INSTITUTE TO ENHANCE PALLIATIVE CARE

PALLIATIVE CARE CASE OF THE MONTH

When Rotating to Methadone is a Good Idea

Susan Hunt, MD

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Case: HM is a 50-year old woman with stage IV (M1c disease) melanoma. She is nearing the end of life, and requires a continuous infusion of opioid to achieve comfort, which she has described to her physician as a pain level of 3/10. She was recently discharged from an acute care hospital on a continuous infusion of IV Dilaudid ® at 4 mg/hour with a PCA of 4 mg every 10 minutes. Over the most recent 24 hours she has required on average 15 mg/hour, and reports her pain level as 6/10. She denies nausea, reports increasing anxiety and depression, and uses a bowel regimen which allows daily bowel movements. She has been admitted to inpatient hospice level of care for pain control. On exam, her CAM is negative for delirium, and she has no myoclonus. She remembers previously being prescribed oral methadone for pain, but this medication was stopped when she had difficulty taking tablets. She has no allergies, and takes no other medications other than mentioned above.

Discussion: HM is a patient for whom we anticipate the need for increasing doses of opioid due to disease progression. She has difficulty taking PO medications and describes anxiety and depression. She is on a continuous infusion and PCA doses of hydromophone, using, on average, 15 mg IV Dilaudid ® / hour, which is equivalent to 300 mg OME/ hour or 7200 mg OME/day. She has no symptoms or signs of opioid toxicity, which can occur with Dilaudid ® as well as morphine (see Palliative Care Case of the Month, November 2011), but for which she is at increased risk as her Dilaudid ® requirement increases. The estimated cost to her hospice for her current Dilaudid ® regimen is $160/day.

Because of her anticipated need for increasing doses of opioids, and her increasing risk of opioid neurotoxicity due to Dilaudid ® metabolites, rotation to IV methadone would be a good next step.

Methadone is a synthetic opioid which can be administered orally, sublingually, or intravenously. It is rapidly distributed to tissues and plasma proteins. Its unbound fraction averages 12%, but is quite variable. Methadone has a very-long half- life, but a much shorter duration of analgesia. Because of the miss-match of half-life (long) and duration of analgesia (short), it is recommended to start with lower doses of medication, and titrate doses only after 7-10 days. Plasma levels of methadone may require 10 days to stabilize, and analgesia may increase with chronic dosing.

Methadone is metabolized in the liver, lacks active metabolites, and is an antagonist of N-methyl-D-aspartate (NMDA) receptors, all of which can reduce the risk of opioid neurotoxicity in patients requiring high doses of opioids and who have, or are at risk for, volume depletion/renal insufficiency.

An approach to rotation to IV methadone for this patient is to rotate her continuous infusion of Dilaudid ® to IV methadone, and keep the Dilaudid ® PCA. The calculations follow: IV Dilaudid ® 4mg/hour = 96 mg/day = PO OME 1920 mg/day. Oral methadone equivalent is 1920/20 or 96 mg/day. IV methadone is calculated by dividing oral methadone by 2: 96 mg po methadone a day /2 =r 48 IV methadone/day. Rounding down, her equianalgesic dose of IV methadone to replace the continuous infusion of IV Dilaudid ® is estimated at 15 mg IV every 8 hours. The rotation is best done in three steps, substituting 1/3 of the IV Dilaudid ® with 1/3 of the IV methadone dose at each step, and monitoring her PCA use to determine how effectively her pain is being controlled. Our patient complains of anxiety and depression. Because methadone is metabolized by CYP2A4 and CYP2B6, it has many drug-drug interactions, including, for example, sertraline.

Attention to every other medication a patient is prescribed, or uses over the counter, is a must, and appropriate adjustment or discontinuation critically important. Some medications alter the methadone level, so that the methadone dose must be adjusted. High doses of methadone can prolong the QTc interval, but for hospice patients, the benefits of methadone usually outweigh this risk.

Resolution of the case: HM agreed to inpatient level of hospice care for her rotation to methadone. She was started on IV methadone 5 mg IV every 8 hours, and her continuous infusion of IV Dilaudid reduced by 1/3. Her PCA use was less over the next few days, and the dose was adjusted downward. After two titrations of methadone, her continuous IV infusion of Dilaudid ® was stopped, and she was continued on IV methadone 15 mg IV every 8 hours, with a Dilaudid PCA at a reduced dose, with improved pain control. The estimated cost of 15 mg IV methadone every 8 hours is approximately $45/day.

References:

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3. Toombs JD. Oral Methadone Dosing for Chronic Pain. *Pain-Topics.org.* March 12, 2008.