Current Studies

1. A Proposed Model to Test the Efficacy of Analgesic Drugs in Horses

Our overriding goal in pursuing this area of research is to develop and refine effective treatment strategies to alleviate pain in horses suffering from trauma or surgery induced pain. Currently, there is no well-established method to determine if a given treatment protocol alleviates pain in horses following injury or surgery. Using a dose of *Escherichia coli* (*E. coli*) endotoxin, Palmer and colleagues evaluated the effects of various doses of *E. coli* endotoxin on joint size and warmth, resistance to palpation, lameness, and overall patient response (whether or not they became febrile or ill). Injecting a dose of 0.125 ng of endotoxin/joint, horses exhibited mild to moderate joint effusion and warmth of the injected joint, mild resistance to palpation of the joint, grade-2 lameness, and no signs of systemic illness. All horses continued to bear weight on the affected leg, and signs of lameness and joint pain began to wane between 36 and 48 hours post injection.

**Hypothesis** - We hypothesized that the injection of *E. coli* endotoxin into the carpal joint will induce a reproducible synovitis to test the effectiveness of analgesic therapies to decrease pain and lameness in horses. In addition, we hypothesized that the administration of intra-articular morphine (5 mg) will provide analgesia that is at least equivalent to a standard dose of IV phenylbutazone, and that the combination of intra-articular morphine and IV phenylbutazone will provide better pain relief than either drug administered alone for at least 24 hours. Parameters of pain that are evaluated include physical characteristics of the horse (attitude, temperature, pulse, respiration), circumference of joint, subjective joint effusion score, complete blood count, analysis of synovial fluid, and subjective and objective analysis of lameness. Lack of response in our horses to this amount of endotoxin administration resulted in a relatively comprehensive dose-response study utilizing doses of as high as 10 mcg. Results of this preliminary study are pending.

2. A Multicenter, Large-scale Evaluation of Pain Behaviors Following Neutering in Dogs

Many veterinarians do not administer analgesics following routine surgical procedures such as ovariohysterectomy and castration, partly because they do not believe the dogs are painful. We are evaluating a large number of dogs from different veterinary practices to determine if they are painful following OHE or castration. We are also evaluating whether duration of surgery, length of skin incision, and preoperative pain medications are related to behavioral signs of pain.

**Hypothesis** - OHE and castration induce acute postoperative pain in dogs. The degree of pain is correlated with the amount of tissue trauma (duration of surgery and length of skin incision), whether or not analgesics are administered, and individual patient characteristics.

**Specific objective #1** - Evaluate the degree of postoperative pain in dogs undergoing elective OHE or castration at multiple veterinary centers.

**Specific objective #2** - Determine if a correlation exists between the amount of tissue trauma (estimated by duration of surgery and length of skin incision) and the degree of postoperative pain.

**Specific objective #3** - Determine if pre-treatment with morphine or nalbuphine or postoperative treatment with ketoprofen decreases the incidence of postoperative pain behaviors.

**Specific objective #4** - Determine if the amount of tissue trauma or analgesic administration (none, morphine, nalbuphine, ketoprofen) correlates with owner evaluation of comfort for three days after surgery. Data has been collected on ~450 dogs and is currently being analyzed.
3. Comparison of Opioid and Alpha-2 Adrenergic Receptor Location and Density in the Horse and Dog Using Radioligand Binding

Our long-term goal is to discover a more effective method to treat pain in horses than currently exists. In order to better understand the horse’s response to pain and analgesic drugs, we need to characterize the neurophysiological processes involved in the modulation of nociceptive information leading to the perception of pain in this species. An understanding of these processes may lead to the use or development of more effective analgesic drugs associated with fewer adverse side effects.

In recognition of the fact that dogs generally have a more desirable response to opioids than horses, we compared the distribution and density of opioid and alpha-2 adrenergic receptors in the horse and dog. We hypothesized that differences in the endogenous opioid and alpha-adrenergic systems are responsible in part, for the marked species differences between horses and dogs in their reaction to opioid drugs. Thus, we tested the hypothesis that the distribution, density, and subtype of opioid and alpha-2 adrenergic receptors within the CNS are significantly different between the horse and dog.

Specific objectives - Compare the distribution and density of mu, kappa, and delta opioid receptors and alpha-2 adrenergic receptors in the cerebral cortex (frontal cortex and somatosensory cortex), thalamus, periaqueductal gray and nucleus raphe magnus of the rostroventral medulla, cerebellum, and dorsal horn of the spinal cord in the dog and horse using autoradiography. Three dogs and three horses that were euthanized as part of separate studies were used in this study.

Pending Grants

1. The Effect of Oral Tramadol and Sustained Release Oral Morphine on Thermal and Mechanical Threshold Testing in the Dog

Our hypothesis is that tramadol is an effective oral analgesic for dogs requiring analgesia for up to 7 days following a painful procedure. Specifically, we hypothesize that tramadol will induce superior analgesia, with fewer adverse side effects, than sustained release oral morphine in dogs. We propose to compare the analgesic efficacy and incidence of side effects of oral tramadol to sustained release oral morphine using thermal threshold and mechanical threshold testing as the noxious stimuli. Three doses of orally administered tramadol (5.0, 10.0, & 20 mg/kg, PO, BID) will be compared to three doses of sustained-release oral morphine (0.5, 1.0, & 2.0 mg/kg, PO, BID) at one, two, and seven days of oral therapy. The results of this proposed research would have direct benefits to any dog-experiencing moderate to severe pain persisting for periods of up to one week or more.

2. Evaluation of a Pulsed Electromagnetic Field to Provide Postoperative Analgesia in the Dog Following Ovariohysterectomy

The purpose of this study is to follow-up on a previous pilot study to determine if pulsed electromagnetic field (PEMF) therapy reduces postoperative pain and anxiety following routine ovariohysterectomy (spay) in dogs. The results of that pilot study, conducted on 16 dogs, suggested that PEMF augmented morphine analgesia thereby improving the control of pain in the postoperative period. We propose to evaluate behaviors in a larger number of dogs (n = 100) in the immediate postoperative period and to obtain owner evaluations for three (3) days postoperatively. The analgesic properties of the PEMF will be evaluated in dogs pretreated, before surgery, with either morphine or fentanyl. Morphine generally provides approximately 4 hours of analgesia following subcutaneous (SQ) administration, whereas fentanyl provides analgesia lasting from 15 minutes to one hour. Thus, we hope to determine if PEMF will augment the effects of morphine, as suggested by the results of the pilot study, and if PEMF will provide analgesia following a short acting opioid. All dogs will receive an analgesic prior to surgery, either fentanyl or morphine; therefore, there will be no true control group (no analgesia). Any dog appearing to be painful will be administered postoperative analgesics.

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