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F05 Cancer Pain - Opioids

(344) Rapid opioid titration protocol for acute on chronic cancer pain in the emergency department setting: a pilot study

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Acute on chronic cancer related pain can be difficult to manage in the emergency department setting. Patients may have significant opioid tolerance, thus rendering the routine doses administered in the emergency department ineffective. Most emergency medicine physicians and nurses are not familiar with the calculations necessary to dose intravenous opioid medication appropriately in the opioid tolerant patient with severe pain. Baseline data from our institution indicate that our patients with severe cancer pain wait a median time of 133 minutes until they receive their first dose of pain medication and 72 minutes until they receive their second dose. Our data also show that a vast majority of our physicians use a "one time" order for their opioid medication rather than an order set with scheduled dosing. To address this, we initiated an ED Cancer Pain Protocol order set with scheduled intravenous opioid medication every 15 minutes until the patients pain score is to their satisfaction or until they have a reduction in their pain score to <5. The protocol accounts for opioid naïve patients and opioid tolerant patients. We also posted an educational worksheet for conversion of common outpatient opioid medications to oral morphine equivalents and calculating the appropriate acute pain dose for opioid tolerant patients. We found that although this practice is common in palliative care settings this was a novel concept for many of our emergency medicine physicians. Our preliminary data indicate that after the protocol was initiated the median time to administration of second opioid dose decreases from 72 min to 41 min. We hope this pilot data will serve as rationale for large scale implementation of this protocol in future collaborating community or academic centers. This project was funded by a grant from the American Cancer society.

(345) Efficacy and safety of subcutaneous methylnaltrexone in advanced illness patients with opioid-induced constipation: a responder analysis

S Nalamachu, J Pergolizzi, R Taylor, N Slatkin, A Barrett, J Yu, E Bortey, C Paterson, and W Forbes; multicenter study sponsored by Progenics Pharmaceuticals Inc., Tarrytown, NY

Opioid-induced constipation (OIC) is a distressing side effect of chronic opioid therapy, evidenced in up to 90% of advanced illness patients taking long-term opioids. Subcutaneous methylnaltrexone (MNTX) has been shown to be efficacious and safe in this patient population, although factors that determine optimal responsiveness have not been elucidated. The objective of this post-hoc analysis was to examine the influence of demographic and baseline characteristics on efficacy and tolerability of MNTX in advanced illness patients with OIC. Data were pooled from 2 randomized, double-blind, placebo (PBO)-controlled, Phase 3 studies (n=287) of MNTX (0.15 and 0.3 mg/kg). Subgroup analyses of the primary outcome measure, proportion of patients with a rescue-free bowel movement (RFBM) within 4 hours of first dose, were conducted for gender (female/male), age (<65/≥65 years), primary diagnosis (cancer/noncancer), and baseline morphine equivalent dose (<150/≥150 mg/d). Overall, 54.1% and 58.2% of patients treated with MNTX 0.15 and 0.3 mg/kg experienced a RFBM within 4 hours, versus 14.6% for PBO-treated patients (P<0.0001 for both doses vs. PBO). Responsiveness to MNTX was significantly greater than PBO in all subgroups (range of MNTX responses: 48.1%-73.3%, range of PBO responses: 10.2%-18.8%, P<0.0001 for nearly all comparisons). The largest differences from PBO were observed for noncancer patients taking MNTX 0.3 mg/kg (70.0% vs. 12.8%, P=0.0002) and for patients maintained on ≥150 mg/d oral morphine taking MNTX 0.3 mg/kg (73.3% vs. 16.7%, P<0.0001). Common adverse events were abdominal pain (pooled MNTX: 27.9%, PBO: 9.8%), flatulence (13.3%, 5.7%) and nausea (10.9%, 4.9%) Tolerability was generally comparable across subgroups. These findings demonstrate that in advanced illness patients with OIC, MNTX produces a rapid and robust laxation response that is consistent across gender, age, primary diagnosis, and baseline opioid use. MNTX 0.3 mg/kg may elicit particularly favorable responses in select subgroups. Development of abstract supported by Salix Pharmaceuticals, Inc.

