Effect of postoperative analgesic protocol on limb function following onychectomy in cats

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Objective—To evaluate the analgesic effects of topical administration of bupivacaine, IM administration of butorphanol, and transdermal administration of fentanyl in cats undergoing onychectomy.

Design—Prospective study.

Animals—27 healthy adult cats.

Procedure—Cats were randomly assigned to 1 of 3 treatment groups, and unilateral (left forefoot) onychectomy was performed. Gait analysis was performed before and 1, 2, 3, and 12 days after surgery. All forces were expressed as a percentage of the cat's body weight.

Results—On day 2, peak vertical force (PVF) was significantly decreased in cats treated with bupivacaine, compared with cats treated with butorphanol or fentanyl. The ratio of left forelimb PVF to PVF of the other 3 limbs was significantly lower on day 2 in cats treated with bupivacaine than in cats treated with fentanyl. No significant differences in vertical impulse (VI) were found between groups on any day. Values for PVF, VI, and the PVF ratio increased progressively following surgery. However, for all 3 groups, values were still significantly decreased, compared with baseline values, 12 days after surgery.

Conclusions and Clinical Relevance—Results suggest that limb function following onychectomy is significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Regardless of the analgesic regimen, limb function was still significantly reduced 12 days after surgery, suggesting that long-term analgesic treatment should be considered for cats undergoing onychectomy. Irrigation of the surgical incisions with bupivacaine prior to wound closure cannot be recommended as the sole method for providing postoperative analgesia in cats undergoing onychectomy. (*J Am Vet Med Assoc* 2005;227:89–93)

Onychectomy is a painful procedure in cats[1,2] and can result in complications if the pain associated with onychectomy is not treated.[3] Unfortunately, cats typically receive analgesic medications for postoperative pain less often than do dogs.[4,5] This disparity could in part be explained by concerns about possible adverse effects in cats following administration of opioid analgesics or by difficulties in recognizing pain in this species.[2,5-9] Nevertheless, analgesics should always be administered to any patient undergoing a procedure that could potentially cause pain,[7] and the inability of animals to communicate should not be interpreted as a lack of pain.

Two major types of analgesics have been used in cats undergoing onychectomy: opioids and local anesthetics. In particular, opioids such as fentanyl citrate and butorphanol have been proven to be safe and effective analgesics in cats.[10-12] Butorphanol, for instance, has been shown to be a more efficacious analgesic than medetomidine in cats that have undergone ovariohysterectomy,[13,14] and transdermal administration of fentanyl has been shown to be an effective, noninvasive, well-tolerated method for delivery of analgesia in cats.[15] In addition, use of transdermal fentanyl patches in cats has not been found to cause lethargy, respiratory depression, excitement, or dysphoria,[11,15] and transdermal fentanyl patches can provide pain relief similar to that associated with butorphanol.[16]

Bupivacaine is a long-acting local anesthetic that has been shown to provide safe and effective analgesia following intrapleural or intra-articular administration in dogs and has been recommended for use in cats.[17-19] However, its effectiveness as an analgesic following onychectomy in cats has been questioned.[20]

Various subjective and objective methods have been used to evaluate the effectiveness of analgesic regimens, but such methods often are unreliable in defining the degree of pain.[6,20,21] Recently, a pressure-platform gait analysis system has been found to be an effective, objective method for evaluating limb function in cats.[22] This system generates values for **peak vertical force (PVF)** and **vertical impulse (VI)** that are comparable to those obtained with traditional force platform gait analysis systems.[23] Peak vertical force is the maximum load applied to the platform during gait analysis and can be used to identify subtle lameness that may be undetectable by physical examination.[24] Vertical impulse is the sum of all vertical loads applied to the platform during the stance phase of gait. Together, PVF and VI have been found to be the most useful measures for evaluating abnormal gaits in animals.[24]

The purpose of the study reported here was to use pressure-platform gait analysis to evaluate the analgesic effects of topical administration of bupivacaine, IM administration of butorphanol, and transdermal administration of fentanyl in cats undergoing onychectomy. We hypothesized that postoperative limb function, as reflected in PVF and VI, would be better

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in cats treated with fentanyl than in cats treated with bupivacaine or butorphanol because of a longer duration of analgesia.

