



The Blue Ridge Poison Center

Tox Talks

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Recognizing and Reducing Risks of Narcotic Analgesic Harm

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Narcotic analgesic medications are frequently prescribed in occupational medicine practice in the treatment of work-related injuries. The toxic hazard severity of these medications can be of far greater magnitude than workplace chemicals, especially when considering the impact on those working and living in close association with the treated individual.

Drugs in the narcotic analgesic category, commonly referred to as opioids based on their actions at mu opioid receptors, can be further classified into three groups: opiates (e.g., codeine, morphine); semisynthetic opioids (e.g., oxycodone, hydrocodone, hydromorphone); and synthetic opioids (e.g., meperidine, propoxyphene, methadone, fentanyl). Recently collected human observational study data have shown significant increases in mortality attributed to use of certain drugs in these opioid subcategories. Methadone has been shown to be a leading direct cause of drug-related deaths in areas such as rural Virginia, where more than 75% of cases have been deemed accidental and nearly two thirds of cases have been attributed to drug source diversion, i.e., nonprescribed use. Narcotic analgesic-induced psychomotor impairment resulting in work-related performance deficits may also be an important contributor to workplace and non-workplace injury and death occurrence. In addition, it is widely acknowledged that opioid dependence and addiction can have a profoundly negative impact on quality of life and availability of support resources.

Opioid-related Risk Factors

It is important for prescribing health care providers, in general, to recognize both drug- and patient-related risk factors for unintended consequences of narcotic analgesic treatment. There are both innate (e.g., genetic) and acquired (e.g., previous use-related) differences within and among individuals in tolerance to the potentially life-threatening

central respiratory depressant effects of opioid medications. These differences apply to the way the body processes the drug through absorption, distribution, metabolism and elimination, as well as how and to what degree key target organ systems, such as the central nervous system, respond to the internally delivered dose of that drug. Drug-related injury risk determinants include the potency, dose, formulation (e.g., regular or extended release), and delivery vehicle (e.g., adhesive skin patch) of the prescribed opioid. It is also important to recognize the potential impact of coadministration of alcohol and/or other substances, including non-opioid as well as opioid drugs, on the way the body processes and target organs respond to the prescribed drug.

Drug-specific Risks

Numerous opioid-related health hazard risks include those that have been recently subject to federal and other regulatory measures. The following list, although by no means complete, raises some important points regarding safety and efficacy of prescription opioid treatment.

Morphine: Improper administration of sustained-release oral formulations of morphine can result in more rapid absorption, higher peak blood concentrations, and more pronounced clinical effects. This is more likely to occur when patients are not adequately informed or fail to observe precautions regarding safe administration of these products, including taking care not to ingest crushed tablets or chewing before swallowing them. In addition, it is important to bear in mind that older individuals and others who have impaired renal function are at increased risk of accumulation of active metabolites of morphine (e.g., morphine 6-glucuronide), which can increase risk of toxicity, even at relatively low doses of morphine.

Codeine: The speed and extent of codeine's metabolism in the body to morphine determines both its analgesic efficacy and its potential for harmful central nervous system depressant effects. It is well recognized that there are segments of the normal population that include those who rapidly and extensively metabolize the parent drug (1-7%) as well as those who are slow/poor metabolizers (7-10%). This means that individuals in the former category may be at risk of central nervous system at doses of codeine that are ineffective for pain control, albeit nonharmful, in the latter group. Thus, it may be of vital importance to take a precautionary approach to size and frequency of initial dosing regimen in individuals where there is uncertainty or concern in this regard.

Methadone – The long elimination half-life and time to attainment of steady state blood and tissue drug concentrations after initiation of methadone treatment, differences between methadone's analgesic and respiratory depressant effect concentration thresholds, and changes in individual tolerance to these effects serve to explain the marked increase in methadone-related mortality during the first few days of such treatment. Treated patient or illicit user noncompliance with safe guidelines for methadone use that include cautious upward titration of daily dose as needed for analgesic efficacy is another important mortality risk determinant that should be well recognized.

Fentanyl: Warning messages have been recently issued regarding risks of fentanyl overdose in children and adults that address the potential for increased transmucosal and oral delivery of this potent opioid. Of particular concern is the potential for harm in infants or toddlers who mouth or chew on discarded fentanyl-containing patches. Patients should also be informed about the increased risks of fentanyl overdose that can result from increased transdermal drug delivery when the integrity of the patch system membrane in contact with the individual's skin is violated and/or the patch is warmed from an external source (e.g., heating pad or hot bath). Prescribing health care providers should also be advised

that, when initiating transdermal fentanyl treatment, even in individuals who may have become tolerant to the effects of other opioids, an approach that incorporates a low starting dose and gradual upward titration to intended effect be taken.

Recommendations

In order to reduce the risks of narcotic analgesic harm in occupational and nonoccupational medicine practice, it is of critical importance that patients and their care providers engage in safe practice measures that include the following:

- Recognize drug- and non-drug-related risk factors for adverse effects of narcotic analgesics.

- Apply safe practice measures that include educating patients and their close living associates in this regard, encouraging close and careful compliance with prescribed treatment, restricting access to medications to those for whom they are prescribed, and applying risk-conservative (i.e., precautionary) approaches to prescribing treatment, including careful consideration regarding drug potency, starting dose, and dose escalation.

- Consider safer alternative therapeutic interventions.

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