The Long-term Analgesic Effectiveness of Opioid Therapy in Chronic Non-Cancer Pain Patients: A Literature Review of Randomized Controlled, Open-label, and Epidemiologic Studies

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INTRODUCTION

- Pain may be the major factor in seeking medical attention in the United States, and chronic pain can have a profound effect on a person’s lifestyle.
- The treatment of patients with pain is multimodal and includes medications, physical therapy, psychological interventions, and non-opioid and opioid analgesics.
- Guidelines and recommendations for the chronic use of opioids have been published by different federal governments, state agencies, and national medical societies, including CDC, Washington State, and AAPM/AAFP.4,14

- Although opioids have a role in a treatment for chronic intractable pain, some argue that the risks of abuse, overdose and death outweigh their potential therapeutic benefits. Many state that there is a scarcity of scientific evidence that demonstrates that opioids are effective “long-term.” These statements represent opinion, in general, and are based on observational cohort studies of patients who had long-term opioid therapy that did not have evidence supporting long-term (12-month) opioid therapy (LOT) or the therapeutic benefit of long-term opioid pain (CNCP) therapy.
- This is not surprising because randomized placebo-controlled trials in patients with severe pain, and studies of patients greater than 3 months duration are in patients who are challenged for a number of reasons, including difficulty obtaining Long-term placebo-controlled trials for ethical reasons.4,14–20
- Recruitment – patients are eligible if they are able to continue long-term placebo trials for ethical reasons.21,22
- Retention of subjects – placebo subjects are likely to drop out and show less improvement over time.
- There is data on patients receiving LOT in numerous studies. Long-term trials (mostly clinical) involving single or placebo (OL) studies, open-label extension (OLE) studies, randomized clinical trials (RCTs) that compared different therapies, and epidemiologic studies, represent a source of useful information to assess the effectiveness of LOT. These measures are important for deciding whether patients benefit from this treatment.
- The patients in these OL studies and the subset of patients in RCTs that elect to continue into OLE studies may actually reflect the real-world patients and results obtained from clinical trials.

METHODS

- We conducted a literature search of published studies of long-term opioid analgesic therapy 6 months in duration in CNCP patients. Studies were included using the search terms “opioid,” “long*,” and/or “therapy” in Medline, Embase, Bioverse, and PubMed, and through March 2016.
- Additional articles were identified through comments, clinical guidelines, literature review, and meta-analysis.

RESULTS and DISCUSSION

- For the literature review, four key outcomes were extracted for each study, where available:
  1. Percent pain therapy was either collected directly from study reports or calculated based on the average number of subjects at the beginning and at the end of the study and the length of the study.
  2. Reported changes from baseline to end of study in ‘pain relief,’ ‘total pain,’ or ‘usual pain’ as measured on the Brief Pain Inventory (BPI), 0 to 10 point or 10 point numeric rating scale, 100 mm visual analog scale, or other scales prior to the start of the study. These RCTs were either placebo controlled or lot RCTs and evaluated and monitored for efficacy and safety (LOT) for patients with chronic non-cancer pain (CNCP).
  3. These RCTs were not placebo-controlled but compared different analgesic therapies, nonpharmacological therapies, or combinations of these therapies. We excluded studies that were ≥12 months in duration (Figure 2).
  4. Eleven studies included data on the physical component and on pain scores.3,15,19,20

- The analysis did not account for variation in imputation methods used for results, placebo-controlled trials, or OLE studies.

CONCLUSIONS

- We performed a comprehensive review of data from 73 studies corresponding to 15 randomized controlled trials (RCTs), 27 OL studies, and 28 epidemiologic studies, for CNCP patients that include assessments or measures changes in pain scores and function.

- The purpose of this study was to provide an up-to-date review of the literature that all studies of LOT (all studies, including RCTs, OLs, OLEs, and epidemiologic studies, for CNCP patients that include assessments or measures changes in pain scores and function.

- The 55 studies which includes RCTs, OL studies, and OLE studies represented 498,594 patients and 11,798 person-years. Among these, 11 cohort studies, 33 OL trials, and 63 OLE trials were ≥12 months in duration (Figure 2).

- Many state that there is a scarcity of scientific evidence that demonstrates that opioids are effective “long-term.” These statements represent opinion, in general, and are based on observational cohort studies of patients who had long-term opioid therapy that did not have evidence supporting long-term (12-month) opioid therapy (LOT) or the therapeutic benefit of long-term opioid pain (CNCP) therapy.

- Although opioids have represented a mainstay treatment for chronic intractable pain, some argue that the risks of abuse, overdose and death outweigh their potential therapeutic benefits. Many state that there is a scarcity of scientific evidence that demonstrates that opioids are effective “long-term.” These statements represent opinion, in general, and are based on observational cohort studies of patients who had long-term opioid therapy that did not have evidence supporting long-term (12-month) opioid therapy (LOT) or the therapeutic benefit of long-term opioid pain (CNCP) therapy.

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