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A07 Meta-Analysis and Systematic Reviews

(136) Adverse event assessment, analysis, and reporting in recent published analgesic clinical trials: ACTTION review and checklist

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The development of valid information about treatment risks and benefits requires consistent and comprehensive data about adverse event assessment and participants' adverse events during randomized clinical trials (RCTs). Despite a 2004 extension of the Consolidated Standards of Reporting Trials (CONSORT) statement recommending the specific harms (i.e., adverse events) information that investigators should report, there is little evidence that published analgesic RCTs adequately adhere to these recommendations. This systematic review builds on prior recommendations by describing a comprehensive checklist for adverse event reporting developed to capture clinically important adverse event information (e.g., the severity of each adverse event causing withdrawal per arm; the duration of adverse events per arm). Using this checklist, we coded adverse event assessment methods and reporting in all 80 double-blind RCTs of non-invasive pharmacologic treatments published in European Journal of Pain, Journal of Pain, and Pain between 2006 and 2011. Across all trials, adverse event reporting was frequently incomplete, inconsistent across trials, and in some cases missing. For example, > 50% of RCTs reported an arbitrarily selected subset of adverse events occurring in the trial and > 40% of trials failed to report any information on serious adverse events [SAEs]. Two specific study characteristics (participant type and sponsor) previously shown to be associated with variability in adverse event reporting were examined. Trials of participants with acute or chronic pain conditions and industry-sponsored trials typically provided more and better quality adverse event data than trials involving healthy volunteers or trials that were not industry sponsored. The results of this review suggest that improved adverse event reporting is needed in analgesic RCTs. We developed an ACTTION adverse event reporting checklist that is intended to assist investigators thoroughly and consistently capture and report these critically important data in publications.

(137) Discrepancies between published and registered primary outcomes in analgesic trials: ACTTION systematic review

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The National Institutes of Health released the trial registry ClinicalTrials.gov to the public in 2000 to increase public reporting and transparency of clinical trials. By 2005, the International Committee of Medical Journal Editors required trial registration for publication. The systematic review we conducted examined whether registered primary outcomes (POs) in analgesic treatment trials correspond with published POs. Trials with publications (n=95) were selected from the Repository of Registered Clinical Trials (RReACT) database, which includes all postherpetic neuralgia, painful diabetic peripheral neuropathy, and fibromyalgia clinical trials registered at ClinicalTrials.gov as of 1/1/2012. POs were identical in 23% of trials; there were discrepancies between registered and published POs in 55% (22% failed to register or publish POs). Common discrepancies were inconsistencies between, or failure to report, the timing of PO assessment in the registry and publication (42%), POs that were more vaguely described in the registry than the publication (38%), or instances where a registered PO was "demoted" to a secondary outcome or omitted from the publication without explanation (16%). When POs were identical, the PO was statistically significant in 81% of the trials. However, when registered and published POs differed, the ultimately published PO was frequently statistically significant (65%), whereas when registered and published POs differed and the publication "demoted" the registered PO, only 1 registered PO was reported as statistically significant, suggesting bias toward publishing statistically significant POs. At best, PO discrepancies may be attributable to carelessness (e.g., failing to report PO assessment timing) or to difficulty uploading registry information. At worst, discrepancies could indicate investigator impropriety (e.g., registering imprecise POs ["pain"], then publishing whichever pain assessment produced statistically significant results). Improvements in registry reporting are needed, as well as greater attention by investigators, journal editors, and reviewers to differences between registered and published POs.

(138) Systematic review of opioid dependence in chronic pain

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Opioid use in the treatment of chronic pain is a complex issue, as people with chronic pain may derive both benefit and harm from their use. The former can include reductions in pain intensity, while the latter can include problematic patterns of use or engagement in activities that meet diagnostic criteria for opioid dependence, a substance use disorder. The identification of individuals who are currently using opioids in a problematic way is of great importance and is highly relevant at the present time given the substantial increases over the past decade in rates of morbidity and mortality associated to prescription opioid misuse. At the present time, however, prevalence estimates of opioid dependence vary widely within the literature, from 0% to 48%. This expansive variation is due to a number of factors including issues of study design and setting, as well as variations in methods and definitions used in order to identify opioid dependence. The purpose of the present project was to perform a comprehensive review of the opioid dependence literature in chronic pain, including a method of evaluating quality of reviewed studies to allow for appropriate weighting of individual studies. This poster will present the results of this review, including an estimate of opioid dependence in those who are prescribed opioids for chronic pain, confidence intervals around this estimate, risk factors for misuse, and guidelines for future study which may assist to increase sensitivity and specificity in accurate identification.

(139) Nalbuphine for the treatment of opioid-induced pruritus: a systematic review

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Opioid-induced pruritus is a common side-effect in patients with acute pain associated with surgery or childbirth. There are several options available to treat opioid-induced pruritus, including nalbuphine. However, it is not known whether nalbuphine offers greater efficacy in treating pruritus without attenuation of analgesia and increase in the incidence of adverse outcomes. A systematic search of studies assessing treatment efficacy of nalbuphine was conducted through Medline, PubMed, Cochrane Library, CINAHL and ProQuest databases. The primary outcome was incidence reduction of pruritus, while the secondary outcomes included analgesia and adverse outcomes. Ten studies that met all inclusion criteria were identified, nine of which were randomized controlled trials and one case report. The incidence of pruritus was higher among patients receiving neuraxial opioids. Nalbuphine provided greater efficacy in treating opioid-induced pruritus when compared to placebo, control or other pharmacologic agents such as diphenhydramine, naloxone and propofol. There was no attenuation of analgesia or increased in sedation with low dose nalbuphine treatment. Further, nalbuphine was associated with incidence reduction of nausea or vomiting; and reversal of respiratory depression. Nalbuphine is superior in treating opioid-induced pruritus when compared to placebo, control, diphenhydramine, naloxone or propofol in patients receiving opioids for acute pain related to surgery or childbirth. Therefore, it is recommended that nalbuphine should be used as first line treatment of opioid-induced pruritus.