Multiple Risks for Patients Using the Transdermal Fentanyl Patch

The transdermal drug administration system, commonly known as "the patch," is a convenient method to administer certain drugs that work best when steady therapeutic blood levels are maintained over time. The scopolamine patch is widely used for prevention of seasickness and is gaining popularity as an extra antinausea safeguard in select patients who need more than the traditional drugs such as ondansetron and dexamethasone to help prevent postoperative nausea and vomiting. Likewise, nicotine patches are popular to help prevent signs and symptoms of nicotine withdrawal associated with acute cessation of cigarette smoking. Patients with severe intractable chronic pain and those suffering relentless pain from a terminal illness who need but may not be able to tolerate high doses of oral opioids can benefit from the use of the transdermal fentanyl system.

Despite the theoretical benefits of maintaining steady-state kinetics with the patch compared to the wide variations of blood levels, termed peaks and troughs, associated with oral administration of most drugs, the transdermal system of administration has numerous drawbacks. The onset of pharmacological activity is very slow because of slow absorption of the drug through the intact skin. For instance, it typically takes 4 hours for circulating plasma levels of scopolamine to even be detected once the patch is applied, and the time to reach peak levels averages 24 hours. Thus the anesthesiologist cannot expect any significant therapeutic effect immediately following an anesthetic unless the scopolamine patch is applied many hours before the start of a procedure. The fentanyl patch takes 24–72 hours to reach steady state, and once it is removed, the residual fentanyl in the skin continues to be absorbed for hours. It takes approximately 17 hours for fentanyl blood levels to drop by 50% once the patch is removed, so fentanyl interactions with sedatives, hypnotics, and other opioids are still possible hours after the patch has been removed. Thus removal of the patch does not quickly eliminate the risk of fentanyl interactions with other drugs.

The rate of absorption of the medication can also be influenced by the degree of blood flow through the skin where the patch is applied. Increased body temperature resulting from a fever, a heating blanket, exposure to a hot, humid environment, or vasodilating anesthetics increases peripheral blood flow to the skin attached to the patch, which subsequently increases the rate of systemic drug absorption. Elevated levels of fentanyl increase the potential for respiratory depression, even in patients with increased opioid tolerance. Additionally, the central nervous system depressant effects of the fentanyl will at least be additive if not potentiated by sedatives, hypnotics, and other opioids administered for procedural sedation. Because fentanyl patches are indicated only for patients who have developed a significant tolerance to other opioids, the patch's high dose can be lethal to opioid-naïve patients. Because fentanyl patches therefore are contraindicated for treatment of acute postoperative pain in opioid-naïve patients, few dentists would ever prescribe them.

It is, however, not unusual for a dental patient wearing a fentanyl patch to be treated in the dental office. For a patient wearing a fentanyl patch, the dentist who is considering using any form of procedural sedation, other than perhaps nitrous oxide–oxygen minimal sedation, must recognize the danger of inadvertently producing a level of sedation that is deeper than intended and deeper than the sedation practitioner can safely manage should respiratory depression, respiratory arrest, upper airway obstruction, laryngospasm, or other complications arise. Additionally, many patients utilizing the fentanyl patch are debilitated, high-risk terminal cancer patients, making them even more prone to oversedation. If the dentist prescribes drugs such as ketoconazole or erythromycin that inhibit cytochrome P450 3A4 hepatic enzymes, plasma levels of fentanyl may rise and precipitate a serious overdose.

Another caution involves patients wearing a fentanyl patch who do not equate their patch with "taking medicine." Because the patch is not swallowed, these patients often do not list the patch in their medical history questionnaire that asks, "Do you take any drugs?" In addition to the concern previously mentioned of the additive effects of fentanyl with sedative medications, one other interaction must be considered when the presence of the patch has not been identified. Dentists who administer opioid agonist-antagonists such as nalbuphine (Nubain), butorphanol (Stadol), or pentazocine (Talwin), or who foolishly use naloxone reversal of opioids to electively speed recovery, will undoubtedly produce an acute opioid abstinence syndrome (acute narcotic withdrawal) that can be extremely unpleasant for the patient and even life threatening.

This possibility is exemplified by a moderate sedationist who was sedating an apparently healthy patient who had indicated on his medical record that he did not take any medications. After several increments of intravenous

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midazolam and nalbuphine had been slowly titrated, the patient became increasingly more restless and disoriented. My answer to his phone call seeking my advice included the following recommendations:

1. This could be the result of disinhibition, so giving more drug is unlikely to improve the situation because the sedationist is not capable of changing to a general anesthetic.
2. This could be the result of opioid reversal by the nalbuphine in a secret opioid abuser. Ask his wife if he ever uses recreational drugs, as the precipitation of opioid abstinence syndrome is a possible diagnosis.

The wife then indicated that her husband absolutely took no drugs, legal or illegal, and was perfectly healthy except for his severe chronic back pain, for which he had been prescribed a fentanyl patch at the pain clinic. Fortunately, the dentist had access to a modest intravenous dose of meperidine, which reversed the effects of the reversal agent and allowed the patient to become more comfortable again.

Because of continued deaths from fentanyl patches, the FDA recently required the manufacturer of the Duragesic patch to print the name and strength on the patch in long-lasting ink in a color that is clearly visible to patients and care givers so that patches are easier to find and identify on the body. Also, used patches still contain a considerable dose of fentanyl that can harm or kill children or pets who find them if they are not disposed of correctly.

In summary, fentanyl patches pose significant risks to patients and dentists who provide various levels of sedation and general anesthesia. A careful and complete past medical history must be recorded that asks about medications taken or prescribed for any route of administration, including the transdermal patch, in addition to medications that the patient is supposed to take but may have electively stopped. Sedative drugs, if administered at all, must be even more carefully and slowly titrated to avoid oversedation or other adverse outcomes resulting from the often high levels of fentanyl already present. The risks associated with the cumulative effects of multiple doses of oral sedatives in the presence of fentanyl almost certainly outweigh the potential benefits for these patients. It is important to avoid administering any drugs with opioid reversal activity unless life-threatening circumstances leave the dentist with no other choice for emergency rescue. Even when the fentanyl patch has been removed, its effects can still be hazardous for the sedationist's patient. Finally, following dental procedures that are likely to produce significant postoperative pain, opioid-containing postoperative analgesics are best prescribed by the pain clinic specialist who is responsible for the fentanyl patch. The management of these patients can be quite complex, so clinical decisions impacting these patients are generally best left to a single prescriber so that all prescriptions comply with his or her overall pain management treatment plan. Because of the multiple risks for patients using the transdermal fentanyl patch, many pain clinic patients have a written contract with their physician that only that physician should prescribe analgesic medications for any indication. Dentists are strongly encouraged to use extreme care when treating these patients who use fentanyl patches and abide by the wishes of the patient's pain specialist.

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