with pain were not alleviated with buprenorphine administered at 0.03 mg/kg every 12 hours. However, other studies[21,22,a] of rodents have revealed that, regardless of the route of administration, buprenorphine improves food and water intake and decreases changes in corticosterone concentrations and pain-related behaviors, compared with responses for control animals.

Gastrointestinal tract stasis in rabbits can be secondary to stress, dietary changes, painful stimuli, disease, or iatrogenic medication. Gastrointestinal tract stasis can become a serious medical condition if not detected, and it can lead to death if not treated appropriately.[23] The purpose of the study reported here was to compare the analgesic and adverse effects after IV administration of buprenorphine and a CRI of lidocaine to New Zealand White rabbits undergoing ovariohysterectomy. Specifically, postoperative gastrointestinal adverse effects and behavioral, physiologic, and metabolic changes were evaluated. We hypothesized that a CRI of lidocaine to rabbits, when used as a postoperative analgesic for ovariohysterectomy, would result in clinically normal surgical recovery without unwanted gastrointestinal tract adverse effects (eg, anorexia or gastrointestinal stasis), compared with results after IV administration of buprenorphine.

Materials and Methods

Animals

Fourteen healthy 12-month-old female New Zealand White rabbits (*Oryctolagus cuniculus*) were enrolled in the study. Mean ± SD body weight was 2.57 ± 0.15 kg. Rabbits were housed in stainless steel cages (1.22 × 1.52 × 1.83 m) and maintained on a light cycle of 12 hours of light and 12 hours of darkness. All rabbits were deemed healthy on the basis of results of physical examinations that included rectal temperature, heart rate, respiratory rate, and mucous membrane color and results of abdominal palpation and auscultation. All rabbits were fed a diet consisting of timothy pellets[b] and timothy hay.[c] Food and water were provided ad libitum. The study was approved by the University of Georgia Institutional Animal Care and Use Committee (No. A2013 04-020-Y1-A3).

Anesthesia and ovariohysterectomy

Rabbits were allowed to acclimate to their cages for 7 days before the start of the study. Food was not withheld from rabbits prior to anesthetic episodes. Anesthesia was induced by IM administration of ketamine hydrochloride[d] (35 mg/kg) and xylazine hydrochloride[e] (2 mg/kg). In addition, meloxicam[f] was administered (1 mg/kg, IM). Rabbits were randomly assigned (simple randomization by use of a spreadsheet application[g]) to 2 treatment groups (7 rabbits/group). Buprenorphine[h] (0.06 mg/kg, IV, q 8 h) was administered to one group, whereas lidocaine hydrochloride[i] (a bolus of 2 mg/kg administered over a

5-minute period followed by a CRI at 100 µg/kg/min administered via a syringe pump[j]) was administered to the other group. Drug administration began after anesthetic induction and continued for 48 hours after surgery. Drug dosages used in the study were determined on the basis of published recommendations.[4,12,16] To maximize the use of the rabbits, the study reported here was conducted concurrently with another study[k] conducted to compare endotracheal intubation and a supraglottic airway device. All anesthesia was performed by an experienced anesthetist (RWS), and surgical procedures were performed by veterinarians (NA, LAB, DDR, MS) in a veterinary surgical residency training program.

When a rabbit was at a good plane of anesthesia, it was placed in a sternal position with the head extended at a 45° angle and the neck hyperextended. The airway was secured with a supraglottic airway device[l] or an endotracheal tube.[m] Ophthalmic ointment[n] was applied to both eyes. Anesthesia was maintained by use of isoflurane[o] in oxygen (400 mL/kg/min) delivered via a Bain nonrebreather circuit. Settings for the isoflurane vaporizer were adjusted to maintain a surgical depth of anesthesia as determined on the basis of muscle relaxation and loss of palpebral and corneal reflexes.

A double-lumen pediatric central line catheter[p] was placed into a single jugular vein of each rabbit, and an isotonic crystalloid solution[q] was administered at a rate of 5.0 mL/kg/h. The central line catheter was sutured in place, and a bandage consisting of cast padding and an elastic wrap was applied. A 24-gauge catheter[r] was placed in a middle auricular artery. Heart rate, ECG, direct arterial blood pressure, respiratory rate, end-tidal partial pressure of CO_2, and rectal temperature were measured every 5 minutes. Body temperature was maintained at 38° to 39°C by use of a warm-water circulating blanket[s] and forced warm air blanket.[t]

In preparation for surgery, the urinary bladder was emptied by gentle manual pressure. The abdominal area was shaved and surgically prepared with chlorohexidine and alcohol. Rabbits then were transported to a surgical suite, and aseptic techniques were used throughout the procedures. Routine ovariohysterectomy was performed on each rabbit by use of a standard 2-cm ventral midline abdominal incision that began approximately 4 cm caudal to the umbilicus. Hemorrhage was controlled with a radiosurgery unit.[u] The uterus was located and exteriorized through the incision by gentle traction. Once the uterus was localized, the fat around each ovarian pedicle was carefully dissected to enable identification of the ovarian vessels; the vessels were double ligated with 3-0 polydioxanone,[v] and the ovaries were removed. Uterine vessels were ligated with transfixing ligatures applied to the cervical serosa. After ligation was completed, each uterine horn was removed cranial to the cervix. The cervical stump was oversewn in a continuous pattern to prevent abdominal urine leakage. The abdominal wall was closed in a simple interrupted pattern by use of 3-0 polydioxanone. An intradermal suture pattern with 3-0 poliglecaprone[w] was used to close the skin. Rabbits were continually monitored until they were able to swallow, the supraglottic airway device or endotracheal tube was removed, and they were able to maintain a sternal position.

When rabbits were fully conscious, they were returned to their cages. Rabbits continued to receive buprenorphine (0.06 mg/kg, IV, q 8 h) or lidocaine (CRI at 100 µg/kg/min) for 48 hours. Syringe casings were used as guards to prevent rabbits from chewing the IV fluid catheters. Crystalloid fluids were administered IV to all rabbits at a rate of 100 mL/kg/d for 48 hours. To maintain consistency, drug infusion rates were subtracted from the total amount of fluids administered. All drugs were prepared by personnel who were not responsible for data collection.

Rabbit evaluation

After rabbits were acclimated to their cages, baseline measurements were obtained. Respiratory rate was visually determined while the rabbits were in their cages. Rabbits then were removed from the cages and manually restrained, and heart rate and gastrointestinal tract sounds were evaluated via thoracic and abdominal auscultation, respectively.

Pain scores were determined for each rabbit starting 48 hours before surgery and continuing until 96 hours after surgery. Rabbits were assessed 3 times/d (between 8 AM and 9 AM, between 12 PM and 1 PM, and between 5 PM and 6 PM). On the day of surgery, additional assessments were performed at 0, 30, 60, 90, 480, and 960 minutes after the end of surgery. Abdominal palpation was also used to elicit behavioral responses to pain.[4] For each abdominal assessment, pain scores were determined by use of a scale of 0 to 2 (0 = no obvious discomfort, no withdrawal, and no vocalization; 1 = obvious discomfort or withdrawal movement but no vocalization; and 2 = obvious discomfort or withdrawal movement with vocalization).[4,24,25] General pain scores were categorized as 0 (no vocalization or teeth grinding), 1 (inconsistent vocalization or teeth grinding), or 2 (continuous vocalization or teeth grinding).[26] Signs of pain were assessed by the same investigators (RWS, JRC, and PR), who were unaware of the treatment group of each rabbit. All of these investigators were trained in assessing and interpreting pain guidelines for this species. Body weight of each rabbit was recorded after each assessment.

