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A single injection of high-concentration buprenorphine significantly reduces food and water intake as well as fecal and urine production in New Zealand White rabbits (*Oryctolagus cuniculus*)

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OBJECTIVE
To evaluate selected gastrointestinal side effects of high-concentration buprenorphine (HCB) in healthy rabbits.

ANIMALS
10 healthy New Zealand White rabbits ranging in body weight between 3.0 and 3.8 kg.

METHODS
Eight, 6-month-old, New Zealand White rabbits received a single injection of HCB SC (0.24 mg/kg). The rabbits were previously randomized to receive SC and oral saline as a control. Two rabbits received saline for the purpose of blinding the outcome assessors. Food and water consumption, fecal and urine production, and fecal pellet number were recorded for all rabbits before HCB administration and the 3 days postinjection.

RESULTS
A clinically and statistically significant decrease in food and water consumption was observed in rabbits receiving an injection of HCB, compared to rabbits receiving saline. In the 24 hours after injection, HCB-treated rabbits consumed a median of 17 g of food (range, 0 to 82 g), while saline-treated rabbits consumed 122 g of food (31 to 181 g). Rabbits receiving HCB injections also produced significantly less feces both in terms of pellet numbers and overall quantity, along with decreased urine production.

CLINICAL RELEVANCE
A single administration of HCB has a clinically significant impact on multiple physiological functions in healthy rabbits. Administration of this drug could potentially worsen clinical signs of anorexia and decrease defecation in healthy rabbits. The effects of HCB on diseased or painful rabbits are not yet known.

Keywords: New Zealand White rabbit, Simbadol, high-concentration buprenorphine, hypomotility, *Oryctolagus cuniculus*

Buprenorphine hydrochloride is a semisynthetic opioid and a partial agonist at the mu receptor.[1] Buprenorphine has been successfully used in both pre- and postoperative analgesia and sedation in the dog and cat with limited side effects such as less vomiting and dysphoria, as compared to other opioid medications.[2–7] It is also gaining popularity in exotic animal medicine, often a common choice for pain control in species such as rabbits.[8] Studies[9–11] have shown various degrees of effectiveness of buprenorphine as a sedative and analgesic for rabbits perioperatively. Although it is an effective analgesic for use in rabbits, buprenorphine does have negative side effects on the gastrointestinal motility of lagomorphs.[9–12] Several formulations of buprenorphine are currently commercially available, including high-concentration buprenorphine (HCB), buprenorphine hydrochloride, and sustained-release buprenorphine.

Opioids reduce gastrointestinal motility.[1,13] Several previous studies[9–12] have suggested that

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the use of buprenorphine postoperatively in rabbits causes severe weight loss, decreased fecal production, and decreased food consumption when compared to rabbits treated with other analgesics such as meloxicam or lidocaine. While the initial effects of buprenorphine tend to be more severe than other nonopioid analgesics, these effects tend to be transient and they are considered sufficiently mild to continue its use for postoperative pain management.[9–12]

A commercially available HCB (Simbadol; Zoetis) is FDA licensed for use in cats. This formulation of buprenorphine is approved for 24 hours of pain relief postoperatively in cats. Although limited, some research[14,15] has been performed investigating its effectiveness in other species. One study[16] performed in rabbits comparing buprenorphine hydrochloride, sustained-release buprenorphine, and HCB suggested that all 3 formulations cause decreased food consumption, weight loss, and decreased fecal pellet production as compared to the control group. These clinical side effects appear to be transient, improving over the 3-day study. The same study[16] also suggests that HCB maintains therapeutic concentrations for up to 14 hours post-SC injection. Another study[17] investigated the pharmacokinetics of HCB and determined that 3 consecutive SC doses of HCB (0.24 mg/kg) every 24 hours had variable accumulation of both buprenorphine and its metabolites. This led to a large variability in terminal half-life.

Building on the limited research on the impact of HCB on basic rabbit physiological parameters, the objective of this study was to determine the potential beneficial or adverse effect of HCB on selected physiological parameters (fecal output, food intake, urine production, and water consumption). We hypothesized that HCB could have a detrimental effect on these select physiological parameters of rabbits.

Methods

Animals

Ten, 6-month-old, intact male, purpose-bred, New Zealand White rabbits (*Oryctolagus cuniculus*) were used. The animals were deemed healthy based on physical exam, hematology, biochemistry, and coagulation assessment results. Body weight ranged between 3.0 and 3.8 kg (mean, 3.4 kg). One animal was known to be bilaterally cryptorchid and another animal had evidence of previous barbering. These animals were previously used for other studies investigating the effect of analgesics and prokinetic drugs and as part of a coagulation study (data not shown). A 1-week washout period intercurred between the studies.

Animals were housed individually in stainless steel cages (KM.CO; Shor-line) with perforated floors that allowed for collection of feces in a tray. Rabbits were fed a standard laboratory rabbit pelleted diet (5321-Laboratory Rabbit Diet; LabDiet, Lank O' Lakes Inc). No hay was provided. Water was provided in 2 glass bottles. Plastic toys hanging from the cage were provided for enrichment for each animal. Animals were kept on a 12-hour light:12-hour dark photoperiod at a set room temperature of 67 °F (19.4 °C) with a humidity range of 30% to 70%. All the rabbits were monitored daily by the outcome assessors. In addition, a licensed veterinarian (JB) visually assessed every rabbit at least once a day. Any concern or abnormal behavior of the animal was reported by the outcome assessor to the veterinarian. There were no specific stopping rules in place in case of anorexia in otherwise normally active rabbits. If the caregivers or the veterinarian were concerned about the clinical conditions of a specific rabbit (eg, in case of lethargy, other systemic illness), they had the option to provide veterinary care to the rabbit. Prior to any procedure, the study was approved by the Oklahoma State University Institutional Animal Care and Use Committee (VM-19-9).

Experimental procedures

Study design—This study was an add-on to a randomized complete crossover trial for which results are described elsewhere.[18,19] During the original randomized complete crossover trial, 10 rabbits were included in the study and lived in the conditions described above for 10 weeks. During these weeks, each animal received once per week a single administration of SC saline, oral saline, or 1 of 8 other treatments. The order of these treatments was randomized for each animal. The results of those treatments have been previously reported.[18,19]

On week 11, 8 animals received SC HCB injection (0.24 mg/kg SC) and 2 were administered SC saline of equal volume.[16] Each one of the 8 rabbits that was administered HCB on week 11 received oral and SC saline in 1 of the earlier 10 weeks and served as their own control in the analysis. Administration of the SC saline to the 2 rabbits during week 11 was uniquely intended to maintain blinding of the operators (caregivers and outcome assessors). Results from the 2 rabbits that received SC saline during week 11 were not included in any of the analyses. Outcome data collection is described in detail below and was identical during each one of the 11 weeks.

Administration of HCB—A caregiver, blinded to the content of the injection, administered the HCB and saline injections. Medications were drawn by a third party who was not present for the treatment administration or the following assessment of the rabbits. An assessor, also blinded to the injection received by the rabbit, collected the data on the days following the treatment as detailed below.

Data collection

Data collection was identical during the entire duration of the study. On the day of treatment (day 0), each animal received a complete physical exam including body weight by the assessors. The enclosure was cleaned and preweighted urinary incontinence pads (Medline Ultrabsorbs Premiun Underpads [Medline Industries] and Disposable Underpads McKesson Classic 23 X 36 Inch Fluff Mat

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Light Absorbency [McKesson Corp]) were placed in a tray underneath the cage. A total of 800 g of pelleted diet was provided. Two water bottles were made available, and the water weight (g) added to each bottle was recorded. The animals were left undisturbed for approximately 24 hours.

Two assessors recorded fecal pellet, cecotroph, and urine output as well as food pellet and water consumption at time 0 and at 24, 48, and 72 hours postinjection. Fecal pellet and cecotroph quantifications were performed separately. Total fecal weight and number of fecal pellets as well as the number and weight of cecotrophes produced over a 24-hour period were recorded. The presence of urine was also recorded, and urine production was indirectly measured by subtracting the weight of urine pad (day 1) from the weight of the same pad the day prior (day 0). Water consumption was determined by subtracting the total weight offered initially (day 0) and remaining water weight 24 hours later (day 1). Cages were prepared for the following 24 hours. Fecal and urine output, water consumption, and food consumption were measured as previously described at 24, 48, and 72 hours after initial drug administration. At the conclusion of this study, the animals were transferred to another study.

Statistical analysis

Continuous variables were reported as median, 25 to 75 percentiles, and range. Generalized linear mixed models were built to explore the effect of HCB compared to placebo on each of the 5 outcomes [food consumed (g), water consumed (mL), fecal production (g), fecal production (number of pellets), and urine production (g)], accounting for paired rabbit analyses. The treatment variable included 1 set of observations for each rabbit after administration of HCB (treatment group) and 2 sets of observations for each rabbit after administration of saline, oral, and injectable (control group). For each outcome, treatment, time, and the interaction between treatment and time were included as fixed effects, and rabbit ID was included as a random effect. The random effect block included the intercept and used the variance component as the random effect covariance type. Results of generalized linear mixed models were reported as estimated marginal means. The Bonferroni correction was applied to the results. Considering a standard statistical significance (alpha) of 0.05, and considering 5 primary outcomes, statistical significance was set at $P < .01$ (alpha/5 = 0.05/5). Analysis was performed with commercial software (SPSS Statistics V.24.0; IBM).

Results

A summary of all the outcomes stratified by treatment administered is reported **(Table 1)**.

Food intake

On day 0, there was no significant difference in food intake when rabbits received different treatments **(Table 2)**. Compared to day 0, on days 1, 2, and 3 postinitial injection, rabbits that received HCB

Table 1—Summary statistics (median values, percentiles, and ranges) of physiological parameters (food consumed, water consumed, fecal volume and quantity, and urine production) in 8 New Zealand White rabbits before and 24, 48, and 72 hours after administration of either high-concentration buprenorphine (HCB) or saline.

	HCB			Saline		
Parameter/time (h)	**Median**	**25 and 75 percentiles**	**Range**	**Median**	**25 and 75 percentiles**	**Range**
Food consumed (g)						
0	121.95	96.85– 142.75	81.4–147	119.65	102.9–138.95	62.1–153.7
24	16.75	0.4–71.45	0–81.5	122.4	106.95–143.8	31.4–180.8
48	46.25	1.4–94.3	0–131.7	123.5	101.85–146.75	63.6–166.5
72	84.75	22.95–101.9	0.7–137.4	128.95	109.65–144.3	95–158.5
Water consumed (mL)						
0	275.05	202.65–335.85	100.3–360.6	247.55	224.2–329.15	185.4–409.2
24	48.55	35.1–55.75	10.6–124.1	310.25	245.85–369.85	123.6–434.8
48	94.5	31.3–158.15	11.1–209.7	263.1	208.5–337.8	176.6–523.1
72	146	67.15–215	27.3–245	288.5	246.3–338.75	128.5–480.8
Fecal production (g)						
0	64.65	21.4–88.75	18.5–98.1	63.85	50.5–81.6	40.4–110.6
24	7.4	2.45–35.95	1.6–46.7	65.6	51.35–91	8.6–117.6
48	19.4	10.4–47.45	2–57.5	69.9	43.8–94.95	11.6–116.7
72	32.75	4.65–52.55	1.8–82.8	68.1	58.35–102.4	45.1–113.4
Fecal pellets (number)						
0	217	188–248	150–269	212	179- 233	92–328
24	59	21–151	7–288	215	186–271	67–352
48	140	19–226	7–279	211	187–280	12–340
72	161	36–225	3–315	239	210–261	161–356
Urine production (mL)						
0	169	141.1–232.3	24.7–248.9	150.3	125.17–203.6	60.6–234.2
24	1.3	0.9–41.95	0.7–73.6	171.55	135.91–204.35	5–270.9
48	81.85	33.5–98.1	0.9–110.4	155.85	122.57–178.55	77.1–340.4
72	81.85	33.55–98.1	0.9–110.4	172	129.71–200.85	70.7–274.4

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Table 2—Results of the generalized linear mixed model including 8 New Zealand White rabbits administered HCB or saline and monitored before and up to 72 hours after treatment.

Model term	Coefficient	95% CI		*P* value
Intercept	118.9	95.8	142.1	< .001*
Baseline				
HCB	Ref			
Control	−0.3	−25.7	25	.979
Time (HCB)				
Time 0	Ref			
24 h	−86.6	−115.9	−57.3	< .001*
48 h	−67	−96.3	−37.7	< .001*
72 h	−49.3	−78.5	−20	.001*
HCB vs control				
HCB vs control at 24 h	89.5	53.7	125.4	< .001*
HCB vs control at 48 h	70.1	70.1	34.2	< .001*
HCB vs control at 72 h	58.7	22.8	94.5	.002*

Food intake (g) was included as dependent variable; treatment (buprenorphine/saline), time, and their interaction as fixed effects; and individual rabbit as random effect. The referent categories for the interaction terms are not shown. The coefficient is the expected change resulting from a change in that term, while the other terms in the model are held constant.

