INSTITUTE TO ENHANCE PALLIATIVE CARE

PALLIATIVE CARE CASE OF THE MONTH

"Do you have something stronger than this dilaudid?" The case for opioid rotation

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Case: Mr CC is a 67-year-old with NSCLC and metastatic disease to his mediastinum and L chest. He was admitted to the hospital for increasing R sternal chest pain over the past month. Pain is described as burning and non-radiating. There are no exacerbating or relieving factors. The pain is so bad that he has anorexia. The month prior to admission, he was started on oxycontin, and his dose was titrated up 160 mg bid with dilaudid 8 mg q3 PRN. Despite dose escalation, his pain was unchanged. While in the hospital, a fentanyl patch and a dilaudid PCA were added to the original regimen. However, no increased analgesia occurred.

A palliative care consult was obtained. His regimen was simplified to a dilaudid continuous intravenous infusion (CI) and PCA. Doses were escalated to 4 mg/hour CI and 4 mg PCA with 8 mg RN dose q1 hour. He reported no change in his pain. Co-analgesics of NSAIDS, Tylenol, dexamethasone, and a TCA were tried. Radiation oncology was consulted and saw no lesions to irradiate. The patient began to complain of worsening pain. As he continued to complain of 7-10/10 pain, the patient was changed to morphine and titrated to 10 mg continuous infusion and 10 mg PCA dose. Marked analgesia was noted. Attempts to transition to methadone were unsuccessful, as his need for morphine PCA doses remained unchanged. Despite initial complaints of sedation on morphine, the patient's pain scores decreased to 3/10. As such, he was continued on morphine and discharged from the hospital on a PCA.

Discussion: Opioid rotation, or trial of an alternative opioid, is commonly practiced when a patient's pain responds poorly to one opioid or intolerable side effects develop. These intolerable side effects may include nausea, vomiting, sedation, or even hyperalgesia. Although rotation is a common practice, a Cochrane review in 2004 found that evidence to support the practice for opioid rotation was anecdotal and in non-controlled studies. Randomized trials were suggested. Since that time, several prospective studies have been performed where opioid analgesic effect was inadequate or side effects to the opioid were intolerable. Studies by both Narabayashi et al. and Wiraz et al. investigated rotation to an alternative long acting opioid, dilaudid or oxycodone. In addition, patients had increased analgesia compared to the prior regimen. Often the effective equianalgesic dose in these studies was greater than the prior dose, suggesting that prior side effects may have been dose limiting. More is being learned about the pharmacokinetics and pharmacodynamics behind opioid metabolism. It is clear that there is variability between individuals. Some of this may be secondary to disease states (i.e. renal or hepatic impairment), or the effect on metabolism by other drugs. Other differences are due to genetic variations.

Inherited differences in opioid receptors, channels, and metabolism to active and inactive compounds have been found. These differences may extend to transporters effecting bioavailability from the GI tract to even penetration of the blood brain barrier. This variability may account for differences in effectiveness and side effects from one patient to another. For example, "non analgesic responders" to methadone were found to have lower blood levels of the drug when compared to the same dose with "responders." This suggests that the "nonresponders" may actually just clear methadone faster. It is frequently cited that 5-10% of the Caucasian population has the inability to convert codeine to its active metabolite, making it an ineffective medication in those individuals. Differences in metabolism have also been found with tramadol and oxycodone. In trying to obtain adequate analgesia with these medications, large doses may be tried with the development of side effects.

When switching to a different opioid, it is recommended to decrease the dose by 25-50% and even greater when switching to methadone. The rationale behind this has been "incomplete cross tolerance" and the concern that a patient may be more sensitive to the side effects of the second opioid, especially sedation. Understanding possible individual genetic variability, gives this practice even more credence.

Mr. CC was tolerating 20 mg IV dilaudid /hour without analgesia. His basal rate of 4 mg/hour dilaudid may be equianalgesic to 20-30 mg IV morphine hour. Given his profound tolerance to IV dilaudid and oral oxycodone, a conservative CI of 7 mg morphine/hour was started with frequent PCA doses available. Even with sub-equianalgesic dosing, he noted marked analgesia.

When doses of an opioid are escalated without apparent benefit and/or with side effects, opioid rotation should be considered. An individual's biochemistry may determine if a particular opioid regimen will be successful and tolerated.

References:

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