Fecal output, food intake, and water consumption were assessed 3 times/d starting 48 hours before surgery and continuing until 96 hours after surgery. Food and water were collected from each food tray and cage and weighed. Fecal output was evaluated through fecal output photographic scores, fecal weights, fecal pellet numbers, and qualitative assessment. All cages were cleaned and feces collected 3

times/d; collected feces was used for daily evaluation. All fecal assessments were performed by 1 investigator (RWS), who was unaware of the treatment group of each rabbit. Photographs of cage trays were used for the fecal output photographic scoring system, which was established to quantitatively and qualitatively assess fecal output. Fecal score was assigned on a scale of 0 to 4 as follows: 0 = poorly formed feces covering < 10% of the tray, 1 = a mixture of poorly formed and normally formed feces covering ≥ 10% of the tray, 2 = multiple piles of mostly normally formed but with some poorly formed densely dispersed feces covering ≥ 30% of the tray, 3 = multiple piles of normally formed feces covering ≥ 50% of the tray, and 4 = multiple piles of normally formed densely dispersed feces covering ≥ 70% of the tray.[6] Fecal scores were summed and the mean was determined for each day. Further qualitative assessment also included categorizing fecal pellets as follows: normal size and appearance of pellets (> 1 cm in diameter; smooth circular to oval form), small size (< 1 cm in diameter; a smooth circular to oval form), and normal size but abnormal appearance (> 1 cm in diameter; rough with no defined shape).

Rabbit behaviors were recorded in a separate room by use of a video camera.[x] Video recording of behavioral data was performed 3 times/d (12 min/recording session) starting 48 hours before surgery and continuing until 96 hours after surgery. Each rabbit was placed in an exercise pen along with a handful of hay, a jingle ball, a water bowl, and a plastic rabbit hut.[y] Rabbit behavior was videotaped so that it could be assessed without the physical presence of an evaluator, and entry into the room was prohibited during the recording period. The first 2 minutes of each video recording was discarded (period that allowed the rabbits to become accustomed to the pen and room). Behaviors were then categorized every 30 seconds for 10 minutes. Behaviors consisted of sitting (sitting fully balanced on all 4 limbs), sprawling (reclining in sternal or half-lateral recumbency with hind limbs, forelimbs, or both extended horizontally), traveling (moving a distance within the pen), foraging (sniffing, rummaging, or eating food), grooming (using paws or mouth to groom any part of the body), exploring (looking at or sniffing the ground when food was not near the animal or taking a single step forward without ambulation), rearing (standing on hind limbs), frolicking (hopping or jumping rapidly and flinging hind limbs to 1 side), crouching (immobile with abdomen tucked in), and drinking (consuming water).[6] All behaviors were accessed by investigators who were not aware of the treatment group for each rabbit.

Blood glucose and cortisol concentrations were measured 24 hours before surgery, at the start of surgery, at the end of surgery, and then every 12 hours after surgery for 96 hours. Blood samples (1 mL) were collected from a saphenous vein by use of a 22-gauge, 0.625-inch needle attached to a 3- or 5-mL syringe. Alternatively, a sample was collected from the jugular

Table 1—Mean ± SD values for physiologic variables in healthy New Zealand White rabbits (n = 6/group) undergoing ovariohysterectomy (day 0 was the day of surgery) that received lidocaine (bolus of 2 mg/kg administered over a 5-minute period followed by CRI at 100 µg/kg/min) or buprenorphine (0.06 mg/kg, IV, q 8 h) beginning during surgery and continuing for 2 days after surgery.

	Day −2			Day −1			Day 0				Day 1			Day 2			Day 3			Day 4		
Variable	AM	Noon	PM	AM	Noon	PM	0 min	30 min	60 min	90 min	480 min	960 min	AM	Noon	PM	AM	Noon	PM	AM	Noon	PM	AM	Noon	PM
Lidocaine group																								
Heart rate (beats/min)	191 ± 19	194 ± 25	191 ± 30	214 ± 23	206 ± 13	203 ± 17	178 ± 30	166 ± 18	171 ± 23	163 ± 23	163 ± 35	173 ± 26	184 ± 69	193 ± 72	197 ± 69	183 ± 21	171 ± 38	204 ± 20	203 ± 18	190 ± 25	199 ± 29	193 ± 42	188 ± 29	201 ± 50
Respiratory rate (breaths/min)	127 ± 32	126 ± 45	143 ± 28	151 ± 42	137 ± 29	146 ± 34	77 ± 34	69 ± 21	76 ± 34	75 ± 17	90 ± 24	97 ± 17	116 ± 27	109 ± 19	111 ± 20	130 ± 41	114 ± 20	126 ± 31	147 ± 27	137 ± 27	143 ± 31	108 ± 17	128 ± 22	145 ± 21
Body weight (kg)	2.53 ± 0.15	2.48 ± 0.14	2.50 ± 0.18	2.49 ± 17	2.45 ± 18	2.47 ± 15	2.46 ± 16	ND	ND	ND	ND	ND	2.47 ± 15	2.45 ± 13	2.41 ± 12	2.42 ± 12	242 ± 10	2.38 ± 10	2.35 ± 18	2.37 ± 15	2.38 ± 15	2.38 ± 14	2.37 ± 14	2.47 ± 15
Food intake (g)	0 ± 0	38 ± 27	38 ± 12	77 ± 30	41 ± 18	44 ± 9	40 ± 11	ND	ND	ND	ND	ND	42 ± 19	49 ± 16	41 ± 14	61 ± 24	47 ± 13	47 ± 16	53 ± 21	48 ± 16	50 ± 16	106 ± 55	37 ± 12	46 ± 9
Water intake (g)	0 ± 0	56 ± 30	64 ± 20	124 ± 72	91 ± 108	54 ± 19	25 ± 13	ND	ND	ND	ND	ND	18 ± 17	23 ± 18	23 ± 12	89 ± 72	62 ± 29	39 ± 9	172 ± 84	116 ± 118	78 ± 70	196 ± 126	48 ± 30	60 ± 16
Buprenorphine group																								
Heart rate (beats/min)	221 ± 41	200 ± 36	213 ± 15	196 ± 29	213 ± 21	216 ± 19	177 ± 13	181 ± 17	178 ± 18	171 ± 20	187 ± 15	207 ± 38	210 ± 33	209 ± 15	199 ± 42	207 ± 30	211 ± 38	200 ± 28	205 ± 23	202 ± 26	205 ± 30	213 ± 27	197 ± 26	213 ± 27
Respiratory rate (breaths/min)	143 ± 39	126 ± 28	154 ± 28	154 ± 30	131 ± 31	121 ± 23	47 ± 4	47 ± 11	51 ± 25	56 ± 20	75 ± 24	101 ± 45	110 ± 51	119 ± 35	120 ± 38	111 ± 22	120 ± 27	113 ± 34	820 ± 27	810 ± 44	760 ± 27	800 ± 30	800 ± 30	680 ± 15
Body weight (kg)	2.62 ± 0.17	2.59 ± 0.19	2.61 ± 0.16	2.62 ± 0.18	2.59 ± 0.17	2.58 ± 0.18	2.57 ± 0.16	ND	ND	ND	ND	ND	2.56 ± 0.15	2.53 ± 0.17	2.52 ± 0.16	2.48 ± 0.18	2.47 ± 0.19	2.48 ± 0.21	2.47 ± 0.23	2.44 ± 0.20	2.45 ± 0.23	2.42 ± 0.15	ND	ND
Food intake (g)	0 ± 0	52 ± 23	77 ± 46	132 ± 45	42 ± 24	88 ± 51	67 ± 32	ND	ND	ND	ND	ND	15 ± 7	18 ± 9	22 ± 9	42 ± 27	42 ± 39	18 ± 11	56 ± 34	45 ± 11	41 ± 30	48 ± 10	ND	ND
Water intake (g)	0 ± 0	50 ± 29	86 ± 55	204 ± 64	69 ± 77	46 ± 28	50 ± 24	ND	ND	ND	ND	ND	48 ± 45	25 ± 14	55 ± 60	85 ± 52	90 ± 109	41 ± 24	144 ± 77	55 ± 35	76 ± 31	80 ± 40	ND	ND

Rabbits were assessed 3 times/d (between 8 AM and 9 AM, between 12 PM and 1 PM [Noon], and between 5 PM and 6 PM).
ND = Not determined.

vein catheter (3 mL of blood was discarded, and a 4-mL blood sample was then obtained). Blood samples were placed into heparinized tubes.[z] Immediately after blood samples were collected, glucose concentrations were measured by use of a handheld biamperometric glucometer[aa] and a benchtop glucose analyzer.[bb] Plasma cortisol concentrations were determined by use of a competitive radioimmunoassay.[cc]

Any rabbit that had a mean pain score of 2, failed to defecate within an 8-hour period, or had weight loss of 10% was removed from the study. A rescue protocol consisted of administration of oxymorphone[dd] (0.2 mg/kg, IM, q 4 h) and assisted feeding of a critical care formula[ee] (30 mL/kg, 2 to 4 times/d) until the rabbits would eat on their own.

