In Motion

Highlighting Articles Advancing Pain Research in Canada and the World

Featured article:

Gilron, I., Jensen, T.S., & Dickenson, A.H. (2013). **Combination pharmacotherapy for management of chronic pain: from bench to bedside.** Lancet Neurology, 12(11), 1084-1095. https://doi.org/10.1016/S1474-4422(13)70193-5

This seminal paper is regarded as a foundational review in the field of pain management, providing a comprehensive appraisal of the potential benefits and mechanisms of combination pharmacotherapy for chronic pain.

Key insights from the study:

- **Fundamental Princples:** Drug combinations to develop for chronic pain involve at least 2 drugs which have maximal efficacy, minimal side effects, and differing drug mechanisms to provide additive, or synergistic, analgesia and non-additive side effects.
- **Enhanced Treatment Outcomes:** Using rigorous research methodology, carefully designed analgesic combination trials add to the evidence base for strategic approaches to combine mechanistically distinct chronic pain therapies for improved patient treatment outcomes.

CPN
CHRONIC PAIN NETWORK

Quick Article Link: https://doi.org/10.1016/S1474-4422(13)70193-5

What happened?

Researchers conducted a comprehensive review of clinical concepts, pain treatment mechanisms, and pivotal clinical trials and pharmacological evaluations of the effectiveness and safety of combination pharmacotherapy as compared to monotherapy in the management of chronic pain, including neuropathic pain and fibromyalgia. They explored how different drug classes, such as opioids, antidepressants, and anticonvulsants, can be strategically combined to improve pain relief and patient outcomes.

Why is it important?

The review provides crucial insights into the diversity of pain mechanisms and the potential for enhanced pain management strategies by combining pharmacological treatments that interact favourably. By using high-quality evidence comparing drug combinations to monotherapies, healthcare providers can better understand the synergistic and additive effects of various drug combinations and implement tailored treatment for patients who do not respond adequately to single-drug interventions, ultimately leading to better patient outcomes and improved quality of life.

What now?

Since this pivotal review in 2013, dozens of clinical trials of combination pharmacotherapy for pain have been conducted, many of which were developed according to these principles. These include influential industry-sponsored clinical trials, and newer Canadian trials including the Chronic Pain Network's "CADENCE" trial of an alpha-lipoic acid+pregabalin combination for fibromyalgia. Two Cochrane Collaboration systematic reviews in the area of fibromyalgia (Thorpe et al, 2017) and Neuropathic Pain (Balanaser et al, 2023) supported in part by the CPN, provide an evidence-based review of the efficacy and safety of rigorously studied drug combinations for chronic pain and highlight current challenges and future directions for research in this field. Most recently, the Canadian Institutes of Health Research has recently funded the PRECISE trial, which is led by patient partner, Chris DeBow, CPN Investigator, Ian Gilron, and other members of the CPN. This new trial will evaluate the combination of melatonin and pregabalin to treat pain and disturbed sleep in people suffering from fibromyalgia.