*P < .01, statistical significance.

had a significant decrease in food intake of 87, 67, and 49 g, respectively. Compared to HCB, the same rabbits administered saline ate on average 90 g more food on day 1, 70 g more food on day 2, and 59 g more food on day 3.

Water intake

On day 0, there was no significant difference in water intake when rabbits received different treatments **(Table 3)**. Compared to day 0, on days 1, 2, and 3 rabbits that received HCB had a significant decrease in water intake of 209, 162, and 120 mL, respectively. Compared to HCB, the same rabbits administered saline drank on average 234 mL more on day 1, 175 mL more on day 2, and 145 mL more on day 3.

Fecal production

On day 0, there was no significant difference in fecal production when rabbits received different treatments **(Table 4)**. Compared to day 0, on days 1 and 2 rabbits that received HCB had a significant decrease in fecal production of 41 and 32 g, respectively. Compared to HCB, the same rabbits administered saline defecated on average 43 g more on day 1.

Number of feces

On day 0, there was no significant difference in number of feces produced when rabbits received different treatments **(Table 5)**. Compared to day 0, on day 1 rabbits that received HCB had a significant decrease in the number of feces of 121 fecal pellets. Compared to HCB, the same rabbits administered saline defecated on average 137 more pellets on day 1.

Table 3—Results of the generalized linear mixed model including 8 New Zealand White rabbits administered HCB or saline and monitored before and up to 72 hours after treatment.

Model term	Coefficient	95% CI		*P* value
Intercept	261	201.3	320.7	< .001*
Baseline				
HCB	Ref			
Control	13.5	−41.7	68.8	.629
Time (HCB)				
Time 0	Ref			
24 h	−209.3	−273	−145.6	< .001*
48 h	−162.4	−226.1	−98.7	< .001*
72 h	−119.9	−183.6	−56.3	< .001*
HCB vs control				
HCB vs control at 24 h	233.8	155.8	311.8	< .001*
HCB vs control at 48 h	175	97	253	< .001*
HCB vs control at 72 h	144.6	144.6	66.6	< .001*

Water intake (g) was included as dependent variable; treatment, time, and their interaction as fixed effects; and individual rabbit as random effect.

See Table 2 for remainder of key.

Table 4—Results of the generalized linear mixed model including 8 New Zealand White rabbits administered HCB or saline and monitored before and up to 72 h after treatment.

Model term	Coefficient	95% CI		*P* value
Intercept	58.3	39.8	76.8	< .001*
Baseline				
HCB	Ref			
Control	9.6	−9.6	28.7	.322
Time (HCB)				
Time 0	Ref			
24 h	−40.8	−62.9	−18.7	< .001*
48 h	−31.5	−53.6	−9.4	.006*
72 h	−25.2	−47.3	−3.1	.026
HCB vs control				
HCB vs control at 24 h	43.4	16.3	70.5	.002*
HCB vs control at 48 h	33.2	6.1	60.2	.017
HCB vs control at 72 h	32.7	5.6	59.8	.019

Fecal production (g) was included as dependent variable; treatment, time, and their interaction as fixed effects; and individual rabbit as random effect.

See Table 2 for remainder of key.

Urine production

On day 0, there was no significant difference in urine production when rabbits received different treatments **(Table 6)**. Compared to day 0, on days 1, 2, and 3 rabbits that received HCB had a significant decrease in urine production of 150, 103, and 103 mL, respectively. Compared to HCB, the same rabbits administered saline urinated on average 160 mL more on day 1, 111 mL more on day 2, and 114 mL more on day 3.

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Table 5—Results of the generalized linear mixed model including 8 New Zealand White rabbits administered HCB or saline and monitored before and up to 72 hours after treatment.

Model term	Coefficient	95% CI		*P* value
Intercept	125.4	161.6	269.1	< .001*
Baseline				
HCB	Ref			
Control	−8.2	−72.7	56.3	.802
Time (HCB)				
Time 0	Ref			
24 h	−121	−195.5	−46.5	.002*
48 h	−83.5	−158	−9	.029
72 h	−70.3	−144.8	4.3	.064
HCB vs control				
HCB vs control at 24 h	136.8	45.5	228	.004*
HCB vs control at 48 h	91.7	0.4	182.9	.049
HCB vs control at 72 h	108.7	17.4	199.9	.02

Fecal production (number of fecal balls) was included as dependent variable; treatment, time, and their interaction as fixed effects; and individual rabbit as random effect.

