

# Management of Opioid-Induced Sedation in Patients With Cancer

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Opioid-induced sedation occurs in 20%–60% of patients receiving opioids (Cherny et al., 2001). In patients with cancer, opioid-induced sedation is usually an unacceptable and undesirable side effect that can impede quality of life. Sedation can be very distressing and sometimes is difficult to manage. Studies show that healthcare professionals have limited understanding of equianalgesia and opioid pharmacology and therefore are unable to treat opioid side effects effectively (Cason, Jones, Brock, Maese, & Milligan, 1999; de Rond et al., 2000; Ferrell & McCaffery, 1997; McCaffery & Ferrell, 1997; Randall-David, Wright, Porterfield, & Lesser, 2003).

A paucity of research exists regarding the management of opioid-induced sedation. Recently, however, more research has been conducted regarding drug combinations that counteract opioid-induced sedation, opioid rotation to improve the adverse effects of opioids, and more invasive routes of opioid administration to produce less sedation. The purpose of this article is to present a review of the literature regarding the combination of opioids with other drugs, opioid rotation, and other, more invasive modalities of opioid administration to manage opioid-induced sedation, with the goal of providing healthcare professionals with information about how to address the sedative effects of opioids.

## Opioid-Induced Sedation

Sedation has been defined as “depression of brain functioning by a medication, mani-

Opioid-induced sedation is a common dose-limiting side effect of opioid therapy that can be very distressing and sometimes is more difficult to manage than pain. Opioid-induced sedation may prohibit patients from participating in certain activities of daily living, which can be a source of considerable distress for patients and their families. The issue presents a therapeutic dilemma for healthcare professionals caring for patients experiencing the side effect. Currently, several therapeutic approaches are used to counteract or minimize the severity of opioid-induced sedation, including reduction of the opioid dose, the addition of other drugs, opioid rotation, and the use of invasive routes of administration. This article will address the management of opioid-induced sedation.

festated by sleepiness, drowsiness, fatigue, slowed brain activity, reduced wakefulness, and impaired performance” (Kay, 2001). Although sedation is one of the most common and troublesome side effects associated with opioid analgesics (Wall & Melzack, 1999), the mechanism of the phenomenon remains elusive. Opioid analgesics are agonists that bind with opioid receptors in the central nervous system and inhibit the firing of individual neurons. The action of opioids at these receptors inhibits the arousal mechanism and decreases content processing, also known as decreased wakefulness and slowed interpretation of the environment, respectively (Young-McCaughan & Miaskowski, 2001).

Sedation is a dose-dependent effect of opioids. Most patients develop tolerance to the sedative effects of opioids within a few days (Cherney, 2000). The dose needed to control pain may cause initial sedation, which eventually subsides even though the

same dose will continue to control pain. If sedation persists, a careful assessment by a healthcare provider is needed, as illustrated in Figure 1. Eliminating other confounding factors, such as central nervous system disease, infection, metabolic disorders, and decreased oxygenation, is important because they are more common causes of sedation in patients with cancer than opioid overdose (Manfredi, Ribeiro, Chandler, & Payne, 1996).

Healthcare professionals should be careful not to mistake “catch-up” sleep as sedation. “Catch-up” sleep is a natural effect of pain relief in those who experience sleep deprivation as a result of chronic, uncontrolled pain. Healthcare professionals should ask patients if they feel an exhaustive type of drowsiness or a drugged feeling. Most are able to differentiate between the two (Abraham, 2000).

Sedation occurs more frequently in the elderly and in patients with diminished creatinine clearance as a result of an accumulation of opioid metabolites (Peterson, Randall, & Paterson, 1990; Sawe, 1986). Studies in which these patients were given morphine, the most commonly used opioid, found that

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