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Avoiding Opioid Analgesics for Treatment of Chronic Low Back Pain

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Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain: A Systematic Review and Meta-analysis

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IMPORTANCE Opioid analgesics are commonly used for low back pain; however, to our knowledge there has been no systematic evaluation of the effect of opioid dose and use of enrichment study design on estimates of treatment effect.

OBJECTIVE To evaluate efficacy and tolerability of opioids in the management of back pain and investigate the effect of opioid dose and use of an enrichment study design on treatment effect.

DATA SOURCES Medline, EMBASE, CENTRAL, CINAHL, and PsycINFO (inception to September 2015) with citation tracking from eligible randomized clinical trials (RCTs).

STUDY SELECTION Placebo-controlled RCTs in any language.

DATA EXTRACTION AND SYNTHESIS Two authors independently extracted data and assessed risk of bias. Data were pooled using a random effects model with strength of evidence assessed using the grading of recommendations assessment, development, and evaluation (GRADE).

MAIN OUTCOMES AND MEASURES The primary outcome measure was pain. Pain and disability outcomes were converted to a common 0 to 100 scale, with effects greater than 20 points considered clinically important.

RESULTS Of 20 included RCTs of opioid analgesics (with a total of 7925 participants), 13 trials (3419 participants) evaluated short-term effects on chronic low back pain, and no placebo-controlled trials enrolled patients with acute low back pain. In half of these 13 trials, at least 50% of participants withdrew owing to adverse events or lack of efficacy. There was moderate-quality evidence that opioid analgesics reduce pain in the short term: mean difference (MD), −10.1 (95% CI, −12.8 to −7.4). Meta-regression revealed a 12.0 point greater pain relief for every 1 log unit increase in morphine equivalent dose (P = .046). Clinically important pain relief was not observed within the dose range evaluated (40.0-240.0-mg morphine equivalents per day). There was no significant effect of enrichment study design.

CONCLUSIONS AND RELEVANCE For people with chronic low back pain who tolerate the medicine, opioid analgesics provide modest short-term pain relief but the effect is not likely to be clinically important within guideline recommended doses. Evidence on long-term efficacy is lacking. The efficacy of opioid analgesics in acute low back pain is unknown.

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According to the Centers for Disease Control and Prevention (CDC), opioid abuse has reached epidemic proportions in the United States[1] and accounted for 28 000 deaths in 2014.[2] Other developed countries are experiencing similar increases in opioid abuse, although not necessarily of the same magnitude as in the United States. Opioid abuse increases proportionately to increased use of these drugs for pain control, which in turn has increased substantially in the past 2 decades. Increased awareness of opioid abuse and the role that prescription opioids have in contributing to opioid abuse necessitates reexamination of the use of opioid analgesia for routine pain management.

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The CDC recently developed and published guidelines for primary care physicians on opioid treatment of chronic noncancer pain exclusive of end-of-life care.[3] The CDC guideline is the most recent in a series of opioid guidelines issued both in the United States and elsewhere based on the best scientific evidence combined with expert opinion and stakeholder review. The CDC review is unique because it benefited from evidence accumulated during the 2 decades when there were unprecedented increases in opioid prescribing for chronic pain. The CDC combined an updated systematic review of scientific evidence with a contextual review of nontrial data (eg, epidemiological data). The guideline authors found no support for long-term use of opioids for chronic pain nor for the use of risk mitigation strategies that were purported to reduce the risks associated with chronic opioid use.[4]

In the 1990s, large increases in opioid prescribing occurred when the medical community was pushed to aggressively control pain while the pharmaceutical industry claimed that this could be done safely. However, this notion ran counter to previous teaching

that opioids were neither effective nor safe for chronic pain management. Despite recognition that opioids are highly addictive, there was hope that addiction would occur only in a few high-risk individuals, would be predictable, and could be controlled using risk mitigation strategies scaled according to a patient's risk for addiction. It was thought that opioids could be widely used, at whatever dose was necessary to reduce pain levels, as long as prescribing was done cautiously. Many patients would benefit, and few would be harmed.