See Table 2 for remainder of key.

Table 6—Results of the generalized linear mixed model including 8 New Zealand White rabbits administered HCB or saline and monitored before and up to 72 hours after treatment.

Model term	Coefficient	95% CI		*P* value
Intercept	169.8	128.4	211.2	< .001*
Baseline				
HCB	Ref			
Control	−13.3	−52.6	26	0.502
Time (HCB)				
Time 0	Ref			
24 h	−149.5	−194.9	−104.1	< .001*
48 h	−102.5	−147.9	−57.1	< .001*
72 h	−102.5	−147.9	−57.1	< .001*
HCB vs control				
HCB vs control at 24 h	159.7	104.1	215.4	< .001*
HCB vs control at 48 h	110.8	55.2	166.4	< .001*
HCB vs control at 72 h	114.4	58.8	170	< .001*

Urine production (grams) was included as dependent variable; treatment, time, and their interaction as fixed effects; and individual rabbit as random effect.

See Table 2 for remainder of key.

Discussion

This study investigated the effects of HCB on selected physiological parameters in New Zealand White rabbits. Extralabel drug use was performed with owner consent and complied with provisions of AMDUCA and 21 CFR §530. Our results show that HCB causes a significant decrease in food and water intake compared to baseline. It also caused a significant decrease in fecal and urine production as compared to control rabbits. These results are consistent with previous studies[9–12,16] that have shown decreased gastrointestinal motility in rabbits who received buprenorphine and HCB.

The exact physiology of opioid effects on the gastrointestinal tract is still being investigated. Opioids act on the central and peripheral nervous systems to exert both analgesic and gastrointestinal effects. Opioids bind to mu, kappa, and delta receptors.[13,20] These receptors are found throughout the gastrointestinal tract, typically concentrating in the enteric neurons, interstitial cells of Cajal, and immune cells.[21] The interstitial cells of Cajal are important to the pace making of gastrointestinal contractions and often contain all 3 opioid receptors, although this is species specific.[21,22] Binding of opioids to these receptors causes a decrease in tonic and segment contraction as well as impaired peristalsis.[23] Receptors located in enteric neurons inhibit acetylcholine release subsequently slowing intestinal motility.[21,23] Despite being a partial mu agonist, buprenorphine has been shown to decrease fecal production and slow gastrointestinal transit times in rabbits.[11–13] The HCB used in this study caused similar gastrointestinal side effects in rabbits. Based on these findings, it is suspected that HCB has similar effects at the mu receptor to buprenorphine.

Studies evaluating buprenorphine's partial antagonistic effects on kappa and delta receptors in the gastrointestinal tract are lacking. A study[24] in humans comparing morphine and buprenorphine epidurals showed that buprenorphine had less gastrointestinal side effects than morphine. Buprenorphine has been suggested to be dosed at a range between 0.02 and 0.1 mg/kg in rabbits.[11] Most studies[9–12] used between 0.04 and 0.06 mg/kg of buprenorphine and found significant effects on gastrointestinal motility. One study[25] evaluating the gastrointestinal function using barium contrast radiography showed that a single high dose of buprenorphine (0.1 mg/kg) did not have significant effects on pyloric and duodenal contractions nor did it increase the time needed for fecal pellets to reach the pelvis. While increasing doses of full mu agonists correlate to more severe gastrointestinal signs, buprenorphine has been shown to exhibit a ceiling effect at higher doses.[26,27] A study in rats performed by Cowan et al[27] suggested that buprenorphine dosed between 0.1 and 1 mg/kg progressively decreased gastrointestinal transit times. Doses between 10 and 30 mg/kg did not have a significant difference in gastrointestinal transit times compared to control values. Higher doses of HCB may show a similar ceiling effect, although the present study evaluated a singular dose. The selected dose of 0.24 mg/kg SCly has been used in prior studies[16,17] that also assessed pharmacokinetic effects. Results showed pharmacokinetic variability as well as variability of accumulation of both parent drug and metabolites.[16,17] Continued research at varied dose ranges should be pursued.

In a study done by Andrews et al,[16] 2 of the 7 rabbits in the HCB group were noted to have neurologic

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side effects after injection. One rabbit made a complete recovery while the other was euthanized due to worsening and severity of neurologic disease. The euthanized rabbit was reported to have had a previous seizure before injection of HCB. None of the 8 rabbits in this study showed any clinical signs of neurologic disease either before, or after, injection of HCB during the morning physical exam of the study. While a complete neurologic exam was not performed, the neurologic signs described by Andrews et al were severe and persistent and likely would have been noted during a daily exam. Future studies may consider regular, complete neurologic exams to better explore this potential side effect.