Statistical analysis

Outcome variables were assessed over time by use of linear mixed models with day, time points within day, treatment, surgery, and interactions as fixed effects and rabbit as random effects.

To assess statistical associations, linear mixed models were used with fecal production and other fecal variables, food intake, water consumption, physiologic variables, and clinical pathological variables as outcome variables; time (day and hour nested within day), treatment, surgery, and interaction effects as fixed explanatory variables; and rabbit as a random effect. Residual plots were used to assess linearity, homogeneity of variances, normality, and outliers. Quantile plots of the residuals by treatment group were used for assessment of normality. Autocorrelation of the residuals over time was assessed by use of the autocorrelation function method. The data satisfied model assumptions. A type III ANOVA was performed on the fixed effects, and post hoc comparisons were performed by use of a Tukey adjustment. Binary data were analyzed with logit mixed models. Scoring data were analyzed by use of ordinal logit mixed models, with score as the outcome ordinal categorical variable; time, treatment, and interactions as fixed variables; and rabbit as a random variable. Residuals were evaluated on graphs. Values of $P < 0.05$ were considered significant. A statistical computing program[ff] was used for all analyses.

Results

Two rabbits (1 from each group) were excluded from the study because of complications with the jugular vein catheter. Thus, results were reported for 6 rabbits/group.

Significant changes were detected in heart rate and respiratory rate of both groups over time. Heart and respiratory rates were significantly ($P < 0.001$) lower on the day of surgery, compared with rates on the days before and after surgery. Heart and respiratory rates did not change over the time periods within a day. During surgery, a significant ($P < 0.001$) decrease in heart and respiratory rates was detected for both groups. The group receiving lidocaine had a significantly ($P = 0.012$) lower heart rate overall (by a mean ± SD of 13 ± 4.4 beats/min) over time. There was not a significant ($P = 0.34$) difference in respiratory rates between the 2 treatment groups. Mean ± SD time from injection to induction of anesthesia was 6.2 ± 1.4 minutes.

For general pain scores, there was no vocalization at any time point. There was no association between signs of pain elicited by palpation and any other observed variables for the rabbits **(Table 1)**.

Surgery significantly ($P < 0.001$) increased plasma cortisol and blood glucose concentrations. Cortisol and glucose concentrations were significantly higher on the day of surgery than on other days. Treatment group did not significantly ($P = 0.2$) affect cortisol concentration; however, blood glucose concentration measured with the benchtop glucose analyzer was significantly ($P < 0.001$) lower for the lidocaine group (by a mean ± SD of 28 mg/dL). The same pattern was evident for the glucose concentration measured with the handheld glucometer, except that there was not a significant ($P = 0.09$) effect of treatment **(Table 2)**.

Body weight decreased significantly ($P < 0.001$) for both groups after surgery and reached the nadir at the end of the study period. However, there was not a significant effect of surgery ($P = 0.37$) or analgesic treatment ($P = 0.31$) on body weight. Body weight did not change throughout each day. Water intake was significantly ($P < 0.001$) decreased for 2 days after surgery, compared with intake before surgery. Within each day, food and water intake were significantly higher in the morning, except for the day after surgery when rabbits consumed more food and water in the evening. Analgesic treatment did not have a significant effect on water consumption over time. Food intake for the buprenorphine group decreased significantly ($P < 0.001$) after surgery (decreased by

Table 2—Mean ± SD values for cortisol and glucose concentrations in healthy New Zealand White rabbits (n = 6/group) undergoing ovariohysterectomy that received lidocaine or buprenorphine beginning during surgery and continuing for 2 days after surgery.

			Day 0		Day 1		Day 2		Day 3		Day 4	
Treatment	Variable	Day –1	Start of surgery	End of surgery	AM	PM	AM	PM	AM	PM	AM	PM
Lidocaine	Cortisol (µg/dL)	0.9 ± 0.8	1.2 ± 1.0	4.3 ± 2.1	1.7 ± 0.9	1.4 ± 1.4	1.1 ± 0.3	1.0 ± 0.4	0.6 ± 0.5	1.0 ± 0.5	0.6 ± 0.5	0.9 ± 0.6
	Glucose (mg/dL)											
	Handheld glucometer	135 ± 14	145 ± 14	201 ± 20	135 ± 9	133 ± 17	151 ± 14	151 ± 13	149 ± 11	145 ± 12	143 ± 6	143 ± 16
	Tabletop analyzer	140 ± 9	178 ± 47	240 ± 27	117 ± 18	124 ± 4	140 ± 6	151 ± 6	140 ± 6	132 ± 12	127 ± 13	137 ± 16
Buprenorphine	Cortisol (µg/dL)	0.8 ± 0.5	1.2 ± 0.8	5.0 ± 1.9	1.7 ± 0.6	2.2 ± 1.2	2.1 ± 1.3	1.4 ± 1.1	0.9 ± 0.6	1.4 ± 1.6	0.8 ± 0.3	0.7 ± 0.4
	Glucose (mg/dL)											
	Handheld glucometer	140 ± 10	188 ± 31	298 ± 30	137 ± 21	157 ± 33	175 ± 31	175 ± 53	164 ± 16	164 ± 17	174 ± 19	160 ± 15
	Tabletop analyzer	140 ± 8	199 ± 19	282 ± 28	125 ± 17	144 ± 38	162 ± 48	160 ± 52	142 ± 12	143 ± 11	145 ± 13	139 ± 9

approx 58%; mean ± SD food consumption was 65.4 ± 7.3 g before surgery and 38.2 ± 3.5 g after surgery). Food intake did not differ significantly ($P = 0.9$) for the lidocaine group. The decrease in food intake for the buprenorphine group was most marked the day after surgery. Overall, food intake was higher for the lidocaine group than the buprenorphine group after surgery (42.1 ± 5.9 g and 29.5 ± 4.5 g, respectively; Table 1).

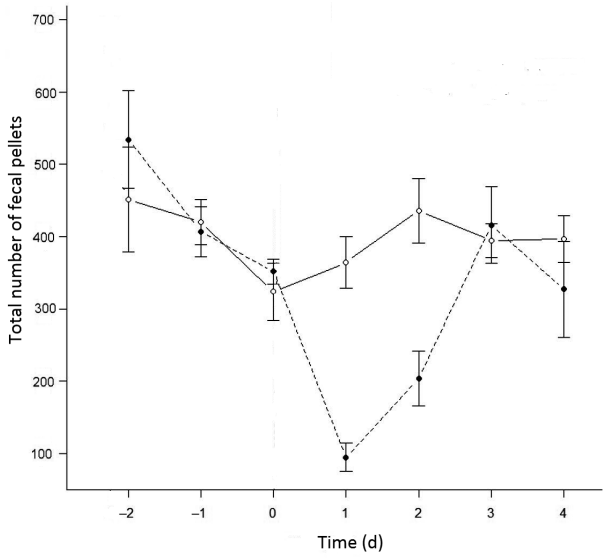

Figure 1—Mean ± SEM total number of fecal pellets for rabbits (n = 6/group) from 2 days before ovariohysterectomy until 4 days after surgery (day 0 was the day of surgery). Rabbits received lidocaine (bolus of 2 mg/kg administered over a 5-minute period followed by CRI at 100 µg/kg/min [white circles]) or buprenorphine (0.06 mg/kg, IV, q 8 h[black circles]) beginning during surgery and continuing for 2 days after surgery. Overall, total number of fecal pellets during the 2 days after surgery was significantly ($P < 0.001$) lower for the buprenorphine treatment than for the lidocaine treatment.

