Evaluating Acute Post-Surgical Pain

J. Gaynor
Colorado State University, Fort Collins, CO, USA.

This summary represents a series of research projects over the last several years investigating the efficacy of several modalities for the alleviation of acute post surgical pain. The first project was performed in research animals while the others involved clinical patients.

Opioid Research

Analgesic Efficacy of Fentanyl Patches in Sheep following Orthopaedic Surgery

The purpose of this study was to compare the analgesic efficacy of transdermal fentanyl and oral phenylbutazone for the treatment of postoperative orthopedic pain. Sixteen ovariectomized sheep underwent ceramic calcium phosphate prosthesis implantation of the knee, with the goal of finding a more effective way of anchoring artificial hips in postmenopausal women. Eight of the sixteen sheep received transdermal fentanyl, while the other eight were administered phenylbutazone. Blood samples were collected preoperatively and at 24, 48, and 72 hours postoperatively to determine plasma cortisol and fentanyl levels. All sixteen sheep had identical abdominal wraps, making their analgesic type indistinguishable to a group of eighteen evaluators, who rated the sheep 24, 48 and 72 hours postoperatively based on a list of criteria, including a quantitative scale and a visual analogue scale. The quantitative scale included categories to rate overall comfort level (0 - 4), movement following the surgery (0 - 4), flock behavior (0 - 3), feeding behavior (0 - 3), and respiratory rate (0 - 3). The visual analogue scale consisted of a ten centimeter horizontal line, marked full weight bearing on one extreme, and non weight bearing on the other extreme, and evaluators were asked to clearly mark their observation. Data were analyzed with a one-way ANOVA for repeated measures. Data were considered significant when P < 0.05. Sheep with transdermal fentanyl had plasma levels consistent with analgesia in other species, and had significantly lower plasma cortisol levels compared to the sheep receiving phenylbutazone. The transdermal fentanyl sheep were also found to be significantly more mobile in the category of movement and had more normal flock behavior, as compared with the oral phenylbutazone group. There were no other differences between the groups. Transdermal fentanyl therefore appears to provide equivalent, if not better analgesia than oral phenylbutazone for postoperative orthopedic pain using the criteria in this study.

Nonsteroidal Anti-Inflammatory Drug Research

The Effect of Preoperative Oral Carprofen on Postoperative Pain in Dogs Undergoing Knee Surgery

Carprofen is an oral nonsteroidal anti-inflammatory drug commonly used for the treatment of chronic osteoarthritic pain. The injectable formulation has some efficacy for the treatment of acute surgical orthopedic pain. The purpose of this project was to assess the efficacy of oral preoperative carprofen for the control of postoperative pain in dogs undergoing knee surgery for repair of ruptured cranial cruciate ligaments. This was a randomized, placebo controlled, parallel study that investigated the effectiveness of carprofen compared to placebo. Nineteen dogs presented to the CSU VTH were entered into the study and randomly assigned to the carprofen group (C)(n=10) or placebo (P)(n=9). Dogs received either a loading dose of carprofen (2.2 mg/kg PO BID) or placebo starting 24 hours prior to surgery including the morning of surgery. The placebo contained lactose and liver flavoring. Pain was assessed using a pain scoring system, visual analog scale, and a loaded pressure threshold device preoperatively, and at 1, 2, 4, 6, 24, and 48 hrs and 10 and 21 days postoperatively. Treatment continued for 21 days. Blood for cortisol analysis was drawn at all assessment times. Data were analyzed using a likelihood based mixed effect model repeated measures. Data were considered significant if p < 0.05. Eight of 10 C dogs and 5/9 P dogs were given at least 1 dose of morphine. The mean relative dose of morphine was greater in the C group at 1 (p= 0.01) and 24 hrs (p=0.02). Heart rate and respiratory rate decreased postoperatively in a similar manner for both groups. There were no significant postoperative differences in cortisol levels or any measured variable. It appears
that the scoring system used was not sensitive enough to detect differences in pain between a known analgesic and a placebo.