In addition to gastrointestinal effects, opioids have been shown to cause decreased urinary output.[27,28] Rats and cats given buprenorphine injections experienced suppressed urine output.[27,28] In a study[32] in cats, those given higher doses of buprenorphine were shown to have the lowest urine output. Urinalysis completed on these cats was within normal parameters. It is important to note that these studies[27,28,32] did not objectively measure urine via urinary catheterization. Studies describing urine output in rabbits receiving buprenorphine are lacking. Cooper et al[10] subjectively measured urinary output in rabbits receiving buprenorphine and noted that the rabbits continued to urinate while given injectable buprenorphine, although they did not quantify or statistically verify these findings. Like cats, urinalysis findings in rabbits receiving high HCB did not note any significant change.[17,28]

Opioids have also been shown to cause urinary retention.[27,31–35] Mu-receptor agonists inhibit bladder afferents at the dorsal horn causing a decreased sensation of fullness.[33] Opioids can also cause decreased detrusor muscle contraction due to their effects on the parasympathetic nervous system.[33,34] Reports in both human and veterinary studies[34–36] have demonstrated the use of morphine can cause urinary retention when given IV or as an epidural. Buprenorphine has been shown to cause urinary retention in humans after oral dosing.[33] Rabbits in the current study showed both decreased water intake and urinary output based on the weights of urinary pads. HCB might have caused a physiologic change leading to decreased water consumption and subsequently decreased output. Further physiologic investigation into buprenorphine's effect on whether urinary retention played a role cannot be determined at this time.

Studies have shown decreased water intake postopioid administration. Studies[29,30] done in rats suggest that opioids decrease overall water intake in a dose-dependent manner. Rats anesthetized with gas anesthesia with subsequent injections of buprenorphine showed decreased water intake as compared to opioid-free anesthesia and single-injection buprenorphine administration.[29] Changes in activity level and circadian rhythm were thought to play a role in this phenomenon.[29,30]

This study has some limitations. First, it included a small sample size and homogenous population. A larger sample size would provide more precise results. The addition of various breeds of rabbits would allow for more generalizable data. Second, this was a nonrandomized add-on to a crossover study, and this could expose the results to potential bias. In particular, a period effect could have confounded the HCB effect. Since all rabbits received HCB during the same week, a different factor related to the week, rather than the drug, could have theoretically been responsible for some of the changes noted in the study. This limitation, while theoretically valid, is contained by the high internal validity of the experimental set-up, including the fact that no other measurable factors changed in the 11 weeks of the study. Third, it could be argued that there could have been some carryover effect from the drugs administered the week before the HCB. However, this seems particularly unlikely since the washout period was of 7 days. In addition, all drugs administered on week 10 and earlier are short-acting medications or placebo and as such are not considered likely to carry any effect after 7 days for administration. Fourth, only healthy rabbits were used in this study. Pain medications can be used in healthy animals undergoing routine procedures (eg gonadectomy) or in diseased or painful animals who could present with ileus at the time of drug administration. The effect of this drug on diseased animals is unknown. Fifth, a singular dose of HCB was used. Buprenorphine is known to have a ceiling effect, and various dose ranges would offer a more comprehensive evaluation of the severity of side effects. Sixth, rabbits were not assessed until they returned to baseline. The complete duration of the effects of HCB is unknown. Finally, the current study measured water intake and urinary output but did not account for possible urinary retention. Imaging and measurements of the bladder throughout the study by a method such as focal abdominal ultrasound would have given a more complete assessment of urinary changes in our population of rabbits. Long-term urinary catheterization can also be considered in conjunction with or in place of ultrasound.

In conclusion, this study was designed to understand the effects of a single-dose HCB SC injection on physiologic function in rabbits. A single injection of HCB (0.24 mg/kg) caused a significant decrease in food and water intake, weight and number of fecal pellets produced, and urine production compared to control rabbits. These changes were clinically and statistically significant for the 72-hour study period. At the current stage, the clinical use of HCB in rabbits at the dose used in our study should take into consideration the side effects reported in this study.

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None reported.

Disclosures

The authors have nothing to disclose. The authors have no financial interests with companies that manufacture products used in this study or with companies that manufacture competing products.

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