A RANDOMIZED TRIAL OF AMITRIPTYLINE VERSUS GABAPENTIN FOR NEUROPATHIC PAIN IN CHILDREN

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Introduction: Treatment of neuropathic pain and complex regional pain syndrome requires a multimodal approach of pharmacologic, physical, and psychological therapies. While amitriptyline and gabapentin are our front line drugs for treating neuropathic pain, no studies have yet compared them directly to determine which drug might be better for relieving pain, disability and sleep disturbances(1,2). Our primary study objective was to compare the efficacy of gabapentin and amitriptyline for treating neuropathic pain in children in a randomized controlled trial (RCT). Secondary objectives were to evaluate changes in children's disability and sleep.

Methods: REB ethical approval was obtained prior to study initiation and patient consent/ascent was obtained prior to commencement of each drug trial. Eligible participants ranged from 8 to 17 years of age. Diagnosis of neuropathic pain (pre 2011 NP classification) was made at The Hospital for Sick Children’s Chronic Pain Clinic. Electrocardiograms were performed on all patients prior to study to rule out conduction abnormalities. Patients were prescribed a regimen of pharmacologic, physical, and psychological therapy. Patients received either gabapentin (300 mg tid) or amitriptyline (10 mg qhs) with capsules matched for size and dosing regimen matched with appropriate placebos for a 6-week, triple-blind (patient, physician, data analyst) RCT. Patients completed weekly interviews to obtain outcomes and attended an in-hospital interview at 6 weeks. Primary outcome was a change in usual (i.e., past week) pain intensity from baseline to 6-weeks as measured by an 11-point Colored Analog Scale (3).

Results: Thirty-four patients (82% female) were randomized to amitriptyline or gabapentin. Two patients allocated to the amitriptyline group were ineligible due to a contraindicated condition identified at start of trial. Three participants were discontinued from gabapentin and amitriptyline groups (2 and 1, respectively) due to adverse events deemed unrelated to study medications. The primary analysis was based on 29 patients having completed the study. Mean pain intensity at baseline was comparable for 2 groups: 6.5±1.4 for amitriptyline and 5.3±2.6 for gabapentin. At the end of the 6-week trial, mean usual pain intensity was 5.0±3.0 for amitriptyline (a difference of -1.5 from baseline) and 3.3±2.4 for gabapentin (a difference of -2.0 from baseline). Usual pain scores did not differ significantly between groups (p > .05, independent sample t-tests).

Discussion: Based on our data, our standard dose of amitriptyline and gabapentin are effective in reducing usual pain intensity ratings in a 6 week trial for children and adolescents with neuropathic pain.

References:
Introduction: Substitution of opioid medication by beta-blockers during laparoscopic cholecystectomy has been shown to reduce both fentanyl consumption and postoperative nausea in the post-anesthesia care unit (PACU) [1]. Increasing evidence suggests an association between opioid use and post-operative chronic pain [2]. There are also laboratory evidences of interaction between opioid and cancer recurrence [3]. In regards to breast cancer, the intensity of acute postoperative pain is a risk factor for the development of post-mastectomy pain syndrome. This study was designed to evaluate possible benefits of opioid-free general anesthesia early in the PACU and on chronicisation of pain in oncological breast surgery.

Method: This prospective, randomised, double-blinded protocol was designed to compare the effect of intraoperative fentanyl versus beta-blockers in breast oncological surgery. This abstract represents the interim analysis of 36 patients. Internal ethics review board approval was obtained. All enrolled patients received a multimodal co-analgesic regimen consisting of acetaminophen, gabapentin, ketorolac and ketamine in addition to dexamethasone and ondansetron. Induction was achieved with propofol and fentanyl 3 μg/kg for the control group (CG, n = 18) or esmolol 1 mg/kg for the beta-blocker group (BB, n = 18) with rocuronium for muscle relaxation. Anesthesia was maintained with sevoflurane in an air/oxygen mixture. Per-operative tachycardia and hypertension were managed with titrated doses of fentanyl 50 μg IV (CG) or metoprolol 2.5 mg IV (BB). Intravenous fentanyl was given as needed in the PACU for both groups. Phone interviews were conducted up to 6 months after surgery to assess presence of chronic pain.

Results: Baseline characteristics were similar between the two groups. No significant difference on postoperative fentanyl use was demonstrated: 43.1 ± 14.2 μg (CC) versus ± 30.7 μg (BB) (P = 0.389). The occurrence of nausea was also similar (27.8%, CC, versus 16.7%, BB) (P = 0.691). There was no significant difference in the incidence of perioperative bradycardia, hypotension and total dose of ephedrine given between the 2 groups. Chronic pain defined by use of opioid medication 6 months after surgery was limited to only one patient in the control group (5.6%) (P = 1).