However, this approach was, in retrospect, incorrect. Evidence failed to support anecdotal reports that many patients experience clinically useful relief from chronic pain by using opioids. Harms were substantial because reliably identifying which patients would fail treatment or abuse these drugs was not possible. Risk mitigation strategies, while sensible precautions, did not completely protect pain patients treated with opioids. Increased prescribing for chronic pain led to increases in opioid abuse and opioid-related deaths.

Is there any role for opioids in treating chronic low back pain? This question was addressed by Abdel Shaheed et al[5] in a report in *JAMA Internal Medicine*. The authors performed a systematic review and meta-analysis assessing the association between use of opioid analgesics and clinical efficacy, tolerability, and dose-dependent effects among patients with low back pain.[5] Low back pain is a common health problem and is among the leading causes of disability worldwide.[6] Low back pain is also the most common reason for prescribing opioids in the primary care setting, which is the predominant source of opioid prescribing.[7] This systematic review differs from prior reports by calculating the relationship of various doses of opioids suggested for use by evidence-based guidelines and relief of back pain. Abdel Shaheed et al[5] evaluated 14 placebo-controlled studies of opioid use for chronic low back pain involving 7295 patients. Of note, in half of these trials, half of the patients withdrew from the studies because of lack of pain relief. There was measurable short-term pain relief (mean difference in pain scales, −10.1; 95% CI, −12.8 to −7.4) and a 12.0-point improvement in pain scores for each 1.0 log unit increase in morphine-equivalent dose. However, for the doses recommended in guidelines (40.0-240.0 morphine milligram equivalents), none of these increased values in measured pain relief achieved clinical significance.

These results are similar to prior reviews and meta-analyses that failed to show short-term benefit of opioids for back pain.[8] The long-term benefits of opioid treatment for back pain have not been evaluated in clinical trials, although the harms associated with long-term opioid use are clear from epidemiological studies, resulting in much uncertainty about whether opioids are appropriate treatment for chronic low back pain. Whether a short course of opioids limited to 3 to 7 days' treatment, as suggested by the new CDC guideline, can help achieve recovery from an acute back sprain or other injury remains an open question—one that has not been addressed in trials and therefore could not be addressed by Abdel Shaheed et al.[5] However, it is increasingly clear that opioids are not helpful for chronic low back pain, and alternative treatments such as exercise and nonopioid analgesics achieve better outcomes.[9]

Low back pain is important because it is a common clinical problem. Despite the uncertainty about how to reduce adverse outcomes associated with chronic opioid prescribing, it is clear that increased prescribing has led to increases in opioid abuse and opioid-related deaths. Risk mitigation strategies might help prevent opioids from getting into the wrong hands and inform users who are unaware of risk, but there is no evidence that development of dependence or addiction can be predicted or prevented. The best way to reduce adverse outcomes is to stop prescribing opioids for common diagnoses like back pain because the available evidence shows they are not effective. It is not necessary to take any risk, however small, when the treatment is not effective and the consequences of adverse outcomes include potential serious harms to individuals, families, and society.

ARTICLE INFORMATION

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REFERENCES

1. Paulozzi LJ. CDC Grand Rounds: Prescription drug overdose: a US epidemic. Centers for Disease Control and Prevention. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6101a3.htm. Accessed May 23, 2016.

2. Rudd RA, Aleshire N, Zibbell JE, Gladden RM; Centers for Disease Control and Prevention. Increases in drug and opioid overdose deaths: United States, 2000-2014. *MMWR Morb Mortal Wkly Rep*. 2016;64(50-51):1378-1382.

3. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*. 2016;315(15):1624-1645.

4. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med*. 2015;162(4):276-286.

5. Abdel Shaheed CA, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, tolerability, and dose-dependent effects of opioid analgesics for low back pain: a systematic review and meta-analysis. *JAMA Intern Med*. doi:10.1001/jamainternmed.2016.1251.

6. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2163-2196.

7. Olsen Y, Daumit GL, Ford DE. Opioid prescriptions by US primary care physicians from 1992 to 2001. *J Pain*. 2006;7(4):225-235.

8. Martell BA, O'Connor PG, Kerns RD, et al. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. *Ann Intern Med*. 2007;146(2):116-127.

9. Deyo RA, Mirza SK, Turner JA, Martin BI. Overtreating chronic back pain: time to back off? *J Am Board Fam Med*. 2009;22(1):62-68.