Clinical Application of Analgesic Techniques  (3-Dec-2002)

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Research in our laboratory has focused on clinical application of analgesic techniques in a wide variety of species. We have evaluated the use of epidural analgesics as well as the optimal volumes for epidurally administering drugs in large/food animal species [1-4]. In small animal species, we have investigated the usefulness of transdermal delivery of fentanyl (e.g. fentanyl patch) to provide analgesia for common clinical surgical procedures [5-7].

Epidural techniques have been useful in a wide variety of species. In large animals, epidural administration of local anesthetic agents, alpha-2 agonist, or opiates are useful for perioperative analgesia, standing surgical procedures, and obstetrics. Cranial migration of agents administered in the caudal epidural region has been predicted based on factors that include age, body weight, and occiput to tail root length. Migration of injectate can be influenced by the size of the epidural space, gravity, posture, spinal cord length, and volume of injectate. In two human studies, increasing age, weight, body-mass index, higher site of injection, decreasing height, increasing volume per spinal segment, and pregnancy all significantly increased spread of local anesthetic injected epidurally. However, in two other investigations, no relationship was found to direction of needle bevel, volume, patient height, weight, and age. In domestic animal species, little information on the effect of cranial drug migration is available for these various factors. Therefore, we have done a series of investigations using a dye marker to determine the effect of volume of injectate on cranial migration following epidural injection in goats, calves, juvenile pigs, and horses.

New methylene blue dye (NMB) was dissolved in 0.9% NaCl at 1.2 mg/ml; yielding a solution that stained tissue and was easily visualized. Varying volumes of dye (0.02 - 0.3 ml/kg, depending on the species studied) were injected at the appropriate space in goats (L7 - S1), calves (S5 - C1), juvenile pigs (L7 - S1), or horses (C1 - 2) at a consistent rate of injection. Within 30 minutes, animals were euthanized; the spinal column transected longitudinally, and the extent of cranial dye migration determined. In goats injected with 0.1, 0.2, or 0.3 ml/kg, the number of stained spinal segments was 3.5 + 0.6, 6.5 + 0.9, and 8.8 + 0.6, respectively. In calves treated with 0.05, 0.1, or 0.15 ml/kg, the number of stained spinal segments was 5 + 0.3, 8 + 0.6, and 8 + 0.6, respectively. In juvenile pigs the number of stained spinal segments was 8 + 1.1, 8 + 0.9, 10 + 1.2, and 18 + 2.0 for 0.05, 0.1, 0.2, and 0.3 ml/kg, respectively. When horses were injected with 0.02 or 0.1 ml/kg the dye migrated a range of 6 - 11 or 11 - 14 spaces, respectively. In each investigation there was a very close fit of the data to a linear model and significant R2 value. The results of these studies have given us a method for estimating cranial migration of epidural injectate based on a volume/kg body weight basis. However, when injecting drugs into the epidural space it is important to note that differing pharmacokinetics will cause variation in cranial migration; particularly lipophilicity and duration of action. The data presented here serve as a useful baseline of information regarding drug migration in the epidural space.

Transdermal drug delivery systems offer several advantages over traditional routes of drug delivery: ease of administration, noninvasiveness, and continuous delivery over an extended time frame. As such these systems have been used to deliver a wide variety of drugs in humans, such as nicotine, estrogen, clonidine, and fentanyl. Transdermal fentanyl has been used for control of chronic pain in humans, and more recently has become an alternate analgesic technique in veterinary medicine. We have investigated the use of transdermal fentanyl for analgesia in canine orthopedic patients and cats presenting for onychectomy; comparing it to common clinical analgesic techniques, epidural morphine and intramuscular butorphanol, respectively.

In dogs we have done two separate investigations, one in a research setting with dogs undergoing experimental orthopedic
surgery, and most recently in clinical patients presenting for a common orthopedic procedure, triple pelvic osteotomy. In the first investigation (research setting) we found that transdermal fentanyl provided postoperative analgesia that was at least equivalent to, and possibly greater than, that provided by epidural morphine. However, in the clinical setting, we found that dogs treated with transdermal fentanyl had a greater incidence of pain in the first 12 hours following surgery, but were better able to bear weight on the operated limb by 48 hours following surgery. Combining results of these two investigations into clinical application for major hindlimb orthopedic procedures, we now recommend use of both epidural morphine and transdermal fentanyl; with epidural morphine providing immediate (first 12 hours) postoperative analgesia and transdermal fentanyl allowing analgesia to continue for up to 2 days following surgery.

Finally, in our most recent investigation, we compared intermittent administration of IM butorphanol to transdermal fentanyl for postoperative analgesia in cats undergoing onychectomy. Other than a lower pain score at 8 hours in the transdermal fentanyl group, we observed no other significant differences between the two treatment groups through 48 hours postoperatively, indicating the two analgesic techniques are nearly equivalent. The advantages of the transdermal system in cats are continuous delivery, noninvasive delivery; compared to intermittent administration of butorphanol via IM injection. Furthermore we found that transdermal fentanyl patches were easily applied to cats and well tolerated for the duration of the study. While the cost of transdermal fentanyl approaches twice that of intermittent administration of butorphanol IM, the ease of use and minimal disturbance to the animal are advantages that may outweigh cost considerations in many situations. Consequently, these results have allowed us to tailor our analgesic approach in cats based on owner preference and animal handling and restraint issues.

We have found that the investigations described above have provided us with useful clinical applications of analgesics in the clinical setting. Future studies will be planned to continue our evaluation of newer analgesics and practical analgesic delivery methods in the clinical setting.

References


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