

# What Is the Evidence?

## **Problem**

A 5-year-old spayed female mixed-breed dog weighing 15 kg (33 lb) was brought to the University of Georgia Small Animal Veterinary Teaching Hospital for fixation of a traumatic fracture of the right femur. Physical examination and preanesthetic hematologic evaluation revealed no other abnormalities, and the dog was deemed a suitable candidate for surgery to repair the fracture. The dog was premedicated with glycopyrrolate (0.005 mg/kg [0.002 mg/lb]), hydromorphone (0.05 mg/kg [0.023 mg/lb]), and midazolam (0.2 mg/kg [0.09 mg/lb]) administered SC. Anesthesia was induced via IV administration of ketamine (5 mg/kg [2.3 mg/lb]) and diazepam (0.25 mg/kg [0.11 mg/lb]) and maintained with isoflurane in oxygen to effect. Thirty minutes prior to surgery, the dog received an epidural injection of 0.5% bupivacaine solution (1 mg/kg [0.45 mg/lb]) into the lumbosacral space.

Surgical fixation of the fracture was achieved without complications, and a low delivered fraction of isoflurane (between 0.75% and 1.25%) was used throughout surgery, which lasted slightly longer than 2 hours. After recovery in the intensive care unit, however, the dog began to have signs of pain and required supplemental analgesia (hydromorphone [0.05 mg/kg]) only 2 hours after surgery, approximately 5 hours after epidural administration of bupivacaine.

## **Clinical Question**

How does epidural administration of bupivacaine or a bupivacaine-opioid combination compare with other analgesic protocols for postoperative analgesia in dogs undergoing orthopedic surgeries involving the hind limbs?

## **Evidentiary Search Strategy**

A search of the PubMed database was performed in September 2010 with all of the following search terms: surgery, epidural, bupivacaine, analgesia, dogs. Approximately 15 retrieved abstracts were reviewed and were omitted because the surgical procedure was not orthopedic in nature or the report had not been peer reviewed. Four additional reports identified through the search were obtained through PubMed online or a library if not available electronically. Reference sections of the initially selected reports were searched for other relevant reports, yielding 1 additional item, for a total of 5 relevant scientific reports.<sup>1-5</sup>

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## **Review of the Evidence**

Four of the scientific reports<sup>1-3,5</sup> that were identified concerned a randomized controlled clinical trial (RCT); the remaining report consisted of a retrospective case series with a nested cohort study.<sup>4</sup> All 5 studies included evaluation of epidural administration of an opioid-bupivacaine combination (morphine-bupivacaine or oxymorphone-bupivacaine). Three of these included epidural administration of morphine, and 2 included epidural administration of bupivacaine alone.

Two RCTs involved evaluation of analgesic effects following epidural administration of saline (0.9% NaCl) solution, morphine, or morphine and bupivacaine in dogs undergoing hind limb orthopedic surgeries. In one of these studies,<sup>1</sup> a group of dogs that received a combination of morphine and bupivacaine (0.2 mg of morphine sulfate/kg and 1 mg of bupivacaine hydrochloride/kg) prior to surgery had a degree of analgesia superior to that obtained in similarly sized groups that received epidural administration of morphine (0.2 mg/kg) alone or saline solution. In this study, a better analgesic outcome was defined as lower pain scores for the first 12 hours after surgery, lower plasma cortisol concentration, and reduced need for rescue analgesia than in the control or morphine group.

The second study<sup>2</sup> involved 41 dogs that received epidurally administered saline solution (placebo), morphine (0.1 mg/kg [0.045 mg/lb]), bupivacaine (1.0 mL of a 5% solution/10-cm distance from the occipital protuberance to the lumbosacral space), or a morphine-bupivacaine combination (given at individual component doses) after surgery. Pain scores did not differ significantly between the morphine and placebo groups or between the morphine and bupivacaine groups, but dogs that received bupivacaine alone did have significantly lower pain scores than did the dogs in the placebo group. The total number of doses of supplemental analgesia required was also significantly lower in the bupivacaine group than in the placebo group. Epidural administration of a combination of morphine and bupivacaine provided the best analgesia; this group had lower pain scores, reduced requirements for supplemental analgesia, and a longer interval to administration of supplemental analgesia than did the morphine and saline solution groups.

In another RCT,<sup>3</sup> comparisons were made among the analgesic effects of oxymorphone (0.05 mg/kg) administered IV, bupivacaine (1 mg/kg) administered epidurally, and an oxymorphone-bupivacaine combination (0.1 mg of oxymorphone/kg and 1 mg of bupivacaine/kg) administered epidurally before surgery. Eight dogs were allocated to each group. Similar to the previously described study,<sup>2</sup> this study<sup>3</sup> found that postoperative analgesia requirements were lower in dogs that received the oxymorphone-bupivacaine combination epidurally than in the

other dogs. Postoperative analgesic requirements, however, were not significantly lower with epidural administration of bupivacaine alone, compared with IV administration of oxymorphone. Only 1 dog in the group that received oxymorphone-bupivacaine epidurally required additional analgesia in the 24-hour period after surgery, whereas 7 dogs that received bupivacaine epidurally and all 8 dogs that received oxymorphone IV required additional analgesia.