Materials and Methods

Cats—Twenty-seven healthy, client- or shelter-owned, adult cats that were scheduled to undergo elective onychectomy were used in the study. Cats were included only if they were > 4 months but < 3 years old, had not received any analgesic or sedative medications within 24 hours prior to examination, and did not have any signs of orthopedic or neurologic disease during an initial physical examination. Informed consent was obtained from owners of cats included in the study. The experimental protocol was approved by the University Committee on Animal Care at Iowa State University.

Experimental protocol—Prior to surgery, cats were randomly assigned to 1 of 3 groups (bupivacaine group, 10 cats; butorphanol group, 9 cats; and fentanyl group, 8 cats). For cats in the fentanyl group, a 25-mg transdermal fentanyl patch[a] was applied to the skin between the scapulae 12 hours before surgery, as described.[11,16] Briefly, hair was clipped from an area large enough to allow a 1-cm margin around the patch, and tape was applied to the skin to remove hair clippings. The patch was applied and held in place for 2 to 3 minutes to ensure maximum adherence. The site was then covered with a bandage.[b] All patches were removed 72 hours after initial application.

Anesthesia was induced with a mixture of ketamine (10 mg/kg [4.5 mg/lb], IM), acepromazine (0.1 mg/kg [0.045 mg/lb], IM), and atropine (0.4 mg/kg [0.18 mg/lb], IM) and maintained with isoflurane delivered with oxygen via a mask. Elastic bandage material[c] was applied as a tourniquet to the left forelimb, cats were placed in lateral recumbency, and the left front paw was aseptically prepared for surgery. Onychectomy was performed by means of disarticulation with a scalpel. Digital incisions were closed with a single interrupted suture of 4-0 chromic gut, and a bandage was applied to the paw. Cats were then allowed to recover from anesthesia. All surgeries were performed by a single individual (MGC).

For cats in the bupivacaine group, a total of 1 mL of 0.75% bupivacaine[d] was used to irrigate the digital incisions prior to closure, as described.[21] For cats in the butorphanol group, butorphanol[e] (0.4 mg/kg, IM) was administered before administration of isoflurane was discontinued and every 4 hours for the first 24 hours after surgery, as described.[19]

For all cats in the study, an accepted subjective pain scoring system[10,16] was used to determine whether rescue analgesia was required. Cats that required rescue analgesia were removed from the study.

Gait analysis—Pressure-platform gait analysis was performed before and 1, 2, 3, and 12 days after surgery. For gait analysis the day after surgery, the bandage was removed from the left forefoot within 1 hour of gait analysis.

A 2 × 0.75-m pressure measurement walkway[f] mounted in the center of and level with a 10-m runway was used for gait analysis. Output from the walkway was linked to a dedicated computer[g] with software[h] designed for collection of gait analysis data. Prior to data acquisition, the walkway sensors were equilibrated and calibrated in accordance with manufacturer's specifications. Before each session, cats were weighed on an electronic scale[i] and allowed to acclimate to the runway area and pressure platform.

Cats were allowed to walk across the pressure platform at a comfortable velocity. Five valid trials were collected for each cat at each session. A trial was considered valid if the cat walked along the runway at a comfortable velocity and each of the 4 limbs fully contacted the pressure measurement walkway at least 2 consecutive times during the pass. Pressure distribution data (PVF and VI) were determined for each footfall for each of the 5 valid trials, and mean values were calculated. Values were then expressed as a percentage of body weight.

Following gait analysis on day 12, the study ended and onychectomy was performed on the right forefoot.

Statistical analyses—Student *t* tests were used to compare age, velocity, and acceleration among groups. Cross-sectional analysis was used to compare PVF, VI, and the PVF ratio (ratio of left forelimb PVF to PVF of the other 3 limbs) among groups while controlling for baseline (day 0) and day 12 values through analysis of covariance. This method was chosen because each day was a repeated measure. It was necessary to control for day 0 and day 12 values because drug effects were not present on these days. When a significant group effect was identified, the Tukey honest significant difference method was used to determine specific group differences. Overall significance for all comparisons was set at $P < 0.05$. The effect of time within treatment group was assessed by use of paired *t* tests. All analyses were performed with standard software.[j]

Results

One cat in the bupivacaine group was removed from the study a few hours after surgery when it was considered to have severe pain on the basis of a visual observation of its behavior, and rescue analgesia was administered. Thus, gait analysis data were available for 9 cats in the butorphanol group, 9 cats in the bupivacaine group, and 8 cats in the fentanyl group.

