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(Abstracts)

Contents

Nonopioid Drug Combinations for Cancer Pain: A Systematic Review

Gursharan Sohi[1], Augusto Caraeni[2], Dwight E. Moulin[3], Camilla Zimmermann[4], Leonie Herx[5], Ian Gilron[1, 6-8]

1 Department of Anesthesiology & Perioperative Medicine, Kingston Health Sciences Centre, Queen's University, Kingston, Ontario, Canada.
2 Fondazione IRCCS—Istituto Nazionale dei Tumori, Italy.
3 Departments of Clinical Neurological Sciences and Oncology, Western University, Canada.
4 Division of Palliative Medicine, Department of Medicine, University of Toronto, Ontario, Canada.
5 Division of Palliative Medicine, Department of Medicine, Queen's University, Kingston, Ontario, Canada.
6 Department of Biomedical & Molecular Sciences, Queen's University, Kingston, Ontario, Canada.
7 Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada.
8 School of Policy Studies, Queen's University, Kingston, Ontario, Canada.

Introduction: Cancer pain – defined as pain caused by neoplastic disease or its treatment – is extremely common, affecting 80% of cancer patients(1, 2). Currently, standard management of cancer pain relies heavily on opioid analgesics which, while effective, are not benign. Several nonopioid analgesic agents have proved efficacious in managing pain, including anticonvulsant and antidepressant drug classes for treating neuropathic pain etiologies. Existing guidelines do not yet account for the implications of nonopioid combinations for use in treating cancer pain(3). The present systematic review sought to summarize the safety & efficacy of nonopioid drug combinations for cancer pain management.

Methods: Ethics approval was not applicable because this study did not involve human or animal research. The protocol for this review has been previously published and registered in the International Prospective Register of Systematic Reviews (CRD42020183689) on August 20th, 2020. A thorough search of three databases (PubMed, EMBASE, CENTRAL) was conducted in addition to a hand-search of the relevant literature and consultation with experts in pain-management. This review included double-blinded randomized controlled trials (RCTs) which compared nonopioid drug combinations to at least one of the combination's individual components and/or placebo for the treatment of cancer pain in adults. Two reviewers independently reviewed titles and abstracts for inclusion, resolving disagreements through consensus. The primary outcome was the proportion of participants reporting ≥30% pain reduction from baseline OR ≥moderate pain relief OR ≥moderate global improvement. Risk of bias was assessed independently by two authors using the guidelines established by the Cochrane Handbook for RCTs(4). One author completed data extraction for eligible studies; it was determined *a priori* that studies would only be analyzed in combination if they were sufficiently similar in order to avoid clinical heterogeneity.

Results: In total, 8134 citations were imported for review. Preliminary results of this systematic literature search have, thus far, identified three RCTs deemed suitable for inclusion. Matsuoka (2019) demonstrated the superiority of duloxetine vs. placebo in combination with pregabalin for cancer pain relief. Minotti (1998) found no significant difference in pain scores between imipramine, codeine and placebo in combination with diclofenac. Finally, Delanian (2019) found no benefit to pentoxifylline, tocopherol, clodronate combined vs. placebo with an 18-month follow up. Meta-analysis was not performed due to substantial between-study heterogeneity.

Discussion: Regimens of nonopioid agents have not been rigorously trialed in the setting of cancer pain, as illustrated by the low yield of RCTs reviewed in the present study. From the included trials, nonopioid combinations of antidepressant and anticonvulsant drugs remain promising for the treatment of neuropathic cancer pain, although the strength of available evidence is insufficient to derive recommendations for clinical practice. We conclude that this subject merits further study to improve pain management options for cancer patients.

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Optimizing Prescription Sizes by Measuring Post-Discharge Opioid Analgesic Use After Common Ambulatory Orthopedic Surgeries: An Online Survey

Kristin McPhail[1], Ryan Amadeo[1], Scott Wolfe[1], Thomas Mutter[1]

1 Department of Anesthesiology, Pain and Perioperative Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada.

Objective: Postoperative opioid analgesic prescriptions are necessary to manage acute postoperative pain, but can convert opioid naïve patients into chronic users[1]. Optimizing opioid prescription sizes requires balancing interindividual variation in perceived needs with the societal obligation to reduce the amount of unnecessary opioids dispensed into the community[2]. To help inform the optimum prescription with actual data[3] instead of expert consensus[2], we surveyed patients to determine the oral morphine equivalents (OME) prescribed and used during their recovery.

Methods: Ethics approval was obtained from the local REB. This was a cross-sectional, self-administered, anonymous online survey of patients who had recently undergone ambulatory orthopedic surgery. It was conducted at a single outpatient surgical center attended by 13 surgeons. Serial postoperative phone calls were used to assess for eligibility, including internet access, English language facility, and discontinuation of postoperative opioids. Interested participants were sent a link to the survey by email. The authorship group developed the survey with attention to readability and input from non medical acquaintances. The primary outcome was OME used by opioid naïve patients. Patients reported the opioid prescribed, the number of pills remaining and initially prescribed (including refills), and the researchers converted the input to OME[4] for analysis. The goal was to construct histograms of OME used to qualitatively inform prescription size planning, with OME expressed in tablets (1tablet =5mg OME). Predictors of OME used were examined using negative binomial models with significance set at $p<0.05$.

Results: 388 (40.0%) of 971 eligible patients completed a survey between January and August 2020, and 330 (85.1%) filled an opioid prescription, median 47 tablets [interquartile range 30-75]. 26.8% of respondents were more than 60 years old, 47.8% were female and >85% received regional anesthesia or a combined technique. The most common surgeries were shoulder arthroscopy (29.9%), knee arthroscopy (16.2%), anterior cruciate ligament reconstruction (9.2%), and bunion/ hammer toe surgery (8.5%). Histograms of OME use tended to be right skewed (see Figure). In multivariable regressions adjusted for age, surgery/ anesthetic type, use of cold therapy, refills received, pain scores and use of non-opioid co-analgesics, the only significant predictor was OME prescribed ($p\leq0.002$). A 25mg OME (5 tablet) increase in prescription size was associated with an 11% (95% confidence interval (CI) 6%-18%) increase in tablets taken for knee surgery and a 5% (95% CI 2%-8%) increase in tablets taken for shoulder arthroscopy. Chronic preoperative opioid users (n=33) were excluded from histograms and models.

Discussion: Histograms of postoperative opioid use can be used to plan prescription sizes and anticipate the need for refills after common ambulatory orthopedic procedures, despite significant interindividual variation. Larger opioid prescription sizes were affirmed as a predictor of increased postoperative opioid use[5], and warrant continued investigation as a potential target for intervention.

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Figure 1. Oral morphine equivalents used after knee arthroscopy (n=53)