Conclusion: Substitution of fentanyl by beta-blockers for breast cancer surgery in the per-operative period did not reduce post-operative pain scores, postoperative fentanyl dosage, did not diminish the occurrence of nausea and did not shorten the time spent in the PACU. Chronic post-mastectomy pain did not differ between the groups although its incidence was much lower than previously described in the literature. This interim analysis suggests that opioid-free anesthesia may be an equivalent technique to traditional anesthesia for this surgical population, although it does not appear to provide any significant advantage on acute or chronic post-mastectomy pain.

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Introduction: In the developed world, adequate pain control is a normal part of surgical care, however, this is not the case in sub-Saharan Africa. Ketamine’s role in postoperative analgesia is documented, yet its use in developing nations has not been well studied.1,2 The purpose of our study is to determine a subcutaneous (SC) dose of ketamine for use in a future randomized control trial (RCT) that is both efficacious in reducing postoperative pain scores, and does not result in significant side effects.

Methods: This study was conducted in a sub-Saharan African nation, and as such, Canadian and African university research ethics board approval, local hospital research committee approval, and individual patient consent to conduct and publish the study were obtained. Thirty-one subjects undergoing major abdominal, orthopedic, or gynecologic surgery were recruited. In addition to standard postoperative care, subjects received five SC doses of ketamine at scheduled intervals: on arrival in recovery room, again that evening, then morning and evening on postoperative day one, and in the morning of postoperative day two. Pain scores were recorded using a zero to ten point numerical rating scale in the recovery room, and on the mornings of postoperative days one and two. Patients received 50 mg of ketamine for both the first and second doses, with the subsequent three doses adjusted according to pain and side effects. We considered a significant reduction in pain to be a change of 3 or more points on a numerical rating scale within a 24-hour period.

Results: Mean pain scores in the recovery room and on postoperative days 1 and 2 were 9.39, 5.07, and 2.41, respectively. The overall mean ketamine dose that was efficacious in pain reduction in the 29 patients without side effects was 0.89 mg/kg.

Discussion: Lack of resources including staffing, analgesic drugs, and proper education on pain control are barriers to the delivery of post-operative pain relief in many sub-Saharan African nations. Most patients enrolled in our study received 100 mcg of fentanyl in the operating room, followed by occasional doses of acetaminophen, NSAIDs, or intra-muscular meperidine. The inclusion of subcutaneous ketamine in addition to all standard analgesic medications resulted in drastic decreases in patients’ postoperative pain scores (see graph). While some of the decrease in pain can be attributed to a differing cultural perception of, and reaction to pain, it is likely that ketamine played a role in improving patient comfort following surgery. As such, we will plan an RCT for determining the efficacy of subcutaneous ketamine in reducing postoperative pain, using a dose of 1.0 mg/kg twice a day.

References:
Introduction: Intrathecal morphine has the potential to provide prolonged analgesia following surgery but this comes at a risk of opioid side effects including the chance of delayed respiratory depression. Controversy remains as to the optimal dose and indications for intrathecal morphine. Current limitations in literature include variability in study design, dosing regimens and lack of outcomes with adequate sample sizes. The purpose of this meta-analysis of randomized controlled trials was to determine the efficacy of intrathecal morphine in reducing pain scores after lumbar spine surgery and the resulting incidence of opioid side effects and analgesia related adverse events.

Methods: A literature search of randomized control trials (RCTs) was conducted. The search yielded greater than 600 citations and a total of 10 trials were selected based on an 'a priori' inclusion criteria. VAS scores were grouped into six-hour time frames. Results were analyzed in terms of low dose (less than 150 mcg) or high dose (more than 150 mcg) ITM, or combined dose (both less than and more than 150 mcg). The incidence of side effect profiles related to ITM dosing was also analyzed. Odds ratios with corresponding confidence intervals were calculated for all outcomes using a random-effects model.

Results: VAS scores were available for all 10 trials, 520 patients were randomized and data was available for 453 patients that met our inclusion criteria. Compared to placebo, the pooled results show that both low and high dose ITM groups had significantly lower VAS scores at 0-6 hours [Weighted Mean difference (WMD) of -23.18 (95% Confidence Interval (CI) of -37.66 to -8.70)), 6-12 hours [WMD -11.76 (CI -22.92 to -0.60]), and 12-18 hours [WMD -12.04 (CI -20.60 to -3.49)]. Compared to the control group, the ITM high and low dose groups combined had a significantly higher incidence of pruritus (Odds Ratio with 95% CI of 3.99 (1.78, 8.91)) as well as a significantly lower incidence of sedation [OR 0.35 (0.12, 1.00)]. There was no significant difference between groups regarding nausea, respiratory depression, urinary retention, and post-dural puncture headache.

Conclusion: The addition of intrathecal morphine provides superior post-operative analgesia up to 18 hours, for lumbar spine surgery. Pruritis is the main side-effect that can be expected regardless of dosing. Despite concern for increased sedation with intrathecal morphine, our study results indicate that the incidence is actually reduced when compared to control group.

References: None cited in Abstract
Introduction: Chronic pain (CP) complaints account for 12-16% of emergency department (ED) visits, with 7% of patients visiting frequently. Increased use of the ED for non-urgent medical conditions such as CP has come to the forefront as ED resources are becoming less accessible. The purpose of this study was to understand factors leading CP patients to present to the ED.