The daily total number and total weight of fecal pellets during the 2 days after surgery was significantly lower for the group receiving buprenorphine, compared with results for the group receiving lidocaine. By the third day after surgery, fecal output was similar between the 2 groups. There was also an overall significant decrease in fecal output after surgery that did not return to preoperative values during the study period **(Figure 1)**. There was a significant ($P = 0.002$) increase in the proportion of abnormal fecal pellets after surgery, compared with the proportion before surgery, with no differences detected between treatment groups. There was also a significant increase in the proportion of small fecal pellets for 3 days after surgery. The group receiving buprenorphine had a significantly ($P < 0.001$) higher proportion of small fecal pellets than did the group receiving lidocaine on the second day after surgery. The buprenorphine group was significantly less likely to have higher fecal scores over time (OR = 0.004; $P < 0.001$) than was the lidocaine group **(Table 3)**.

The buprenorphine group was more likely to have higher scores for sitting (OR = 4.7; $P < 0.001$; **Figure 2**) and crouching (OR = 42.9; $P < 0.001$) after surgery than was the lidocaine group; however, the buprenorphine group was less likely to have higher scores for sprawling (OR = 0.38; $P = 0.037$), foraging (OR = 0.33; $P < 0.001$; **Figure 3**), and frolicking (OR = 0.50; $P = 0.012$; **Figure 4**) after surgery than was the lidocaine group. The likelihood of having higher

Table 3—Mean ± SD values for fecal output for healthy New Zealand White rabbits (n = 6/group) undergoing ovariohysterectomy that received lidocaine or buprenorphine beginning during surgery and continuing for 2 days after surgery.

				Day 0					
Treatment	Variable	Day –2	Day –1	Before surgery	After surgery	Day 1	Day 2	Day 3	Day 4
Lidocaine	No. of normal fecal pellets	409 ± 82	426 ± 189	630 ± 116	317 ± 104	276 ± 77	360 ± 128	311 ± 40	353 ± 73
	No. of small fecal pellets	4 ± 5	10 ± 15	11 ± 18	3 ± 5	51 ± 38	43 ± 26	53 ± 62	22 ± 32
	No. of abnormal fecal pellets	6 ± 7	14 ± 10	16 ± 13	3 ± 3	32 ± 23	32 ± 19	33 ± 13	22 ± 22
	Total No. of fecal pellets	420 ± 82	451 ± 192	657 ± 117	324 ± 104	364 ± 95	436 ± 117	394 ± 57	397 ± 72
	Fecal score	3 ± 1	3 ± 1	4 ± 0	3 ± 1	3 ± 1	3 ± 0	3 ± 1	3 ± 1
	Fecal weight (g)	136 ± 39	146 ± 56	201 ± 74	85 ± 28	93 ± 35	110 ± 36	101 ± 37	93 ± 6
Buprenorphine	No. of normal fecal pellets	420 ± 52	533 ± 151	536 ± 165	335 ± 40	48 ± 40	131 ± 78	106 ± 100	91 ± 106
	No. of small fecal pellets	4 ± 9	3 ± 7	3 ± 8	1 ± 2	37 ± 27	57 ± 37	71 ± 76	45 ± 52
	No. of abnormal fecal pellets	12 ± 9	12 ± 12	13 ± 9	15 ± 10	10 ± 10	15 ± 8	37 ± 35	35 ± 47
	Total No. of fecal pellets	407 ± 92	534 ± 179	553 ± 162	351 ± 46	95 ± 51	204 ± 102	416 ± 130	327 ± 163
	Fecal score	4 ± 0	4 ± 0	4 ± 0	3 ± 1	1 ± 1	1 ± 1	2 ± 1	2 ± 1
	Fecal weight (g)	149 ± 39	200 ± 55	201 ± 84	117 ± 43	13 ± 11	31 ± 19	72 ± 23	75 ± 45

Rabbits were assessed 3 times/d; values were summed for each day. Fecal pellets were classified as having normal size and appearance (> 1 cm in diameter; smooth circular to oval form), small size (< 1 cm in diameter; smooth circular to oval form), or normal size but abnormal appearance (> 1 cm in diameter; rough with no defined shape). Fecal score was assigned on a scale of 0 to 4 as follows: 0 = poorly formed feces covering < 10% of the tray, 1 = a mixture of poorly formed and normally formed feces covering ≥ 10% of the tray, 2 = multiple piles of mostly normally formed but with some poorly formed densely dispersed feces covering ≥ 30% of the tray, 3 = multiple piles of normally formed feces covering ≥ 50% of the tray, and 4 = multiple piles of normally formed densely dispersed feces covering ≥ 70% of the tray.

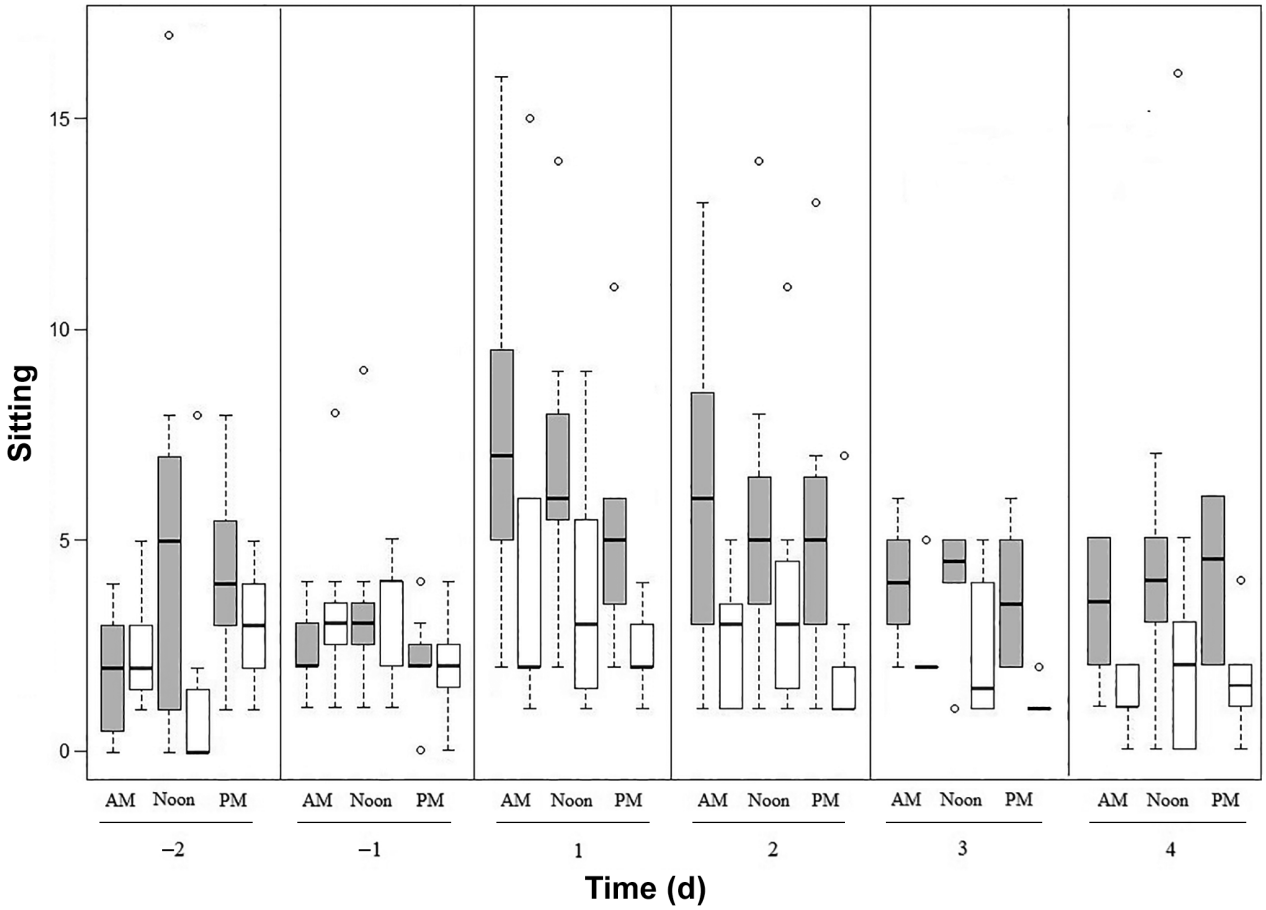

Figure 2—Box-and-whisker plots of sitting behavior of rabbits (n = 6/group) from 2 days before ovariohysterectomy until 4 days after surgery. Rabbits received a CRI of lidocaine (white boxes) or buprenorphine administered IV (gray boxes) beginning during surgery and for 2 days after surgery. Rabbits were assessed 3 times/d (between 8 AM and 9 AM, between 12 PM and 1 PM [Noon], and between 5 PM and 6 PM). Sitting was defined as sitting fully balanced on all 4 limbs; value reported is the number of behaviors counted every 30 seconds for 10 minutes. Each box represents the interquartile range, the horizontal line in each box represents the median, the whiskers represent the minimum and maximum, and the circles represent outliers. Overall, sitting scores were significantly (OR, 4.7; $P < 0.001$) higher for the buprenorphine treatment than for the lidocaine treatment.

