Alternatives to Oral Opioids for Cancer Pain

In managing cancer pain, an alternative to the oral route of opioid administration may be considered under several circumstances. For example, the oral route may not be feasible due to impaired swallowing, gastrointestinal obstruction, poor absorption, or altered mental status. If analgesia is not attained due to rapidly escalating pain, side effects are intolerable, or combination therapy with adjuvant analgesics is desired, an alternate route of opioid administration may be preferable.

Although the reported percentage of patients requiring alternate routes of opioid administration varies in different studies due to a multitude of factors, Drs. Mercandante and Fulfaro note that many patients will require at least one route conversion during their terminal disease course. Clinicians should be highly skilled in pain assessment and familiar with equianalgesic opioid dose ratios. In order to best serve their patients with complex requirements for pain and symptom management, practitioners should also know the advantages and disadvantages of the different routes of opioid administration.

In this paper, the authors review and briefly discuss easily manageable alternatives to the oral route of opioid administration for use at home. They recommend the subcutaneous route as the standard alternative to the oral route, and state that it is equianalgesic to the intravenous route. They suggest that there may be fewer side effects with subcutaneous than oral morphine due to lesser conversion to morphine metabolites with the subcutaneous route.

Another advantage of subcutaneous administration is that certain adjuvant agents for pain and symptom control may be combined with an opioid in a single infusion.[1] In the cancer setting, contraindications to subcutaneous administration include skin conditions (tumor or allergy). Most cancer patients with advanced, incurable disease are immunosuppressed, but the benefit of symptom control very often outweighs the risk of infection posed by the subcutaneous route.

Routes of Administration

There is not enough information in the literature on the use of sustained-release preparations given by the rectal route. For patients with an intact rectum and little stool formation, the rectal route may be preferable to parenteral infusions or injections. Although poor bioavailability and erratic metabolite production limit the use of rectal morphine, a drug with better bioavailability and negligible metabolite formation, such as oxycodone, may prove to be superior when given rectally. The authors note that dose titration of the commercially available transdermal fentanyl preparation (Duragesic) is often difficult to accomplish and that the conversion from morphine to this formulation has yet to be firmly established. Nonetheless, patient acceptance is high when dosing can be established. There are limited reports of the combination of transdermal fentanyl with other opioids to achieve higher total dose or to treat breakthrough pain. Iontophoresis is under development as a technique for managing breakthrough pain, and may soon reach the United States market. The oral transmucosal route is better with other opioids than with morphine. A preparation of oral transmucosal fentanyl (Actiq) has just been approved in the United States for breakthrough cancer pain. The clinical use of the intranasal and inhalational routes is still limited. Intranasal preparations of strong opioid agonists are not yet available. The indications for and dosing of inhalational opioids to treat dyspnea are presented in the paper. The authors do not discuss the intravenous route, which may be preferred if permanent venous access has been established.

Factors to Consider When Changing Routes of Administration

When changing from the oral to an alternate route of opioid administration, there are several issues to address. In practice, the clinician should consider the following:
1. the indication to change to a different opioid;
2. the conversion ratio across route(s);
3. the conversion ratio to different agent(s), if applicable;
4. dosing and volume for different route(s) and agent(s);
5. the indication to add an adjuvant agent; and
6. the feasibility of combining the opioid and adjuvant agent in a single route.

Once the above questions have been answered, the best therapeutic option can be chosen, taking into account the temporal course of pain, overall goals of therapy, available support in the home, and financial resources.

Regarding the temporal course of pain, continuous and breakthrough pain must be distinguished by careful assessment. Breakthrough pain can be defined as pain emerging in the setting of continuous analgesic administration via parenteral infusion, sustained-release oral or rectal schedule, or transdermal application. Breakthrough pain may be further categorized as pain due to end-of-dose failure, incident or provoked pain, or spontaneous pain that is often neuropathic.

When determining the alternative to oral administration, one must decide whether the route used to treat breakthrough pain will be the same as or different from the route used for continuous analgesia. Possible combinations are listed in Table 1.

**Conclusions**
The authors have reminded us that the oral route of opioid administration is preferred for cancer pain relief. Yet, we are slowly learning that not only alternate routes of opioid administration but also nonopioid pharmacologic and nonpharmacologic methods of analgesia should be considered earlier in the disease course. Much research remains to be done, however, to establish clinical criteria for selecting among the ever-increasing number of analgesic therapies available.

**References:**

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