The retrospective cohort study<sup>4</sup> involved evaluation of the analgesic effects of preoperative epidural administration of morphine with or without bupivacaine in 18 dogs that underwent 2 separate surgical procedures. Dogs in the epidural morphine (0.1 to 0.4 mg/kg [0.045 to 0.18 mg/lb]) and epidural morphine-bupivacaine (0.6 to 2.0 mg of bupivacaine/kg [0.27 to 0.9 mg/lb] added to morphine doses) groups were compared with those that received oxymorphone (0.05 to 0.2 mg/kg, IM) and ketoprofen (2.2 mg/kg [1 mg/lb], SC), and were found to have longer lasting analgesia after surgery, although not necessarily a better quality of analgesia. The only distinction made between the morphine and morphine-bupivacaine groups was that the morphine-bupivacaine group had significantly longer lasting analgesia than the group that received morphine alone.

The final RCT<sup>5</sup> involved comparison of the degree of postoperative analgesia between dogs undergoing elective tibial plateau leveling osteotomies that received morphine-bupivacaine (0.1 mg of morphine/kg and 0.1 mL of 0.5% bupivacaine/kg) epidurally, bupivacaine (0.2 mL/kg) intra-articularly and saline solution epidurally, or a control treatment (saline solution epidurally and intra-articularly). Degree of analgesia was assessed with a visual analogue scale, a multifactorial pain score, and measurement of the pressure nociceptive threshold. Interval to administration of the first postoperative dose of analgesic was significantly longer for the epidural (mean, 9.1 hours) and intra-articular (mean, 7.3 hours) treatments than for the control treatment, but no significant difference was evident between the epidural and intra-articular treatments. Overall pain scores did not differ significantly between any of the 3 groups, as all dogs received hydro-morphone IV as needed to provide sufficient analgesia.

Given the aforementioned evidence, what decision would you make?

## Decision and Outcome

Assessment of pain in animals can be subjective, despite efforts to quantify its presence and intensity through use of scoring systems and measurement of stress hormone concentrations. In many instances, a low sensitivity exists for detecting subtle differences between groups in which different analgesic drugs or routes of administration are used. Most of the reports we identified indicated that duration of analgesia is maintained longer with epidural administration of a local anesthetic, compared with IV administration of opioids; however, clear evidence for a superior quality of analgesia was not demonstrated for all types of epidural analgesic treatment. Two reports<sup>2,3</sup> had conflicting results regarding a decreased requirement for additional analgesia after epidural administration of bupivacaine,<sup>2,3</sup> which may be

indicative of differences between studies (eg, timing of epidural administration) or attributable to the challenge for observers to accurately detect and quantify pain.

Epidural administration of an opioid-bupivacaine combination had the most evidence for provision of subjectively improved analgesia<sup>1-3</sup> as well as, in 1 study,<sup>1</sup> lower plasma cortisol concentrations, relative to other analgesic strategies. Various mechanisms have been proposed to account for the superior analgesia provided by opioid-local anesthetic combinations relative to epidural administration of either drug alone; however, the synergistic behavior between these 2 drug classes appears clinically evident on the basis of the literature reviewed here.

Finally, although good evidence exists to suggest that epidural administration of a morphine-bupivacaine combination provides superior analgesia, 1 report<sup>5</sup> also indicated that alternative approaches, such as intra-articular administration of bupivacaine for dogs undergoing joint surgeries, may provide equivalent analgesic effects with regard to duration and requirement for additional IV doses of analgesics.

In the scenario reported here, the epidural administration of bupivacaine prior to fracture fixation appeared effective during surgery, as evidenced by the low requirement for isoflurane and stable plane of anesthesia during surgical manipulation. Postoperatively, however, supplemental analgesia was required within 2 hours after surgery. The literature suggested that postoperative analgesia for hind limb orthopedic surgeries may be enhanced by epidural analgesic administration, particularly with the use of opioid-local anesthetic combinations, which appear to provide longer-lasting analgesia and reduce the need for additional analgesic administration. Therefore, epidural administration of morphine and bupivacaine, rather than epidural administration of bupivacaine alone, may provide enhanced postoperative analgesia as well as intraoperative analgesic and anesthetic benefits. Regardless of drug type, however, epidural administration should still be used in conjunction with repeated pain assessments and multimodal analgesic strategies. Clinically, it is indicated to use combined local anesthetic and opioid epidural protocols, and such a protocol could have provided superior postoperative analgesia in the case discussed in this report.

## References

1. Kona-Boun JJ, Cuveliez S, Troncy E. Evaluation of epidural administration of morphine or morphine and bupivacaine for postoperative analgesia after premedication with an opioid analgesic and orthopedic surgery in dogs. *J Am Vet Med Assoc* 2006;229:1103-1112.
2. Hendrix PK, Raffae MR, Robinson EP, et al. Epidural administration of bupivacaine, morphine, or their combination for postoperative analgesia in dogs. *J Am Vet Med Assoc* 1996;209:598-607.
3. Torske KE, Dyson DH, Pettifer G. End tidal halothane concentration and postoperative analgesia requirements in dogs: a comparison between intravenous oxymorphone and epidural bupivacaine alone and in combination with oxymorphone. *Can Vet J* 1998;39:361-369.
4. Troncy E, Junot S, Keroack S, et al. Results of preemptive epidural administration of morphine with or without bupivacaine in dogs and cats undergoing surgery: 265 cases (1997-1999). *J Am Vet Med Assoc* 2002;221:666-672.
5. Hoelzler MG, Harvey RC, Lidbetter DA, et al. Comparison of perioperative analgesic protocols for dogs undergoing tibial plateau leveling osteotomy. *Vet Surg* 2005;34:337-344.