scores for traveling (OR = 0.63; $P = 0.067$), grooming (OR = 1.27; $P = 0.54$), exploring (OR = 0.83: $P = 0.49$), rearing (OR = 1.17; $P = 0.68$), and drinking (OR = 0.84; $P = 0.69$) did not differ significantly between treatments after surgery. Crouching and grooming scores increased significantly ($P = 0.01$ and $P < 0.001$, respectively) over time after surgery, regardless of treatment **(Figure 5)**. Similarly, scores for frolicking, exploring, and traveling decreased significantly ($P < 0.001$) over time after surgery, regardless of treatment.

Discussion

Surgery, such as ovariohysterectomy, induces physiologic stress responses that result in neural and endocrine alterations.[27] Tissue injury during and after surgery stimulates the activation of nociceptors.[28] Untreated pain can lead to activation of the complement cascade, cytokine systems, arachidonic acid cascade, and sympathetic nervous system.[28] Activation of the sympathetic nervous system may result in tachycardia, arrhythmias, vasoconstriction, altered cardiac output, and increased myocardial oxygen demand and can also lead to gastrointestinal ileus.[28] Providing preemptive analgesia may reduce the nervous system response to noxious input as well as reduce postoperative pain and requirements for analgesic drugs.[29] Gastrointestinal tract stasis in lagomorphs can become a life-threatening condition if not detected and treated promptly.[30] Ileus frequently occurs as a response to environmental stress, dietary changes, disease, and pain.[30] Rapid medical intervention through analgesia is crucial to alleviate this condition when it is secondary to pain.[30]

Currently, few adequate behavioral variables have been developed for assessment of rabbits. Healthy rabbits usually are bright, alert, active, and extremely inquisitive.[1,31] However, animals that are anxious or scared will become immobile and hide their typical behaviors, making it extremely challenging to perform an assessment.[31] Furthermore, large variations in behavior can occur because of individual differences, which can

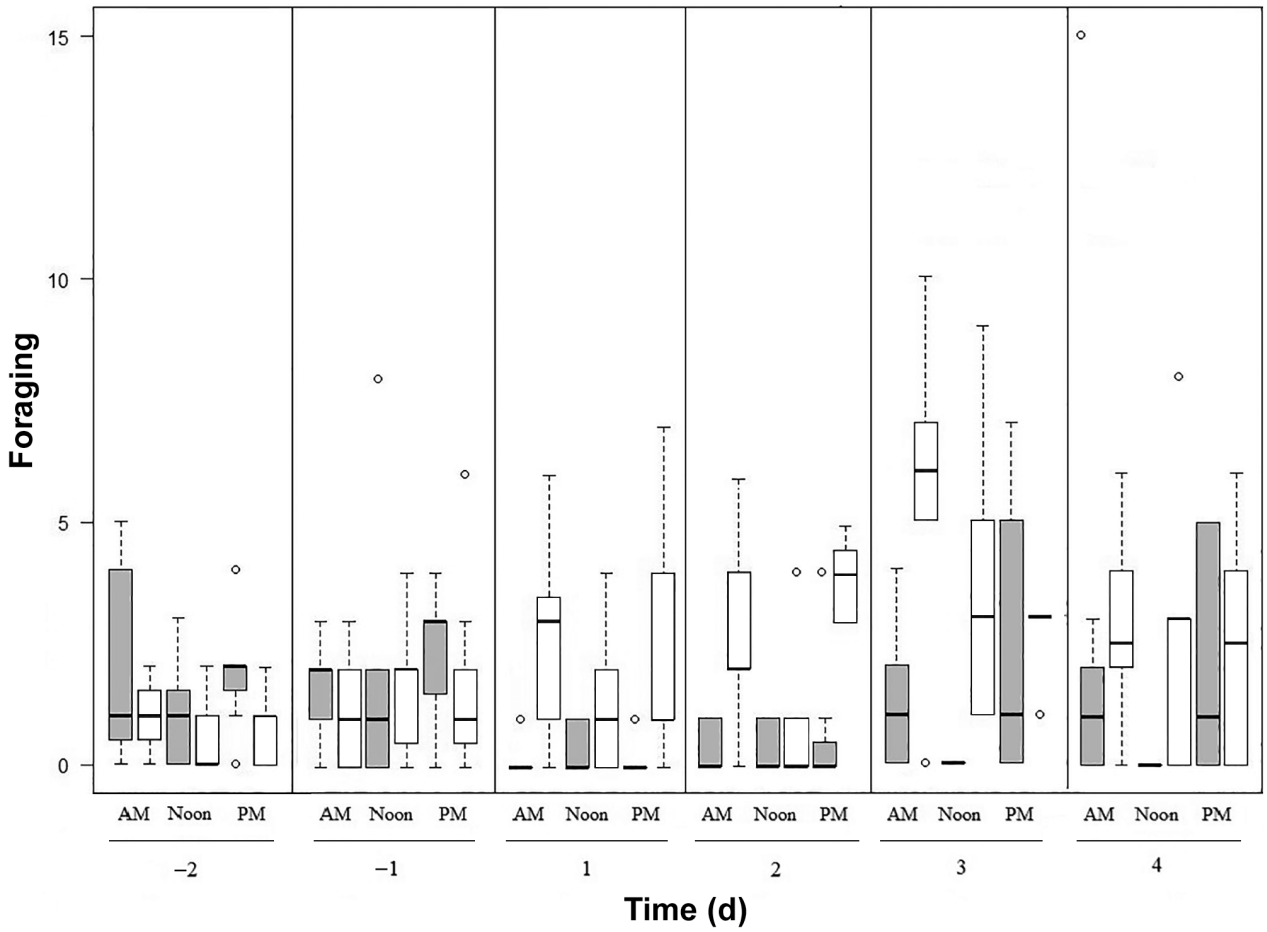

Figure 3—Box-and-whisker plots of foraging behavior of rabbits (n = 6/group) from 2 days before ovariohysterectomy until 4 days after surgery. Rabbits received a CRI of lidocaine (white boxes) or buprenorphine administered IV (gray boxes) beginning during surgery and for 2 days after surgery. Foraging was defined as sniffing, rummaging, or eating food; value reported is the number of behaviors counted every 30 seconds for 10 minutes. Overall, foraging scores were significantly (OR, 0.33; $P < 0.001$) lower for the buprenorphine treatment than for the lidocaine treatment. ***See*** Figure 2 for remainder of key.

