Editorial

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OPAL trial: challenging the use of opioid analgesics for acute low back pain and neck pain: a milestone in evidence-based medicine

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Introduction

Low back pain (LBP) and neck pain are serious health problems in the general population. The 1-year prevalence of neck pain in the general population is 10–15%, and of LBP is 15–45%. Females report neck pain more frequently than males[1,2]. Lower back and neck pain is the leading cause of disability; with that being said among the 154 conditions, low back and neck pain had the highest healthcare spending in the United States with an estimated $134.5 billion in 2016[3,4]. Psychological factors (e.g. stress, some cognitive factors, and sleep problems) and individual/biological factors (e.g. preexisting neuromuscular or autoimmune disorders, aging, and genetics) both contribute to the development of neck pain[5]. To date, there is no definitive treatment to cure it. Furthermore, in 2020, 619 million people were affected by this condition globally. With an estimation to increase about 843 million by 2050[6]. Therefore, the need for effective treatment is undeniable. Being a burdensome health condition for many patients' worldwide, low back and neck pain has long become a topic of interest for researchers to find an effective treatment. This article sheds light on the OPAL trial which discussed the use of opioids in acute low back and neck pain.

Body

Various pharmacological agents like non-steroidal anti-inflammatory drugs, which are typically recommended as the initial treatment, along with opioids, muscle relaxants, and antidepressants, are employed to address this persistent ailment that significantly impacts an individual's life quality[7].

In 2020, prescription opioids remained the most commonly misused prescription drug in the United States. Despite guideline recommendations and the widespread use of opioid analgesics, there is no rigorous evidence to support their use for acute LBP and neck pain[8].

To evaluate the efficacy and safety of a judicious short course of an opioid analgesic for acute LBP and neck pain, OPAL triple-blinded, placebo-controlled randomized trial was conducted. Between 29 February 2016 and 10 March 2022, a total of 347 patients having a median age of 44.7 years, were enroled for 12 weeks or less. Included individuals had either LBP (between the 12th rib and buttock crease) or neck pain (below the occiput to the furthest point of the cervical spine), with or without extending to the leg (for back pain) or arm (for neck pain). Their pain episode lasted no more than 12 weeks, following a pain-free month, and they had at least moderately severe pain (measured by modified SF-36 item 7). This item assessed the intensity of their back or neck pain over the past week, allowing responses from "none" to "very severe." Participants were randomly assigned in a 1:1 ratio into two groups. One group received guideline-recommended care plus an opioid (oxycodone–naloxone, up to 20 mg oxycodone orally per day) while the other received guideline- recommended care and an identical placebo, for up to 6 weeks. The primary outcome evaluated was pain severity at 6 weeks measured with the pain severity subscale of the Brief Pain Inventory (10-point scale). Pain scores at week 6 for the opioids and placebo groups averaged 2.78 and 2.25, respectively. The researchers were astonished to find out that the two groups did not differ much in the terms of pain severity after 12 weeks. However, by 52 weeks, the pain score for the opioids group was 2.37, while that for the placebo group was 1.81. Thus, it was concluded that opioids should not be recommended for acute non-specific LBP or neck pain[9].

Secondary outcomes showed minimal benefits or no differences compared to placebo. Adverse event reporting was similar between groups, except for more cases of nausea, constipation, and dizziness with opioids. Opioid participants displayed higher risk of misuse at week 52 via the Current Opioid Misuse Measure, indicating greater potential for addiction and problematic behaviour[9].

Furthermore, previous data suggested that many patients develop opioid dependence, meaning that cessation causes an unpleasant withdrawal syndrome (such as agitation, insomnia, diarrhoea, vxcrhinorrhea, piloerection, and hyperalgesia) with the prolonged use of opioids drugs, Hyperalgesia is a common feature of opioid withdrawal that also occurs with experimental pain when opioids are stopped[10].

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Conclusion

In conclusion, OPAL is the world's first placebo-controlled trial for the use of opioid analgesics in people with acute LBP or neck pain, which provided a rigorous evidence for the appropriate and judicious use of this medicine. The study comprehensively evaluated the efficacy and safety of short-term opioid analgesics for acute low back and neck pain, addressing the dearth of robust evidence supporting their widespread prescription. Involving 347 patients with a median age of 44.7 and pain lasting up to 12 weeks, participants were randomly assigned to receive recommended care plus oxycodone–naloxone or recommended care plus a placebo over a 6-week period. Unexpectedly, pain severity at 6 and 12 weeks showed no significant differences between groups, while pain scores at 52 weeks were higher in the opioid group than the placebo group, indicating potential long-term drawbacks of opioid use. These findings have noteworthy clinical implications, urging a reevaluation of routine opioid prescriptions for acute non-specific low back and neck pain due to limited pain relief benefits, coupled with an elevated risk of adverse events and misuse. Healthcare providers should exercise caution when considering opioids, critically assessing both short-term and long-term outcomes. However, results of this trial are limited as 42% of the sample was non-compliant. In addition, other multiple modalities ought to be implemented for reporting of pain in order to decrease the bias and strengthen the objectivity of the study including numerical pain scales as well as verbal and visual analogue scales. Henceforth, further clinical and meta-analytic studies need to be done which would demonstrate the unwavering commitment of researchers and healthcare professionals to discover effective treatments for such a disease.

Ethical approval

This study does not involve human subjects, animals, or any other ethical considerations. As such, ethical approval was not required for this article.

Consent

This study does not involve the collection of personal data or identifiable information from individuals. As such, informed consent was not required for this article.

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Author contribution

S.M.M.A.: conceptualization, review, and editing. A.F.: writing original draft. R.S.: proofreading and final editing.

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