Mean ± SE ages of cats in the bupivacaine, butorphanol, and fentanyl groups were 16.6 ± 4.2 months, 12.9 ± 2.8 months, and 30.6 ± 9.1 months, respectively. There were no significant differences in age among groups, and age was not significantly associated with PVF. Mean ± SD velocities during gait analysis for cats in the bupivacaine, butorphanol, and fentanyl groups were 0.76 ± 0.09 m/s, 0.76 ± 0.08 m/s, and 0.81 ± 0.06 m/s, respectively. There were no significant differences in velocity or acceleration among groups.

On day 2, PVF was significantly ($P < 0.01$) lower for cats in the bupivacaine group than for cats in the other 2 groups (**Figure 1**). Significant differences among groups

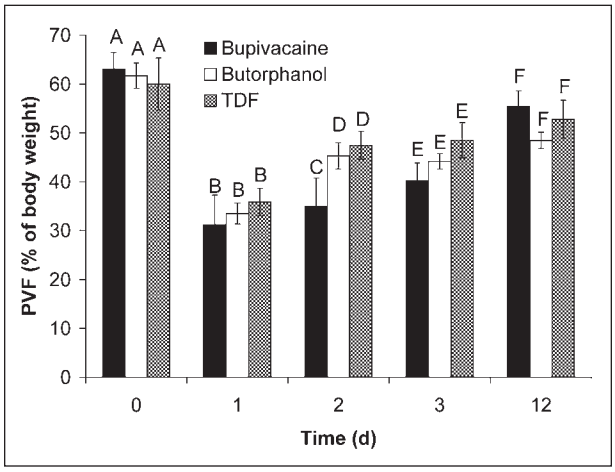

Figure 1—Mean peak vertical force (PVF) of the left forelimb, expressed as a percentage of body weight, in cats that underwent unilateral onychectomy and received bupivacaine topically (n = 9), butorphanol IM (9), or fentanyl transdermally (TDF; 8) for postoperative analgesia. Error bars represent SEM. Columns with different letters were significantly ($P < 0.05$) different.

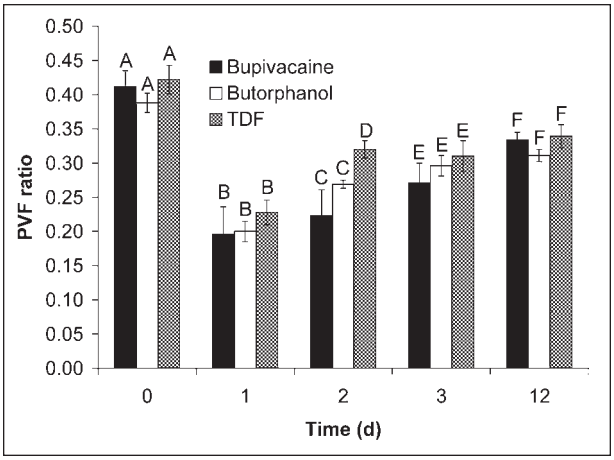

Figure 2—Mean of the ratio of left forelimb PVF to PVF of the remaining 3 limbs for cats that underwent unilateral onychectomy and received bupivacaine topically (n = 9), butorphanol IM (9), or fentanyl transdermally (8) for postoperative analgesia. *See* Figure 1 for key.

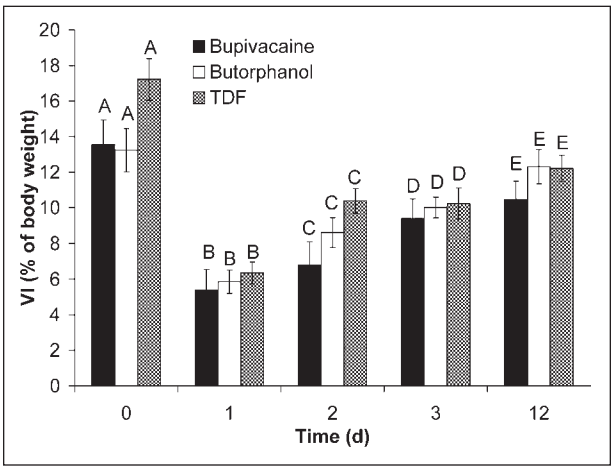

Figure 3—Mean vertical impulse (VI) of the left forelimb in cats that underwent unilateral onychectomy and received bupivacaine topically (n = 9), butorphanol IM (9), or fentanyl transdermally (8) for postoperative analgesia. *See* Figure 1 for key.