make it hard to perform and interpret behavioral pain studies. To ensure rabbits displayed normal behavior, it was important that they were in an environment in which they believed they were safe and where external contact was limited. In the study reported here, rabbits were monitored externally with the use of a video camera, and the first 2 minutes of the video recordings were not assessed to allow each animal to become accustomed to the exercise pen and room. Analgesia studies[1,2,4] of laboratory medicine animals have revealed that changes in posture, locomotion, or gait may be indicators of pain. Rabbits receiving buprenorphine had higher odds of behavior consisting of a decrease in motion (eg, sitting and crouching), whereas rabbits receiving lidocaine had an increase in behaviors that were involved with movement (eg, traveling and frolicking). Rabbits treated with lidocaine had a higher prevalence of sprawling, which could have been associated with relaxation. The prevalence of behaviors associated with motion and relaxation was higher during the first 48 hours after surgery when the rabbits were receiving a CRI of lidocaine. No differences were detected in behaviors of traveling, grooming, exploring, rearing, and drinking between groups or between preoperative and postoperative observations. Crouching and grooming behaviors increased whereas frolicking, exploring, and traveling behaviors decreased in both groups during the postoperative period. Grooming behaviors may have been falsely increased after surgery because some of the rabbits became fixated on the bandage surrounding the central venous catheter. No differences in behaviors were observed over the course of a day; however, patterns were evident over the course of several days. These results differ from those of another postoperative study[6] in which rabbits were less active in the morning than in the afternoon. Decreases in overall activity and changes in specific behaviors related to stress were consistent with results of other studies[2,4] that have associated these responses with pain stimuli in rabbits. A study[2] conducted to evaluate meloxicam and buprenorphine revealed that inactive behaviors were reliable indicators of signs of pain. Although a decrease in postoperative activity (frolicking, foraging, exploring, and traveling) was evi-

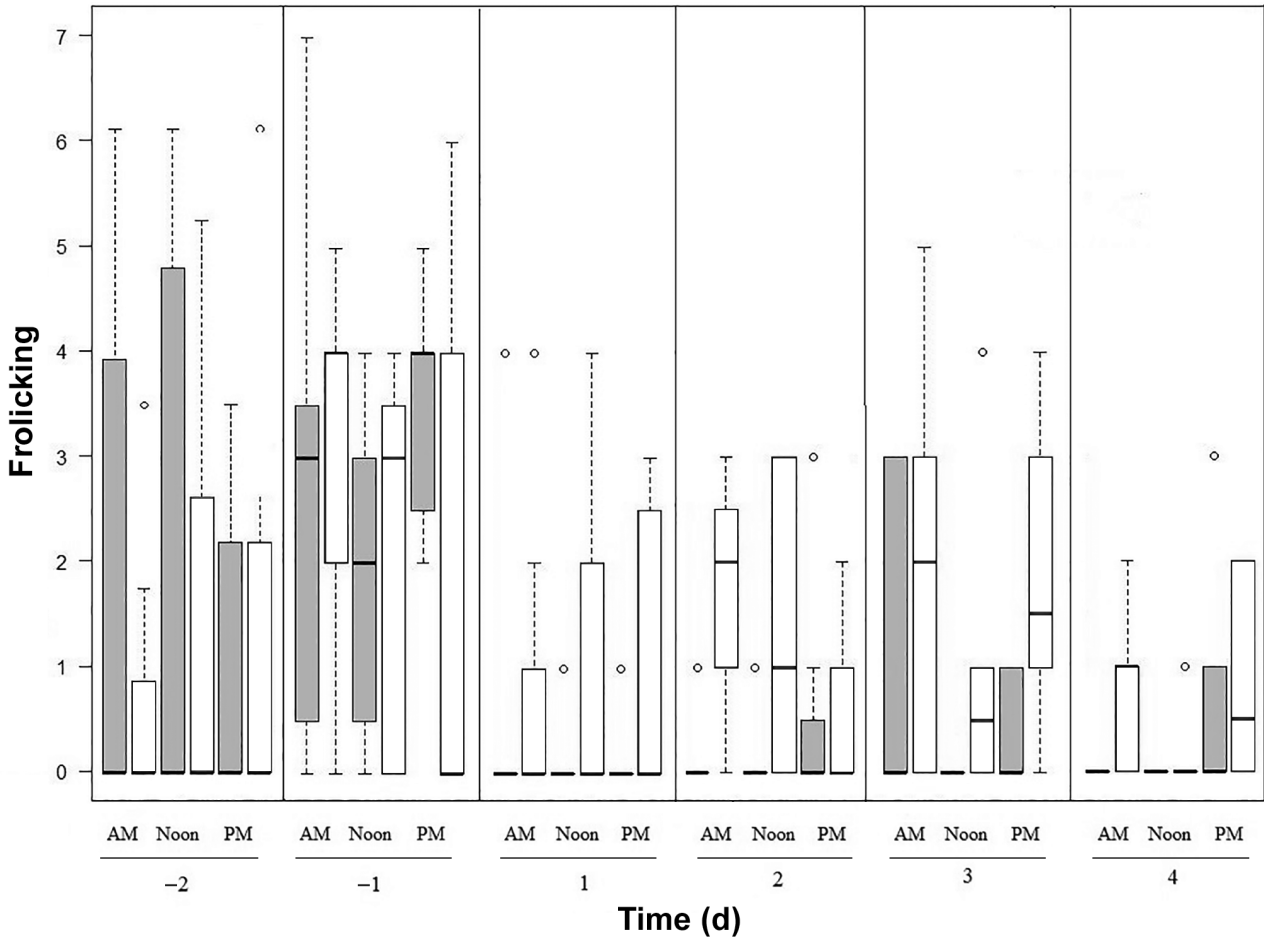

Figure 4—Box-and-whisker plots of frolicking behavior of rabbits (n = 6/group) from 2 days before ovariohysterectomy until 4 days after surgery. Rabbits received a CRI of lidocaine (white boxes) or buprenorphine administered IV (gray boxes) beginning during surgery and for 2 days after surgery. Frolicking was defined as hopping or jumping rapidly and flinging the hind limbs to 1 side; value reported is the number of behaviors counted every 30 seconds for 10 minutes. Overall, frolicking scores were significantly (OR, 0.50; $P = 0.012$) lower for the buprenorphine treatment than for the lidocaine treatment. ***See*** Figure 2 for remainder of key.

dent for both groups of the present study, the lidocaine group was less affected than the buprenorphine group, which suggested that a lidocaine CRI might provide better analgesia. Although efforts were made to ensure consistency of the methods, factors other than pain (eg, analgesic adverse effects, possible unobserved sedation, repeated handling, and sample collections) may have influenced behavioral changes.

Changes in heart and respiratory rates may be consistent with pain, but they also can be caused by a variety of other factors.[27] Heart rate and respiratory rate are under multifaceted physiologic influences and may be altered,[27] as was observed for both groups on the day of surgery compared with before and after surgery. Changes observed in the present study were most likely a result of the anesthetic drugs, volatile inhalation agent, and analgesic agents used.[29] Although buprenorphine and lidocaine can cause bradycardia, lidocaine is an antiarrhythmic drug that decreases heart rate by blocking sodium channels, which decreases the rate of heart contractions.[11] Although a significantly lower heart rate was detected for the lidocaine group, the overall heart rate of the lidocaine group was only 13 beats/min lower than the heart rate of the buprenorphine group, and all measurements remained within reference limits. No differences in respiratory rate were detected between the 2 groups. Heart rate and respiratory rate were constant over time for both groups. Although time was allowed before surgery for the rabbits to become accustomed to their surroundings, it is unlikely that the rabbits were fully acclimated. Stress may have caused similar changes in heart rate and respiratory rates for both groups, which thus reduced the usefulness of these physiologic variables as indicators of pain in the study reported here. More sophisticated techniques for evaluation of heart rate and respiratory rate may be needed to enable use of these variables to assess pain in rabbits.

