Efficacy of long-acting methadone using a combination of oral and injectable formulations in postoperative dogs.

Kansas State University, College of Veterinary Medicine

ABSTRACT
The purpose of the study was to evaluate the perioperative efficacy and tolerability of subcutaneous methadone/flucloxacin followed by oral methadone/flucloxacin/naltrexone (methadone/flucloxacin) compared to intramuscular buprenorphine followed by oral codeine (buprenorphine).

RESULTS AND DISCUSSION
Propofol was additionally needed for intubation in 8/120 (buprenorphine) and 2/119 (methadone/flucloxacin) dogs. The castration, ovariohysterectomy and ovariohysterectomy result in postoperative pain in dogs. Controlling postoperative pain can be difficult due to need for frequent drug administration and lack of oral opioid formulations. Although NSAIDs can be administered orally once daily, they alone are only moderately effective in controlling postoperative pain in canine ovariohysterectomies and castrations. We have developed oral and injectable long-acting methadone formulations which provide 24 hours of high efficacy analgesia with just two doses. Inclusion of the pharmacokinetic enhancer flucloxacin increases the oral bioavailability and duration of methadone effect. Long-acting methadone was effective and well tolerated in postoperative dogs.

INTRODUCTION
Numerous studies have shown common surgical procedures, such as ovariohysterectomy and ovariohysterectomy, result in postoperative pain in dogs. Controlling postoperative pain can be difficult due to need for frequent drug administration and lack of oral opioid formulations. Although NSAIDs can be administered orally once daily, they alone are only moderately effective in controlling postoperative pain in canine ovariohysterectomies and castrations. We have developed oral and injectable long-acting methadone formulations which provide 24 hours of high efficacy analgesia with just two doses. Inclusion of the pharmacokinetic enhancer flucloxacin increases the oral bioavailability and duration of methadone effect. Long-acting methadone was effective and well tolerated in postoperative dogs.

MATERIALS AND METHODS
Enrollment = 239 healthy dogs from local shelters, to undergo routine soft tissue surgery (ovariohysterectomy, ovariohysterectomy, or ovariohysterectomy) with or without ovariohysterectomy. There were no treatments, allocated to treatment by week.

Buprenorphine/dexmedetomidine (buprenorphine): n= 44 male, 76 female (120 total dogs)
• Buprenorphine: 0.02 mg/kg SC ± 12:30P and postoperative (0.01 mg/kg SC ± 4:00P)
• Coderone: 1-2 mg/kg PO q 8h and NSAID (carprofen or meloxicam) starting post night

Long-acting methadone (methadone/flucloxacin): n=47 male, 72 female (119 total dogs)
• Methadone/flucloxacin (0.5/2.5 mg/kg SC pre- ± 9:00A and postoperative ± 4:00P)
• Methadone/flucloxacin/naltrexone (0.5/2.5/125 mg/kg PO) q12h started ± 8h postoperative: (7:00 the following day) with an NSAID (carprofen or meloxicam)

Anesthesia, surgery and monitoring
All dogs were also administered acepromazine, ketamine/midazolam, and isoflurane
• Propofol administered if the patient was unable to inivate with ketamine/medazolam

Student anesthetists performed the anesthesia under faculty supervision
• Anesthetic monitoring included capnography (end tidal CO2; ETCO2): 8 dogs continuous, 7 dogs intermittent per day, HR, RR, doppler blood pressure and isoflurane concentration
• Surgery started at ± 2:30P with 10% isoflurane in oxygen
• Student surgeons performed standardized surgeries under faculty supervision
• Postoperative monitoring included the Glasgow Composite Pain Score (GCPS) and sedation assessed as none (0), slight (1), moderate (2), profound (3), or unresponsive (4)
• Serum chemistry profiles determined before and ± 48 hours after Tuesday surgery

SUMMARY AND CONCLUSIONS
Long-acting methadone was effective in providing preoperative sedation and lowered the need for additional anesthetic induction agents in soft tissue surgery dogs. Dogs administered long-acting methadone had slightly higher mean ETCO2 and lower mean isoflurane concentrations to maintain anesthesia compared to buprenorphine. Additional intraoperative sedation was provided if indicated and monitored at 15 minute intervals from frequency of methadone/flucloxacin compared to buprenorphine. Long-acting methadone required less rescue analgesia or intra/postoperative sedation compared to buprenorphine. There were no clinically relevant changes in serum chemistry profiles in either treatment.

LONG-ACTING METHADONE

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