Methods: This is a prospective, cross-sectional mixed-method study. Surveys and one-on-one interviews were conducted by medical residents during 30 randomly selected ED shifts between July - August 2013. Included study participants had: 1) pain as a primary concern for their visit; and 2) pain lasting greater than 3 months. The following validated surveys were used to assess each patient: Brief Pain Inventory, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, Insomnia Severity Index-7, Posttraumatic Stress Disorder Checklist-Civilian Version, and Screener and Opioid Assessment for Patients with Pain. Demographic information was collected. The study protocol was approved by our institution’s research ethics board.

Results: 59 patients met the inclusion criteria. Patients were predominantly women (64.4%), caucasian (79.9%), and had a family physician (85%). Average patient age was 46.4 years (SD=16.8). The primary reason for an ED visit was an inability to cope with pain (Table 1). Mental health problems were common: 61% had moderate to severe depression, 44.1% had moderate or severe anxiety, 44.1% had posttraumatic stress disorder (PTSD), 45.8% had clinical insomnia, and 42.4% demonstrated opioid misuse. There were no statistically significant differences between males and females. 79.7% of patients had visited the ED in the previous 12 months for their CP. Patients were primarily interested in: more effective medications (50.8%), having a health professional explain the cause of their pain (47.5%) and a Pain Clinic referral (40.7%)

Discussion: Poor coping strategies have been associated with increased pain, depression, disability and poor psychological adjustment. Poor coping strategies may also explain why CP patients seek help from the ED. We found that the majority of patients were interested in alternative methods to address their CP. The ED is not the ideal setting for management of complex CP issues. Interventions that target CP patients may lead to a better use of resources and improve social and clinical outcomes. These interventions should target adaptive coping strategies and address the high levels of depression, anxiety, insomnia and PTSD seen in this group. Understanding these factors may aid in the implementation of an interdisciplinary pain program to specifically address CP patients seeking help from the ED.

References:
1. Australas Emerg Nurs J 2013 16: 30-36
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<tr>
<th>Reason for ED Visit</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>&quot;I couldn’t cope with my pain&quot;</td>
<td>61%</td>
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<tr>
<td>&quot;I was worried about what was causing my pain&quot;</td>
<td>15.3%</td>
</tr>
<tr>
<td>&quot;My doctor advised me to come&quot;</td>
<td>10.2%</td>
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<tr>
<td>&quot;My family and/or friends thought I should come&quot;</td>
<td>5.1%</td>
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Introduction: The present study investigated whether pain and brain responses to pain stimulation are modulated during transcutaneous electrical nerve stimulation (TENS) treatment. We compared pain perception and brain responses to pain stimulation with and without TENS treatment in healthy volunteers.

Methods: Twenty-four participants aged 22.46 ± 3.92 years were recruited. Local ethics committee approval was obtained. During functional magnetic resonance imaging (fMRI) scanning, thermal pain was applied to the lateral skin of the left lower leg through a thermode that was located between the cathodes (fibular head level) and anodes (ankle level) of the TENS device. The same pain experiments were conducted twice for each participant, once with the TENS treatment (TENS condition) and once without (control condition). The participants were given an advance visual cue 2 s prior to pain stimulation. Participants then received a 15-second, 45°C pain stimulation, followed by a 30-second resting period. This 47-second (2+15+30) block was repeated 10 times in both conditions. We selected TENS intensities that were strong yet comfortable for each individual participant. In the TENS condition, TENS (80 Hz, 60 μs, 15 s) was applied to participants at the time pain stimulation started. When pain stimulation ended, TENS application ended. In the control condition, pain was applied to participants in the same way it was in the TENS condition, but without TENS treatment. For the first 5 seconds of the 15-second TENS application period, participants in the TENS condition received their own comfortable TENS intensity (CTI); for the second 5-second period, they received CTI plus 1 mA; and for the third 5-second period, they received CTI plus 2 mA. Pain threshold (°C) was defined as the lowest temperature at which the participants reported pain. Ratings were assessed using a numerical rating scale; 0 = no pain/anxiety/unpleasantness; 100 = maximum imaginable pain/anxiety/unpleasantness. Images were acquired using a 3T MRI scanner.

Results: Pain thresholds were significantly lower in the control condition than in the TENS condition (p < 0.001). Pain and unpleasantness ratings were significantly higher in the control condition than in the TENS condition (p < 0.001). The anterior cingulum and bilateral thalamus were activated more significantly during pain stimulation in the control condition than in the TENS condition (false discovery rate = 0.05). The postcentral cortex and superior parietal cortex were activated more significantly during pain stimulation in the TENS condition than in the control condition (false positive rate = 0.05).

Discussion: The postcentral cortex and superior parietal cortex may be activated by TENS. Activation of the postcentral cortex and superior parietal cortex may reduce pain perception during TENS treatment.

References: