Commentary (Grossman/Nesbit): Opioid Rotation in Cancer Patients: Pros and Cons

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The overall strategy for appropriate management of cancer pain has been well described in algorithms that are the result of cooperative efforts by experts from many disciplines and cancer centers within North America.[1] Conceptually, the approach to cancer pain is straightforward. The etiology of the pain must be evaluated rapidly, and important aspects of the patient's history and physical examination that could influence treatment approaches must be identified. Therapeutic options available to patients with cancer pain are extensive and, if properly applied, result in prompt and excellent pain relief for most patients.

Opioid 'Rotation'

However, even with the available algorithms and guidelines crafted by experts, the key to success rests in the individual health-care provider's careful attention to details. When patients have persistent pain, clinicians are often eager to "rotate" to another opioid in hopes that this will be more effective or better tolerated. As the authors of this manuscript note, although formal studies confirming the efficacy of this approach are lacking, there is theoretical justification for this practice. Different opioids may target different receptors, patients may be more sensitive to the side effects of one agent than those of another, available opioids may have a somewhat different toxicity profile, opioids vary in cost and convenience, and some opioids have metabolites that can exacerbate toxicities in patients with hepatic or renal dysfunction. Nevertheless, it is clear that there is a price to pay for converting from one opioid to another. Doses are usually titrated downward to account for incomplete cross-tolerance. This can result in higher pain scores, at least temporarily, without a guarantee that the new agent will be more efficacious or less toxic. Serious over- or underdosing can occur as a result of nonlinear conversions (eg, with methadone) or the effect of concomitant hepatic p450 enzyme inducers (eg, codeine). Furthermore, it has been documented that physicians have significant difficulties performing equianalgesic conversions from one opioid or route of administration to another.[2] As opioid rotation could result in worse analgesia, we suggest the following steps be considered when patients present with poor pain control or excessive toxicities attributable to their opioid therapy.

1. Reassess the etiology of the pain
It is essential to reevaluate the possible mechanism of the patient's pain syndrome. If the pain syndrome has a neuropathic component, coanalgesics may play a significant role in achieving good pain control. Does the etiology of the pain demand therapeutic interventions other than symptomatic relief? A patient with an epidural cord compression may achieve some level of analgesia with opioids, but steroids and radiation therapy are more definitive interventions. Rotating to another opioid may be warranted after a thorough reassessment of the pain and consideration of additional therapies.

2. Determine opioid responsiveness
Opioid responsiveness is defined as the level of analgesia achieved by dose titration to either acceptable analgesia or intolerable side effects.[3] Factors that influence opioid responsiveness have been elucidated in the literature. These include pain mechanisms, tolerance, disease progression, opioid metabolites, routes of administration, and others. Opioid nonresponsiveness cannot be determined after a single opioid has been utilized. Portenoy reports that 10% to 30% of patients experience poor opioid responsiveness.[4] Opioid responsiveness may be increased by preventing tolerance through the use of N-methyl-D-aspartate (NMDA) antagonists (ie, methadone, ketamine, or dextromethorphan).[5]

3. Titrate fully before moving to another opioid

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In their article, Estfan et al describe the potential pitfalls of routine opioid rotation. It is incumbent upon the physician to aggressively titrate the opioid that the patient is receiving to acceptable analgesia or intolerable side effects before subjecting the patient to opioid rotation. It is not uncommon to note that patients "benefiting" from opioid rotation are in reality benefiting from a higher dose of opioids, as calculated by parenteral morphine equivalents per day, rather than the new agent. **4. Manage side effects fully**

Physicians hoping to reduce opioid-induced side effects by rotating to another opioid do this without knowing that the second agent will be any less toxic than the first. Therefore, they are obligated to make a serious attempt at managing opioid side effects before changing drugs. The appropriate management of sedation, nausea, pruritis, and constipation are well outlined in several of the complete cancer pain algorithms available online and in print. **5. Use available opioid conversion tools**

Studies have documented the difficulties that physicians and nurses have in converting patients appropriately from one opioid or route to another.[2] As a result, opioid conversion tables and nomograms are used for educational purposes. During the past decade, opioid conversion software has become available. The newest of these programs can be downloaded free of charge for the Palm OS and Windows CE operating systems from [www.hopkinsopioidprogram.org](http://www.hopkinsopioidprogram.org).[6] This program converts all current medications to parenteral morphine equivalents and then converts the results to any other opioid regimen, for any available formulation. The Hopkins website will also soon offer a Web-based version of this opioid conversion software. **6. Exercise caution with agents that can be difficult to titrate and convert**

There are inherent difficulties in titrating and performing equianalgesic conversions involving methadone and fentanyl. Methadone's long and variable elimination half-life may lead to drug accumulation and adverse effects. Equianalgesic conversions are particularly difficult, because methadone appears to increase in potency as the opioid dose increases.[7] Conversions to and from methadone should be individualized, and careful clinical monitoring is essential. Transdermal fentanyl can be difficult to titrate due to its long dosing interval. Furthermore, conversions involving transdermal fentanyl have been poorly studied, contributing to the complexity of its conversions. **7. Consider interventional analgesia**

Neurolytic blocks are an option in selected patients with localized or regional pain. For example, percutaneous celiac plexus neurolysis can be performed as an outpatient procedure and may provide better analgesia and fewer side effects in patients who have pain originating in the pancreas, stomach, gallbladder, or other upper abdominal viscera. When indicated, this procedure or others[8] may provide pain relief and allow required doses of opioids to be significantly reduced. Although cancer pain can be well controlled with available therapies, providing adequate analgesia to patients without significant toxicities takes time, effort, and careful monitoring. Opioid rotation clearly has a role in this process, but it is only one tool in the armamentarium of a multidisciplinary cancer pain team.

**Disclosures:**

The authors have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

**References:**


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