were not found on days 1, 3, and 12, although the *P* value for day 1 was close to the established value for significance ($P = 0.054$). Similarly, the ratio of left forelimb PVF to PVF of the other 3 limbs (ie, the PVF ratio) was significantly ($P = 0.015$) lower on day 2 in cats treated with bupivacaine than in cats treated with fentanyl, but was not significantly different from the value for cats treated with butorphanol (**Figure 2**). There were no significant differences in VI among groups on any day (**Figure 3**).

In all 3 groups, PVF, VI, and the PVF ratio were significantly decreased the day after surgery, compared with baseline values. Values increased progressively during the subsequent days. However, for all 3 groups, PVF, VI, and the PVF ratio were still significantly decreased, compared with baseline values, 12 days after surgery.

Discussion

In a strict sense, inclusion of a control group of cats in the present study that did not receive any analgesics may have been advantageous but was not considered because previous research has indicated that this procedure is painful and that cats should be treated with analgesics postoperatively.[25] We found that IM administration of butorphanol and transdermal administration of fentanyl provided similar degrees of analgesia, but that topical administration of bupivacaine was less effective. This most likely reflects the duration of action of bupivacaine (ie, 3 to 10 hours[3]) and the fact that it was administered only once (ie, just prior to closure of the digital incisions). We elected to evaluate the analgesic effects of topical bupivacaine administration because it was our opinion that this procedure is used in clinical veterinary practice. Although our results may have been different if bupivacaine had been infiltrated in the area, rather than administered topically, topical and infiltrative administration of local anesthetics have been found to be equally effective in providing analgesia following total ear canal ablation in dogs.[26]

Our findings are supported by a report[3] that the duration of action of bupivacaine is between 3 and 10 hours. In contrast, results of a previous study[18] suggested that bupivacaine may provide 24 hours of analgesia in dogs. In that study, however, bupivacaine was administered intra-articularly following surgery for rupture of the cranial cruciate ligament, and the intra-articular route of administration may have affected the duration of action or availability of the drug. The shorter apparent duration of action for bupivacaine in the present study may also be attributable, in part, to loss of some of the drug from the incision during suture closure or dilution with blood, either of which could have decreased the effectiveness of the drug.[21] It has also been suggested that injection of bupivacaine may itself cause some mild discomfort[17,21] that could possibly persist for several hours or days. However, the authors are not aware of any information documenting this phenomenon in cats.

In the present study, transdermal administration of fentanyl and IM administration of butorphanol resulted in similar degrees of analgesia, in that results of gait analyses were not significantly different between these groups during the 12 days after surgery. These findings are consistent with results of previous studies[10,16] on the analgesic efficacy of fentanyl and butorphanol in cats. Although we found these treatment regimens provided similar degrees of analgesia in this clinical situation, different results could occur in a different clinical situation or species. Different species have different degrees of skin permeability to fentanyl owing to differences in diffusion and thickness of the stratum corneum.[11] Fentanyl is a highly lipophilic narcotic that selectively diffuses to lipid-rich tissues, such as the stratum corneum of the epidermis.[15] The stratum corneum of haired skin in cats varies from 3 to 20 µm thick, which may suspend diffusion of the drug.[27] Individual cats that are treated with transdermal fentanyl patches had these species differences as well as individual variations in plasma fentanyl concentrations over a 48-hour period. In cats, plasma fentanyl concentration has been reported to range from 0.3 to 7 ng/mL during the 48 hours after application of a transdermal fentanyl patch to the lateral aspect of the thorax.[16] When a transdermal fentanyl patch was applied in the dorsal cervical region of

a group of cats, plasma fentanyl concentration ranged from 0.50 to 6.38 ng/mL 12 hours after patch application.[11]

Following patch removal in dogs, plasma fentanyl concentration rapidly decreases, with a reported half-life of 1.39 hours[11,28]; however, plasma concentration in cats decreases at a much slower rate after patch removal.[11] One possible explanation for the greater half-life of fentanyl in cats is the presence of a cutaneous depot of fentanyl beneath the patch; this phenomenon has been observed in humans.[11] Information on the plasma concentration of fentanyl associated with effective analgesia in cats with superficial or orthopedic pain would be of value in defining the most effective analgesic protocol following onychectomy.

