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Pretreatment with duloxetine may prevent chemotherapy-induced neuropathic pain: A pilot study

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Statement of the Problem and Objectives: Approximately 70% of patients receiving oxaliplatin for colorectal cancer develop painful oxaliplatin-induced peripheral neuropathy (OIPN-P). OIPN-P can persist up to 11 years after treatment is stopped, affecting quality of life and contributing to falls, depression and sleep loss. OIPN-P also necessitates decreased dosage during treatment, thereby decreasing treatment effectiveness and increasing mortality risk. The serotonin and norepinephrine reuptake inhibitor, duloxetine is approved for treating OIPN-P, but is effective only in about 50% of patients. Recent work is suggestive that pretreating with tricyclic drugs can prevent onset of OIPN-P, but these drugs have serious side effects. We investigated whether pretreatment with duloxetine would prevent onset of OIPN-P in male and female rats in a model of oxaliplatin-induced hyperalgesia.

Methodology: Rats were pretreated with duloxetine (15 mg; PO) for 7 days prior to and through oxaliplatin treatment and for 20 days post oxaliplatin treatment. Rats were then tested for 6 days after all treatment stopped. The measure used was a 15 g von Frey filament applied to the left foot, which measures hyperalgesia, a sign of neuropathic pain.

Findings: We found that rats pretreated with duloxetine presented with significantly less hyperalgesia through the testing period compared to control and notably for the six days after all treatment stopped ($p \leq 0.003$; $p \leq 0.13$; males and females resp.).

Conclusion and Significance: These pilot study findings are suggestive of the need for further study to determine whether pretreatment with duloxetine can prevent onset of OIPN-P.

Recent Publications:

- Holden J E, Wagner, M A and Reeves B (2018) Anatomical Evidence for Lateral Hypothalamic Innervation of the Pontine A7 Catecholamine Cell Group in Rat. *Neuroscience Letters* 668:80- 85.
- Wagner M A, Jeong Y, Banerjee T, Yang J and Holden J E (2016) Sex differences in hypothalamic-mediated tonic norepinephrine release for thermal hyperalgesia in rats. *Neuroscience* 324:420-9.
- Wardach J, Wagner M, Jeong Y and Holden J E (2016) Lateral hypothalamic stimulation reduces thermal hyperalgesia through spinally descending orexin-A neurons in neuropathic pain. *Western Journal of Nursing Research* 38(3):292-307.
- Holden J E, Wang E, Moes J R, Wagner M, Maduko A and Jeong Y (2014) Differences in carbachol dose, pain condition and sex following lateral hypothalamic stimulation. *Neuroscience* 270:226- 35.

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- Jeong Y, Moes J R, Wagner M and Holden J E (2012) The posterior hypothalamus exerts opposing effects on nociception via the A7 catecholamine cell group in rat. *Neuroscience* 227:144-153.

Biography

Janean E Holden, PhD, RN, FAAN is the Barbara A. Therrien Collegiate Professor of Nursing. She received her PhD from the University of Michigan and did Post-doctoral research in Pharmacology at the University of Illinois at Chicago. Her research focus is on the role of the hypothalamus in descending pain modulation with emphasis on the role of norepinephrine in the spinal cord.

Notes: