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(396) Nicotine effect on the efficacy of hydrocodone and oxycodone in chronic pain patients

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Hydrocodone and oxycodone are frequently prescribed for the control of moderate to severe pain. Smoking cigarettes however, has been reported to decrease the efficacy of hydrocodone in chronic pain patients. This study compared the efficacy of hydrocodone and oxycodone in smokers and nonsmokers. Following IRB approval signed informed consent , smokers and nonsmokers with chronic low back pain were assigned randomly to one of four groups, (Group I, hydrocodone-nonsmoker, Group II, hydrocodone-smoker, group III, oxycodone-non-smoker, Group IV, oxycodone-non-smoker) each consisting of thirty patients to receive equivalent doses of hydrocodone or oxycodone daily for 30 days for pain relief. Each patient was prescribed hydrocodone 7.5 mg with acetaminophen 325 mg in Groups I and II every 6 hours while patients in Groups III and IV received oxycodone 5mg with acetaminophen 325 mg, every 6 hours as needed. Patient VAS pain scores (0-10) were recorded daily. Urine continine, hydrocodone/hydromorphone and oxycodone/oxymorphone levels were done at the beginning and end of this study and CYP450 2D6 and 3A4/3A5 genetic tests were done at the beginning. Statistical analysis was done using Student's t test and the Mann-Whitney test where indicated with $p \leq 0.05$ considered significant. There were no demographic differences between the groups. The mass of hydrocodone consumed and the pain scores within the hydrocodone groups were higher in Group II, while the oxycodone groups did not statistically differ ($p \leq 0.05$) at the end of the 30 day study. Smokers prescribed hydrocodone had significantly ($p \leq 0.05$) less pain relief than nonsmokers while there were no significant difference within the oxycodone groups. It is concluded that hydrocodone efficacy within groups is less in cigarette smokers while oxycodone efficacy within groups does not appear to be significantly affected by cigarettes in the population studied. The reason for this finding is unknown.

(397) Transdermal fentanyl compared to transdermal buprenorphine on descending pain modulation in human experimental models

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Transdermal preparation of fentanyl, a μ-receptor agonist, and buprenorphine, a partial μ-receptor agonist and K-receptor antagonist, are used in the treatment of moderate to severe pain. This literature review aimed to compare the effect of these two transdermal patches on descending pain inhibition in human experimental pain models to determine rational treatment guidelines. A Pubmed search was performed using key words transdermal fentanyl and transdermal buprenorphine and 4 randomized double-blind placebo controlled studies were evaluated for levels of evidence. Experimental pain models aimed to induce deep pain, superficial pain, allodynia, and hyperalgesia. Pain stimulus included pressure at the tibial bone, pressure distal to the elbow joint, cutaneous thermal stimulation, cold pressor test, cutaneous electrical stimulation, nerve-growth factor induced muscle soreness, UVB light burn injury, and intradermal capsaicin. Both low dose transdermal buprenorphine and fentanyl provided significant analgesic effect compared to placebo. Buprenorphine and fentanyl showed tissue-differentiated analgesic effects, which may be useful in understanding individual treatment response. Buprenorphine appeared to have a greater effect on bone associated pain and fentanyl appeared to have a greater effect on cold pressure induced pain. Incidences of adverse effects were similar between fentanyl and buprenorphine. However, human experimental pain models were performed in healthy subjects, and may not accurately represent response in chronic pain patients.

F16 Opioids in Non-Cancer Pain

(398) Individual differences in endogenous opioid function predict analgesic responses to morphine

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Factors contributing to differential responses to opioid analgesic medications across individuals are not well understood. This study tested whether individual differences in endogenous opioid systems contribute to variability in responses to a prototypic exogenous opioid analgesic. Participants included 18 healthy individuals and 26 individuals with chronic low back pain (LBP), all using no opioid analgesics. Participants attended 3 identical sessions during which they received either intravenous naloxone (8mg), morphine sulfate (0.08mg/kg), or saline placebo, and then underwent an ischemic forearm pain task followed by a computerized heat pain task (Medoc TSA-II). Within-subject differences between acute pain responses in the placebo condition versus the naloxone and morphine conditions were derived as indices of endogenous opioid function and exogenous opioid analgesic responses, respectively. Correlation analyses indicated significant inverse associations between endogenous opioid function and exogenous opioid responses for ischemic threshold ($r = -0.46$, $p<.01$) and tolerance ($r = -0.63$, $p<.001$), intra-task numeric intensity ratings (NRS; $r = -0.70$, $p<.001$), and post-task McGill Pain Questionnaire (MPQ) Sensory ($r = -0.43$, $p<.01$) and Total ($r = -0.41$, $p<.01$) scores. All thermal pain task outcomes revealed significant inverse associations between endogenous opioid function and exogenous opioid responses, including heat pain threshold ($r = -0.43$, $p<.01$) and tolerance ($r = -0.60$, $p<.001$); MPQ Sensory ($r = -0.65$, $p<.001$), Affective ($r = -0.63$, $p<.001$), and Total ($r = -0.64$, $p<.001$) scores, and visual analog pain intensity ($r = -0.50$, $p<.001$) and unpleasantness ($r = -0.45$, $p<.01$) measures. Ten of these 12 correlations remained significant after controlling for differences in placebo pain level (partial correlations). Multivariate analyses indicated that independent of LBP status, endogenous opioid function indices for both ischemic and thermal tasks predicted the set of morphine responses for the respective pain task. Results highlight that individual differences in endogenous opioid function account for substantial inter-individual variability in morphine analgesic responses. Findings may have implications for personalized pain medicine.

(399) Duration of use of extended-release oxycodone and morphine among adults with cancer and non-cancer pain

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Duration of use of extended-release (ER) opioids in US clinical practice has not been extensively published in the literature. The objective of this study was to assess duration of ER oxycodone and ER morphine use, two commonly used ER opioids, among cancer and non-cancer pain patients. Using data from a national commercial insurance database (MarketScan; January 2008 through September 2011), patients ≥18 years old with a new ER oxycodone or ER morphine prescription and 24 months insurance enrollment (6 months before and 18 months after index prescription) were identified. Existing patients (those with prior prescriptions in the 6 month baseline period) were excluded. The primary measure was duration of continuous use (no gaps in supply ≥15 days; sensitivity analysis ≥30 days). Survival analysis was used to compare time to discontinuation of continuous use. There were 43,519 new ER oxycodone users and 22,414 new ER morphine users. Cancer diagnoses were identified for 9% of ER oxycodone and 10% of ER morphine patients. Most patients discontinued use by 3 or 6 months (ER oxycodone: 80% and 86%, respectively; ER morphine: 72% and 81%, respectively). Time-to-event analysis indicates a rapid drop in continuous use in the first month (>50% decline), a less rapid decline between months 1 and 6 (ER oxycodone: approximately 30% to 15%; ER morphine: approximately 45% to 20%), and appear relatively stable (approximately 10-20%) thereafter, indicating that patients treated for 6 months will likely continue for up to 18 months. ER oxycodone results were similar regardless of cancer diagnosis; ER morphine patients without a cancer diagnosis were slightly more likely to continue longer term treatment than those with a cancer diagnosis. Overall, most patients dispensed a new ER oxycodone or ER morphine prescription had a non-malignant pain condition and less than one in five received continuous treatment for >6 months.