Clinical Alert

Volume 6, Number 2
Spring 2009

Maryland Department of Health and Mental Hygiene

Office of Health Care Quality
Spring Grove Center
55 Wade Avenue
Catonsville, MD 21228

Martin O'Malley, *Governor*
Anthony G. Brown, *Lt. Governor*
John M. Colmers, *Secretary, DHMH*
Wendy Kronmiller *Director, OHCQ*

Transdermal Fentanyl Safety

Jack Bengio, Student Pharmacist
Mary Lynn McPherson, Pharm.D., BCPS, Professor, University of Maryland School of Pharmacy
Tricia Tomsko Nay, MD, CMD, CHCQM, FAAFP, FAIHQ, FAAHPM, Medical Director, Office of Health Care Quality

Transdermal fentanyl is a potent opioid pain medication that is given and absorbed through the skin. Dosing mistakes with fentanyl can have harmful and sometimes fatal consequences. Although fentanyl dosing errors can occur with intravenous, transdermal, or transmucosal fentanyl forms, transdermal fentanyl (TDF) is the most commonly used and misused formulation. The following case illustrates the need for attention to detail when dosing TDF.

Case: JR is an 85 year old female in a long-term care facility. She is alert and makes her own health care decisions. She has osteoarthritis, osteoporosis, vertebral compression fractures, and intractable back pain. She complained of moderate to severe back pain most of every day, that she consistently rates between 6 and 10 (on an "0 = no pain to 10 = worst imaginable pain" scale). She weighs 75 pounds. Her physician ordered acetaminophen 1,000 mg by mouth every six hours as needed for pain.

Several weeks later JR still had moderately severe constant pain despite nearly around-the-clock use of acetaminophen. The physician discontinued the scheduled acetaminophen and orders Percocet® (oxycodone/acetaminophen 5mg/325mg), one tablet by mouth every six hours as needed for pain. The patient requested all four doses daily. Three days after beginning Percocet therapy, the nurses' note indicates the patient complained of back pain and was medicated with Percocet® at 11:30 a.m., her scheduled time for the medication. At 12:30 p.m. the patient indicated that there was no relief, so the physician ordered a Duragesic® (fentanyl) 75 mcg transdermal patch every 72 hours to be applied topically to the chest wall. The patch was placed at 2:00 p.m. The following day at 11:00 a.m., the nurses' notes indicate the patient was very lethargic. She opened her eyes but did not speak and her respiratory rate was eight breaths per minute. Immediately notified, the physician ordered the fentanyl patch to be removed. The patient was sent to the hospital via 911 per the physician's orders.

EMS gave the patient two doses of Narcan® (naloxone) with short-term improvement. The patient arrived at the Emergency Room and was found to be unresponsive with a respiratory rate of six breaths per minute. The patient was intubated and admitted to the Intensive Care Unit where she remained on a Narcan® drip for two days. She subsequently developed aspiration pneumonia. After eight days in the hospital, she was stable enough to return to the nursing home.

Discussion: Some major differences between fentanyl and other opioids are its greater potency (about 75-100 times more potent than morphine) and its greater lipid solubility. Because of its lipophilic nature, rapid perfusion across the blood-brain barrier occurs with a quick onset of action once the drug is absorbed from its administration site. Having this in mind, let's analyze the three most glaring problems in this case:

1). Do No Harm! Only patients who are considered "opioid-tolerant" should be switched to TDF. "Opioid-tolerance" is defined as daily ingestion of at least 60 mg of morphine, 30 mg of oral oxycodone, or 8 mg of oral hydromorphone or an equianalgesic dose of another opioid for at least one week.[1] This patient had not been receiving opioids for at least one week (only for three days) and she did not meet the total daily requirement of 30 mg of oxycodone (she was receiving 20 mg/day of oral oxycodone), therefore she did not meet the definition of "opioid-tolerant."

2). Weight matters! The patient was a 75 pound, elderly female. The Duragesic® package insert states "Duragesic® should be used with caution in elderly, cachectic, or debilitated patients as they may have altered pharmacokinetics due to poor fat stores, muscle wasting or altered clearance."[1] As this patient is elderly and has a low body weight, she may have an altered response to TDF. As well, transdermal fentanyl is NOT indicated for

Continued

Clinical Alert

Maryland Department of Health and Mental Hygiene
Office of Health Care Quality
Spring Grove Center, Bland Bryant Building, 55 Wade Avenue
Catonsville, MD 21228

Clinical Alert
is published periodically by the
Office of Health Care Quality

For additional information contact
Tricia Nay, MD, CMD, FAAFP, FAAHPM
Medical Director, OHCQ
Phone: 410-402-8007
Email: *pnay@dhmh.state.md.us*

unstable or breakthrough pain, regardless of the situation. It is too difficult to quickly achieve pain relief in a patient with uncontrolled pain using a drug delivery system that can take days to achieve steady state. By rapidly increasing the patch strength, the patient may become toxic when steady-state is finally achieved. Manufacturer recommendations are to increase initially after three days of beginning therapy, then no sooner than every six days.

DOSE CONVERSION GUIDELINES

Current Analgesic	Daily Dosage (mg/d)			
Oral morphine	60-134	135-224	225-314	315-404
IM/IV morphine	10-22	23-37	38-52	53-67
Oral oxycodone	30-67	67.5-112	112.5-157	157.5-202
IM/IV oxycodone	15-33	33.1-56	56.1-78	78.1-101
Oral codeine	150-447	448-747	748-1047	1048-1347
Oral hydromorphone	8-17	17.1-28	28.1-39	39.1-51
IV hydromorphone	1.5-3.4	3.5-5.6	5.7-7.9	8-10
IM meperidine	75-165	166-278	279-390	391-503
Oral methadone	20-44	45-74	75-104	105-134
IM methadone	10-22	23-37	38-52	53-67
	⇓	⇓	⇓	⇓
Recommended DURAGESIC® Dose	25 mcg/h	50 mcg/h	75 mcg/h	100 mcg/h

3). Do the math! The calculation of the initial dose of TDF was inappropriate in this case. First, the patient was not sufficiently opioid tolerant to warrant a switch to TDF. Looking at the chart above (ref: *www.duragesic.com*), TDF 75 mcg would be equivalent to 112.5-157 mg oral oxycodone per day. (The patient was receiving oxycodone 20 mg per day.) There is a TDF 12 mcg patch, which would be approximately equivalent to 15-20 mg of oral oxycodone per day; if the physician felt TDF was an appropriate intervention for this patient, this would have been the appropriate strength to begin with. The order for Percocet® could have remained in place for breakthrough pain. The initial effect of the patch may take from three to six days to be seen, so the dose should not be increased after one day, since the drug is still being absorbed into the body. Rather, we should figure out how much and how often the breakthrough medication was used over at least two days, and then convert this amount to an equivalent fentanyl dose. However, remember that this patient was fairly cachectic and TDF was not the best intervention for her, even if the physician had started with the much more reasonable dose of TDF 12 mcg.

In conclusion, the most important concepts the provider must understand regarding TDF are as follows:

- What patients should receive TDF? Patients with a normal body habitus who are "opioid-tolerant."
- What type of pain warrants TDF? Stable moderate to severe pain. It is too difficult to chase escalating pain with a long-acting drug delivery system.
- How do you safely convert from oral opioids to TDF? Be sure to consult a recommended chart such as one shown in this ***Alert***. Consult with an experienced pharmacist if needed.

Remember, do no harm, weight matters, and do the math!

References:

1. Duragesic (Fentanyl Transdermal System) Prescribing Information. Accessed online at *www.duragesic.com/duragesic/shared/pi/duragesic.pdf#zoom=100*, January 22, 2009.