**Acupuncture Research**

**Acupuncture for Cruciate Repair Pain - A Retrospective Study**

Medical records were searched for dogs receiving acupuncture for cranial cruciate ligament repair in 1998. An equivalent number of dog records were searched for patients having the same procedure but not receiving acupuncture post-operatively. There were 19 dogs in each group. All dogs were anesthetized in an equivalent manner: opioid, tranquilizer, and anticholinergic as premedication, hypnotic for induction, and gas anesthesia for maintenance. The acupuncture group received acupuncture at the end of the procedure prior to awakening. The following technique was used: GB 33 - GB 34; LIV 8 - SP 9, Xiyan. Each pair of points was connected to an electroacupuncture unit using 2.5 Hz, AC, continuous stimulation for 20 minutes. Output was adjusted to achieve a vigorous muscle twitch. No twitch developed with the Xiyan points even with maximal output. Dogs receiving acupuncture were anecdotally rated as being more comfortable by attending student doctors. Dogs receiving acupuncture required less doses of postoperative morphine and less postoperative sedation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acupuncture</th>
<th>Nonacupuncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number in group</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Intra-articular bupivacaine</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Intra-articular morphine</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Intra-articular morphine + bupivacaine</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Fentanyl patch</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Epidural</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Immediate postoperative morphine</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>2 or more doses of postoperative morphine</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Additional sedation</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

**Acupuncture Analgesia following Stifle Surgery in Dogs**

Acupuncture has been used for many years in veterinary medicine but little objective information exists as to its efficacy or lack thereof. The purpose of this study was to objectively evaluate the efficacy of acupuncture following stifle surgery in dogs.

Thirty dogs were randomly assigned to one of three groups: acupuncture (A), morphine (M), or placebo (P). Dogs underwent a standard anesthetic to undergo tibial plateau leveling osteotomy for correction of ruptured cranial cruciate. Group A had needles placed around the operated stifle in pairs at GB 33 and GB 34, LIV 8 and SP 9 and XIYAN. Each pair was connected to an electroacupuncture device with continuous stimulation at 2.5 HZ, alternating current for 20 minutes prior to extubation. Group M received morphine (0.1 mg/kg, IV) immediately after extubation. Group P had six needles placed in a systematic manner around the operated stifle in areas believed to NOT be acupuncture points or meridians for 20 minutes prior to extubation. Dogs were assessed by a blinded observer prior to surgery over 24 hours using a multidimensional pain scale, a visual analog scale (VAS) and a pain threshold device. Blood was also drawn at those times for determination of plasma cortisol concentration.

There were no statistical differences between groups in age, weight, pain score, VAS, pressure threshold or cortisol levels. Group A dogs tended to receive morphine earlier than other groups, while Group A and M dogs tended to receive a lower total dose of morphine over 24 hours compared to Group P dogs.

Placebo acupuncture-induced analgesia indicates that accuracy of needle placement may not be important. Acupuncture and placebo acupuncture appear to provide the same degree of analgesia as IV morphine.

**Projects Submitted for Funding**

**Quantitative Evaluation of Carprofen and Acupuncture Analgesic Efficacy in Dogs**

Purpose: The purpose of this study is to simultaneously study the pharmacokinetics and pharmacodynamics of clinically relevant doses of oral and injectable carprofen, which are believed to be efficacious. Additionally, this study will quantitatively assess the differences in analgesia between acupuncture and carprofen by use of quantitative somatosensory
testing.
The specific objectives are:

1. To determine the pharmacokinetics of injectable carprofen.
2. To determine the pharmacokinetics of oral carprofen.
3. To determine the pharmacodynamics of oral carprofen.
4. To determine the pharmacodynamics of injectable carprofen.
5. To determine the effective analgesic plasma levels of carprofen.
6. To determine the analgesic efficacy of acupuncture.

Future

The next step is to take the available information and start transferring it to geriatric and cancer patients whose physiology may differ from the normal patient. We hope to determine if the thermal threshold, and pharmacokinetics / pharmacodynamics of various analgesic drugs in these patients differs from the research setting so that we can provide better and potentially more appropriate analgesia.

All rights reserved. This document is available on-line at www.ivis.org. Document No. P0521.1202.