The pain scoring system used in the present study was based on systems previously published for analgesic studies[6] of rabbits and small animals. No

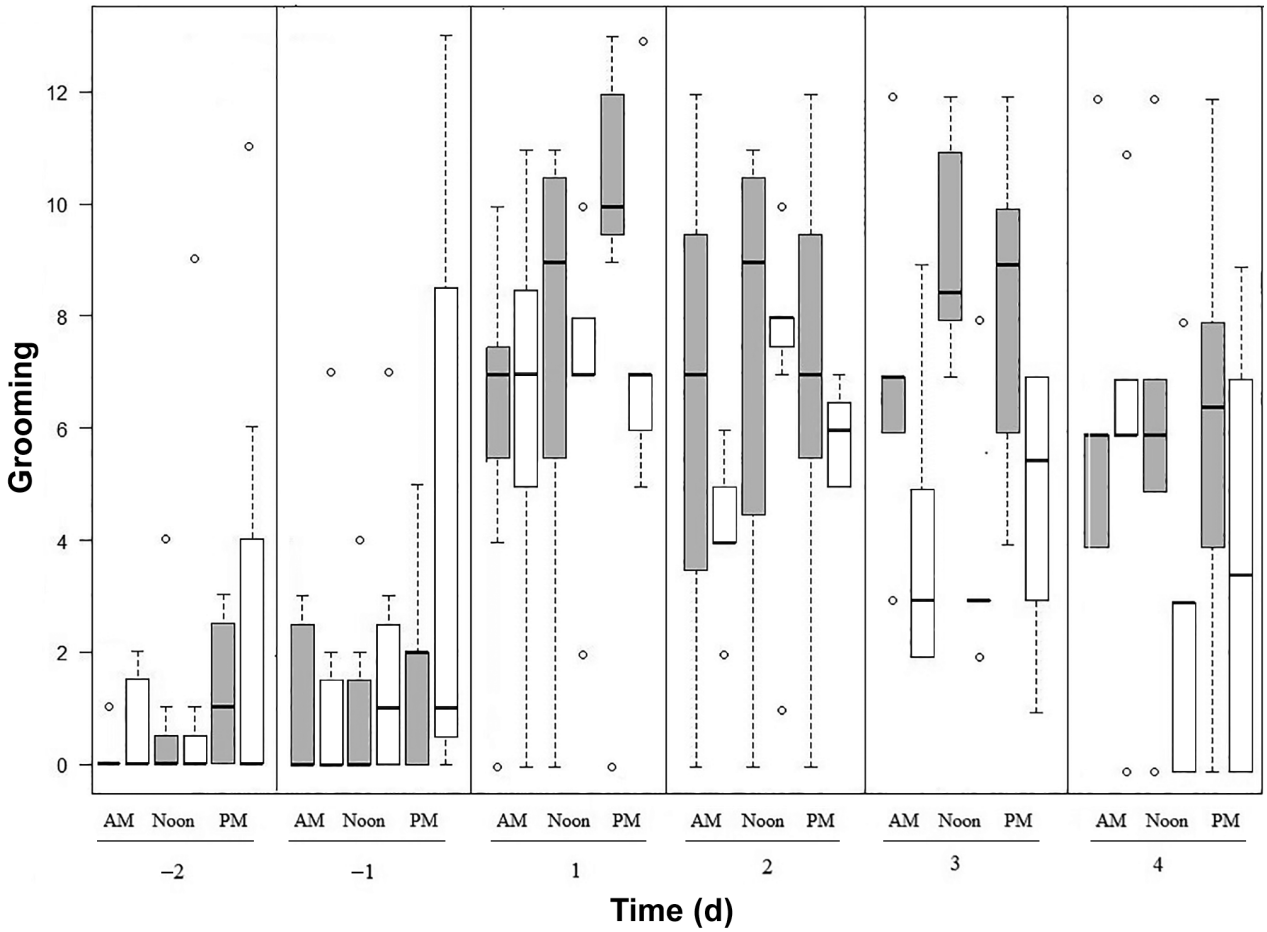

Figure 5—Box-and-whisker plots of grooming behavior of rabbits (n = 6/group) from 2 days before ovariohysterectomy until 4 days after surgery. Rabbits received a CRI of lidocaine (white boxes) or buprenorphine administered IV (gray boxes) beginning during surgery and for 2 days after surgery. Grooming was defined as using the paws or mouth to groom any part of the body; value reported is the number of behaviors counted every 30 seconds for 10 minutes. Grooming scores increased significantly ($P < 0.001$) over time after surgery, regardless of treatment. ***See*** Figure 2 for remainder of key.

differences in pain scores between groups were detected. There was no vocalization at any time point and no association between results for abdominal palpation and any other variables. It was possible that both buprenorphine and lidocaine had similar analgesic effects or that the rabbits instinctively hid their signs of pain and responses were not recognized. Additionally, the analgesic properties of meloxicam given to all rabbits before surgery could have had an overriding effect on pain responses.

Investigators have found that animals with signs of pain after surgery will frequently reduce food and water intake.[6,21,32] This reduction in intake as well as the visceral and generalized pain are major contributing factors to gastrointestinal tract stasis. Clinical signs associated with ileus include decreased or absent fecal output, change in fecal morphology, weight loss, and a decrease in gastrointestinal tract motility.[30] Significant weight loss of rabbits was detected during the present study. The lowest body weight was at the end of the study period; there was not a significant effect of surgery or analgesic treatment on body weight. The amount of weight loss was not of clinical concern (mean loss of 80 g for the lidocaine group and 110 g for the buprenorphine group after surgery) and could have been attributable to stress, change of environment, or insufficient acclimation time. Body weight did not change significantly throughout each day. Food and water intake also decreased over time, with significant decreases after surgery, compared with intakes before surgery. These findings were consistent with findings for another study[6] in which investigators compared effects of meloxicam, buprenorphine, fentanyl, and ketoprofen after ovariohysterectomy and found that food and water consumption were reduced for 2 to 7 days after surgery. Within each day, food and water intake were significantly higher in the morning, except for the day after surgery when rabbits consumed more food and water in the evening. These differences could have been attributable to the crepuscular nature of lagomorphs or the study design, given that the last time point for each day was between 5 PM and 6 PM; thus, the rabbits had more time to drink water and consume the diet before the first assessment the next morning. The increase in food and water consumption in the evening

of the first day after surgery could have been attributable to the earlier painful stimuli or to the sedative effects of anesthesia. Because there were differences in the intervals for recovery, sedation, and the duration of surgery, food and water intake were not recorded on the day of surgery to retain consistency among the rabbits. Although there was a decrease in consumption over time, compared with consumption on the day after surgery, a significant increase in food intake after surgery was detected for the lidocaine group. This increase in consumption, compared with that for the buprenorphine group, indicated possible analgesic or prokinetic properties of lidocaine in rabbits. No differences in water consumption were detected between groups. All rabbits in the study received fluids IV at maintenance rates beginning on the day of surgery until 48 hours after surgery, and it is unknown how the IV administration of these fluids affected water consumption.

Decreased production or alteration in fecal consistency can be an important sign of serious gastrointestinal ileus.[30] The buprenorphine group had a lower likelihood of having higher photographic fecal scores over time, compared with results for the lidocaine group. Additionally, a substantial decrease in the daily total number and weight of fecal pellets and an increase in the amount of smaller pellets were evident for the buprenorphine group after surgery, compared with results for the lidocaine group. However, an overall decrease in fecal output after surgery was evident for both groups, with output not returning to preoperative amounts during the study period. There were also similar increases in abnormal-appearing fecal pellets after surgery for both groups. These results could have been attributable to the decrease in food intake after surgery, effects of surgical noxious stimuli, or effects of anesthesia. In the study reported here, lidocaine CRI had a more positive contribution to normal fecal output than did buprenorphine, which could have been a result of the analgesic effects of lidocaine or its intestinal prokinetic effects.

However, it should be mentioned that a control group was not included; therefore, it could not be ascertained whether buprenorphine decreased or lidocaine increased fecal output. In equids, lidocaine is commonly administered IV after colic surgery.[12] Studies[12,33–35] of horses have revealed that lidocaine decreases the duration and severity of postoperative ileus, decreases signs of gastrointestinal tract pain, and improves survival times. These effects are postulated to be attributable to a combination of direct excitatory effects on intestinal smooth muscle, blockade of inhibitory spinal and peritoneal sympathetic reflexes, and anti-inflammatory and antiendotoxin actions.[34,35] Another explanation for the decrease in fecal output in the buprenorphine group relative to the lidocaine group was that, similar to other opioids, buprenorphine may have led to gastrointestinal tract dysfunction. Although adverse effects are limited because of a ceiling effect, buprenorphine reduces gastric emptying and intestinal peristalsis by directly acting on μ-opioid receptors in the myenteric plexus of the intestinal tract.[36]

Further confirmation of a possible benefit of lidocaine was detected 3 days after surgery, when both drugs were discontinued and fecal output and fecal architecture became comparatively similar (Figures 1 and 2). Studies[1,4,6] of analgesia in rabbits have revealed a similar decrease in fecal production a few days after surgery. Multiple surgical factors and reduction in postsurgical food and water intake play important roles in the decrease in fecal output. Similar results were evident when effects of meloxicam, buprenorphine, ketoprofen, and fentanyl were compared.[1,4,6] To our knowledge, the study reported here was the first in which a significant difference was detected between treatment groups and there were beneficial (or less detrimental) effects of lidocaine over buprenorphine for gastrointestinal tract function in rabbits.