Results of the present study indicate that IM administration of butorphanol is a reasonable analgesic regimen for cats undergoing onychectomy. It has been documented previously that cats that receive butorphanol IV have lower subjective lameness scores the day after discharge, compared with cats given a placebo (saline [0.9% NaCl] solution),[19] but perioperative IM administration of butorphanol at doses ranging from 0.05 to 0.4 mg/kg (0.023 to 0.18 mg/lb) has also been associated with adequate analgesia.[13] In the present study, butorphanol was administered before administration of isoflurane was discontinued, which may have contributed to its efficacy.

In previous studies[16,19,20,29,30] of the effectiveness of various analgesic regimens and surgical techniques, onychectomy was performed bilaterally. However, this may complicate evaluations, as both forelimbs would be expected to be painful following surgery. We suggest that unilateral onychectomy allows for a better evaluation of limb function and degree of pain, as it provides the animal the choice to use the limb on which surgery was performed or to ambulate only with the 3 remaining limbs. Although all cats consistently used the left forelimb by 2 days after surgery, some cats had clinical evidence of non–weight-bearing lameness during gait analyses after surgery. We did not include an evaluation of patient behavior as an indicator of pain in the present study because the interpretation of cat behavior seems to be wrought with subjectivity. In addition, we did not collect other objective parameters of pain (eg, heart rate and serum cortisol concentration) because we were more concerned with the long-term effects of the procedure (ie, 1 through 12 days after surgery) than with the immediate postoperative effects (ie, the first 24 hours after surgery).

The gait analysis system in the present study measured limb function, not strictly limb pain, and it is possible that a cat could have had normal limb function but still be in pain. However, this was not apparent, in that PVF, VI, and the PVF ratio were all less than baseline values at all times after surgery in all cats. It is also possible that factors other than pain (eg, incisional inflammation, early infection, tendonitis, and suture reactivity) could have contributed to the decrease in limb function. However, we are not aware of a better method for evaluating pain in cats 1 to 12 days after limb surgery and believe that our method was at least as good a method of evaluating limb pain as any method that has been described. In addition, ground reaction forces have commonly been used as a measure of limb pain in dogs with osteoarthritis.

Although cats were permitted to walk across the pressure platform at a comfortable pace, no significant differences in velocity or acceleration were detected among groups on any day. In addition, we were able to collect satisfactory gait data for every cat. Despite its limitations, the pressure-platform gait analysis system is considered an acceptable alternative to force platform gait analysis systems and can be regarded as an acceptable objective method for evaluating limb function in cats.[23]

On the basis of results of the present study, topical administration of bupivacaine cannot be recommended as a method for obtaining postoperative analgesia in cats undergoing onychectomy. Limb function, as reflected in PVF and the PVF ratio, was significantly better in cats treated with fentanyl transdermally or butorphanol IM than in cats treated with bupivacaine topically. Although a previous study[22] revealed that ground reaction forces recorded 6 months after surgery in cats that had undergone onychectomy were similar to forces in cats that had not undergone surgery, limb function in cats in the present study was still significantly decreased 12 days after surgery. Thus, providing analgesia for the duration of this period should be strongly considered.

a. Duragesic, Janssen Pharmaceutical Products, Titusville, NJ.
b. Expandover, Kendall Co, Mansfield, Mass.
c. Vetrap, 3M Animal Care Products, Saint Paul, Minn.
d. Marcaine, Abbott Laboratories, North Chicago, Ill.
e. Torbugesic, Fort Dodge Animal Health, Fort Dodge, Iowa.
f. Tekscan Inc, South Boston, Mass.
g. Latitude CPx personal laptop, Dell Computer Corp, Round Rock, Tex.
h. I-Scan, version 4.20, Tekscan, South Boston, Mass.
i. Vet-50 electronic scale, Detecto-Cardinal Scale Manufacturing Co, Webb City, Mo.
j. JMP, version 5.1.1, SAS Institute, Cary, NC.

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