(346) Effect of subcutaneous methylnaltrexone on patient-reported outcomes in advanced illness patients with opioid-induced constipation

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Opioid-induced constipation (OIC) is a common side effect of opioid therapy that can be more distressing to chronic pain patients than the underlying pain syndrome. Subcutaneous methylnaltrexone (MNTX) has demonstrated efficacy in increasing the frequency of rescue-free bowel movements (RFBMs) in advanced illness patients with OIC. Addressing more subjective, patient-reported outcomes (PROs) in OIC patients may lead to improved symptom control, quality of life, and satisfaction with therapy. The objective of this analysis was to examine the impact of MNTX on PROs of constipation distress, BM difficulty, and Global Clinical Impression of Change (GCIC), all pre-specified secondary efficacy assessments in a 2-week, randomized, double-blind, placebo (PBO)-controlled trial. Advanced illness patients (n=133) maintained on stable doses of opioids, and who had failed prior laxative therapy, were treated every other day with MNTX 0.15 mg/kg or PBO. Demographic and baseline characteristics were similar between groups. At baseline, 60% and 63% of patients in the PBO and MNTX groups reported "quite a bit" or "very much" constipation-related distress. On Day 1 of treatment, 52.7% of MNTX treated patients reported that constipation distress had "improved" vs. 29.7% of PBO-treated patients, a finding that persisted throughout the study. For doses of MNTX and PBO that resulted in a RFBM within 4 hours, the BM difficulty was rated as "moderate," "considerable," or "great" for 33.0% (58 of 176) of doses in the MNTX group vs. 50.0% (24 of 48) of doses in the PBO group. Regarding CGIC, 73.5% (Day 7) and 67.9% (Day 14) of MNTX-treated patients reported that bowel status was "Better," vs. 35.1% and 44.6% of PBO-treated patients. These PRO findings complement objective assessments of MNTX-related improvements in bowel function, and indicate that MNTX decreases symptom severity across several dimensions in patients with advanced illness. Development of abstract supported by Salix Pharmaceuticals, Inc.

F08 Cannabinoids

(347) Effect of smoked cannabis on painful diabetic peripheral neuropathy

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There is emerging evidence that the cannabinoids are effective in neuropathic pain. A randomized, double-blinded, placebo controlled crossover design methodology was conducted in sixteen patients with painful diabetic peripheral neuropathy (7 women, 9 men). Subjects participated in four sessions where they were exposed to placebo, low (1% tetrahydrocannabinol, THC), medium (4% THC), or high (7% THC) dose of cannabis. Baseline spontaneous pain, evoked pain and cognitive testing were performed. Subjects were then administered aerosolized cannabis or placebo and the pain intensity and subjective highness score was measured at 5, 15, 30, 45, 60 minutes and then every 30 minutes for an additional 3 hours. Cognitive testing was performed at 5 and 30 minutes and then every 30 minutes for an additional 3 hours. Area under the spontaneous pain versus time curve was the primary endpoint. Overall effect of cannabis dose on spontaneous pain was significant (p=0.029) with only the high dose reaching significance (p=0.013). There was an overall difference in mean lowest achieved spontaneous pain score between groups (0.044) with the high dose achieving the lowest mean pain score (p=0.017). There was a trend for significant effects of the cannabis on evoked pain. Overall effects for brush (p=0.085) and pin prick (p=0.199) pain trended toward significance with the high dose most effective (brush p=0.057, pin prick p=0.144). There was a dose dependent increase in the subjective highness score reported after cannabis exposure which persisted into the late time course. There was a significant difference in two of the three neuropsychological tests (Paced Auditory Serial Addition Test, p=0.005; Trail Making Test B, p=0.049; Trail Making Test A, p=0.362). These results are consistent with evidence in other neuropathic pain syndromes and suggest additional research is warranted.