Original Article

Differences in the Prevalence and Severity of Side Effects Based on Type of Analgesic Prescription in Patients with Chronic Cancer Pain

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Abstract

An understanding of the relationship between the type of analgesic prescription and the prevalence and severity of side effects is crucial in making appropriate treatment decisions. The purposes of this study were to determine if there were differences in the prevalence of side effects among four different types of analgesic prescriptions (i.e., no opioid, only an as needed (PRN) opioid, only an around-the-clock (ATC) opioid, or an ATC + PRN opioid); to determine if there were differences in the severity of side effects among the four prescription groups; and to determine the relationships between the total dose of opioid analgesic medication prescribed and taken and the severity of side effects. As part of a larger study, 174 cancer patients with bone metastasis reported their analgesic use and the prevalence and severity of 11 side effects. Significant differences ($P < 0.05$) were found in prevalence rates for seven of the side effects among the four prescription groups. The highest prevalence rates were found in the only ATC and ATC + PRN groups. Significant differences were found in the severity scores for five of the side effects, with the highest severity scores reported by patients in the only ATC and ATC + PRN groups. Significant positive correlations were found between the severity of six of the side effects and the total dose of opioid prescribed and taken. Risk factors for analgesic-induced side effects are ATC and ATC + PRN prescription types and higher doses of opioid analgesics. J Pain Symptom Manage 2007;33:67–77.

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Introduction

Side effects of analgesic medications are a well-documented barrier to successful pain management. These side effects limit the titration of analgesics to achieve optimal pain control and decrease the patient's quality of life.[1,2] Side effects commonly associated with chronic administration of various classes of analgesic medications include gastrointestinal (e.g., nausea, vomiting, indigestion, constipation), central nervous system (e.g., drowsiness, difficulty concentrating, hallucinations/nightmares, light-headedness, poor coordination, lack of energy), and autonomic nervous system (e.g., urinary retention, xerostomia) effects. The recently revised clinical practice guideline for cancer pain management[3] noted that analgesic medications should be titrated to achieve effective analgesia with tolerable side effects.

An understanding of the relationships between the type of analgesic prescription and the prevalence and severity of side effects is crucial in making appropriate treatment decisions for both pain control and side effect management. However, very little data are available on the differences in either the prevalence or the severity of side effects associated with different types of analgesic prescriptions. In addition, no data exist on the relationships between the severity of side effects and the total dose of opioid analgesics prescribed or taken. Therefore, the purposes of this study, in a sample of oncology outpatients with pain from bone metastasis, were to determine if there were differences in the prevalence of side effects among four different types of analgesic prescriptions (i.e., no opioid, only an as needed (PRN) opioid, only an around-the-clock (ATC) opioid, or an ATC + PRN opioid); to determine if there were differences in the severity of side effects among the four different types of analgesic prescriptions; and to determine the relationships between the total dose of opioid analgesic prescribed and taken and the severity of side effects.

Literature Review

A number of systematic reviews have evaluated the prevalence of analgesic side effects associated with the treatment of cancer[1,4] and chronic noncancer[5–9] pain. Most prevalence rates were derived from adverse event data reported as a part of studies of new analgesics. In these reviews, constipation with opioid use ranged from 27% to 70%; nausea and vomiting from 10% to 30%; sedation from 20% to 70%; and poor sleep or difficulty sleeping from 19% to 31%. However, the majority of the studies included in these systematic reviews were short-term trials (i.e., less than 28 days) with opioid analgesics. Therefore, little is known about the prevalence and severity of side effects in patients who are taking opioids for longer than one month.

A few studies have provided limited data on the relationship between opioid-induced side effects and total opioid dose.[10,11] While the primary purpose of these studies was not to evaluate the prevalence and severity of analgesic side effects or the relationship between total dose and severity of side effects, some information can be extrapolated from this work. Boureau et al.[10] compared the efficacy and adverse effects of controlled-release morphine suspension and controlled-release morphine tablets for chronic cancer pain in a crossover study of 44 patients. The prevalence rates for those side effects that persisted throughout the two-week study ranged from 75.8% to 78.8% for constipation, 57.1% to 75.0% for nausea, 50.0% for vomiting, and 69.0% to 86.2% for daytime drowsiness. While the mean daily dose of oral morphine was reported to be 108 mg ± 57, no data were reported on the relationship between opioid dose and severity of these side effects.

Comparing the safety and efficacy of morphine immediate-release tablets and sustained-release morphine tablets, Walsh et al.[11] found that 9%–10% of study participants experienced nausea and 35% experienced sedation.