Several studies have been conducted to evaluate acute cortisol and glucose responses as a method of determining the extent and duration of distress associated with painful stimuli in large and small animals.[28,37,38] Pain is a potent stressor and may induce excess stimulation of the hypothalamic-pituitary-adrenal axis, which causes increases in blood concentrations of cortisol and glucose.[29] In the study reported here, surgery significantly increased plasma cortisol and blood glucose concentrations overall. Concentrations of cortisol and glucose were significantly higher the day of surgery, compared with concentrations on other days. No significant differences in cortisol concentrations were detected between the lidocaine and buprenorphine groups; however, without a control group, it could not be determined whether both treatments had an effect on cortisol concentrations. Blood glucose concentrations were significantly lower for the lidocaine group (mean of 28 mg/dL lower), compared with concentrations for the buprenorphine group, with similar glucose concentrations between the handheld glucometer and benchtop glucose analyzer. Anesthesia, handling, and other stressors can cause transient but nonsustained increases in both glucose and cortisol concentrations.[39] Although we could not account for all variables, efforts were made to ensure similar, consistent methods between both groups. Thus, the lower glucose values for the lidocaine group may have been clinically important.

All rabbits tolerated both drug treatments well. Throughout the study, no rabbits met the criteria for the rescue protocol, which suggested that both drugs provided sufficient analgesia or that the criteria were not sensitive enough to differentiate signs of substantial pain. Because no pain scale is 100% sensitive, the goal of surgical analgesia should be to anticipate pain on the basis of previous experience and scientific knowledge and ultimately prevent it.[40] Minor differences in surgical procedures could have caused dif-

ferences in the amount of pain of each rabbit. To reduce effects of these factors, equally skilled surgeons performed the surgeries, and gentle tissue handling, a standard length of incision, and standard surgical techniques were used.

The magnitude of sedation or inactivity induced by administration of buprenorphine or lidocaine to rabbits is unknown and should be considered a factor when evaluating pain and therapeutic efficacy. Both drugs can cause deep sedation in other species, but abnormal mentation may affect results. Additionally, pain perception of individual animals for identical stimuli may differ each time the stimulus is applied.

Few studies have been conducted to investigate the pharmacodynamics of meloxicam in rabbits. In 1 study,[4] meloxicam (0.2 mg/kg, SC, q 24 h for 48 hours after surgery) had results similar to those for buprenorphine (0.03 mg/kg, IM, q 12 h for 48 hours after surgery). All rabbits in that study[4] had a decrease in food consumption, fecal production, and body weight, which indicated that meloxicam was comparable to buprenorphine with regard to postoperative effects. However, pharmacokinetic data have indicated that rabbits need a high dose of meloxicam because of their high drug metabolism. A dose of 1 mg of meloxicam/kg results in drug concentrations comparable to those associated with adequate analgesia for 24 hours in humans.[41] The effects of meloxicam on rabbits in the present study were not known; however, on the basis of pharmacokinetic data for rabbits, it appears that meloxicam is rapidly eliminated.

A major limitation of the present study was the lack of a control group. Although inclusion of a control group would have been ideal in a research setting, a group of rabbits in which pain was induced without any form of analgesic control was not considered appropriate for ethical reasons. It is unknown how results for a control group would have differed from results for the 2 groups in the study.

Another limitation of the present study was the sample size. Because of logistics, time, expense, and the use of animals in a pain control or analgesic study, the sample size of each group was limited. Additional studies with larger sample sizes might be needed to confirm results of the study reported here.

In the present study, a number of behaviors were evident as potential indicators of pain in rabbits after ovariohysterectomy. Other variables such as body weight, food consumption, and fecal output were also used to measure analgesic effectiveness. Results of this study were comparable to results of other published postoperative buprenorphine trials of lagomorphs; however, to our knowledge, this was the first study in which surgical and postoperative analgesic effects of lidocaine were documented in this species. Administration of a CRI of lidocaine at the dose and rate used in this study may be a useful adjunct for a more balanced anesthetic and analgesic regimen in rabbits. Lidocaine is a useful analgesic because of its multiple locations of action and its positive effects on gastrointestinal tract motility and fecal output. In the study reported here, lidocaine CRI appeared to result in better analgesia than for buprenorphine alone; however, further studies should be conducted with combinations of lidocaine and buprenorphine because such combinations could potentially result in an even better analgesic response.

Acknowledgments

Supported in part by Docsinnovent Company and Oxbow Animal Health Company.

Presented as an abstract at the 2nd Biennial International Conference on Avian Herpetological and Exotic Mammal Medicine, Paris, April 2015.

The authors thank Lynn Reece, Lisa Reno, and Ethan Karstedt for technical assistance and Michal Kohles for technical consultation.

Footnotes

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b. Timothy hay pellets, Oxbow Animal Health, Murdock, Neb.
c. Timothy hay, Oxbow Animal Health, Murdock, Neb.
d. Ketaset, 100 mg/mL, Fort Dodge Animal Health, Fort Dodge, Iowa.
e. TranquiVed, 20 mg/mL, VEDCO, St Joseph, Mo.
f. Loxicam, 5 mg/mL, Norbook, Overland Park, Kan.
g. Microsoft Excel 2010, Microsoft, Redmond, Wash.
h. Buprenex, 0.3 mg/mL, Hospira, Lake Forest, Ill.
i. Lidocaine hydrochloride, 20 mg/mL, Hospira, Lake Forest, Ill.
j. Medfusion 2010i syringe pump, Medex Co, Duluth, Ga.
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l. V-gel size R4, Docs Innovent Rusch, Teleflex Medical, Kernen, Germany.
m. 3.5-mm cuffed endotracheal tube, Rusch, Teleflex Medical, Kernen, Germany.
n. Puralube vet ointment, Western Medical Supply, Arcadia, Calif.
o. Piramal Critical Care Inc, Bethlehem, Pa.
p. 4F 13-cm 0.018-inch-diameter catheter, Arrow International Inc, Reading, Pa.
q. LRS, Abbott Laboratories, North Chicago, Ill.
r. Baxter Healthcare Corp, Irvine, Calif.
s. Baxter K 100 heat therapy pump, Baxter Healthcare Corp, Deerfield, Ill.
t. Bair Hugger, Arizant Healthcare Inc, Saint Paul, Minn.
u. Ellman Surgitron 4.0 dual RF/120 IEC electrosurgical unit, Ellman Inc, Hicksville, NY.
v. 3-0 PDS, WEBMAX, Patterson Veterinary, Devens, Mass.
w. 3-0 Monocryl, Maxon, Covidien, Mansfield, Mass.
x. Sony Handycam HDR-CX405 camcorder, Sony, San Diego, Calif.
y. Large igloo hide-out, Kaytee Products, Chilton, Wis.
z. BD Microtainer tubes, Becton Dickinson Company, Franklin Lakes, NJ.
aa. AlphaTRAK, Abbott Laboratories, Abbott Park, Ill.
bb. Olympus AU640e, Olympus America Inc, Center Valley, Pa.
cc. Siemens Immulite 100, cortisol assay kit No. LKC01, Siemens Healthcare Diagnostics, Malvern, Pa.
dd. OPANA, oxymorphone hydrochloride (1 mg/mL), Endo Pharmaceuticals Inc, Greenville, NC.
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