TITRATION: PRACTICAL CONSIDERATIONS FOR PATIENTS AND PROVIDERS

- Titration to optimal effect is the central principle in the treatment of diseases with medications. This principle is seldom effectively applied to the treatment of chronic pain with opioids, because of irrational fears of respiratory depression, addiction, and ever-present threat of regulatory sanctions.

- Titration of opioids is complete when:
  1. The patient has regained optimal functioning, or
  2. Intolerable side effects have occurred. (This most commonly occurs with morphine or methadone.)

If one of these conditions has not been met, the patient has been robbed of an opportunity to lead a healthy life. There is no ceiling dose to limit the use of most opioids used in the treatment of chronic pain.

- Uncontrolled pain is a medical emergency. While it goes under-treated, the patient's health deteriorates. The current practice of making patients wait for their next appointment, which is often a month away, before the next increment in titration, is bad medicine.

- Dosages should be started low whenever a new medication is started, even if the patient already has a tolerance to other opioids. Increments should be smaller at first, allowing the patient to develop tolerance to undesired side effects, most of which occur at low dosages.

- In order to avoid the risk of respiratory depression, the interval between increases must be long enough for the patient to experience the full effect of the previous dose, which occurs when peak blood levels are achieved. With IV administration, time to peak blood level is only a few minutes. With immediate release oral preparations, peak blood levels occur in 20-30 minutes. With time released medications this takes at least an hour.

- If titration is performed at peak blood levels, only a 25%-100% increment in dosage should be administered. If a full dosing interval has passed, the dose should be 125%-200% of the previous dose.

- Pain is a moving target, making titration an ongoing process from hour to hour, and day to day. The conception that tolerance to the pain controlling effects of opioids doesn't or shouldn't occur is, in an academic sense, essentially sound, but can be misleading to the practitioner when a patient's pain levels increase after a period of stability.

A frequently overlooked fact in pain management is that as patients recover from long periods of debilitation caused by under treated or untreated pain, gradually increasing activity levels provoke corresponding increase in pain levels, and the need for increased dosages of opioids. Practitioners who don't anticipate this development are likely to become suspicious, and balk at performing the necessary titrations, which usually proceed over the course of several months.

When pain levels increase unexpectedly, the possibility of progression of disease should be entertained and evaluated if indicated. Titration should not be withheld.

- The dosage curve in the treatment of severely debilitated patients recovering from chronic pain is bell-shaped. Dosages increase gradually over the course of several months as the patient's activity level increases. Once the patient achieves full activity, the nervous system begins to heal, and dosages can be expected to diminish.

- Patients will often report satisfaction with under treatment of pain, for several reasons:

1. They are afraid of becoming addicted.

2. They feel morally righteous about keeping their dosages low, not understanding that they do so at the expense of their health.

3. Many have been tossed out of practices for complaining about continuing pain, and for asking for more medication. Half a loaf is better than none.

4. Under treated patients seldom realize the qualitatively different realm of functioning in which they would exist if they were titrated properly. Most profoundly disabled patients have not experienced this, and understandably have no idea what benefits might result.

Dr. Russell Portenoy is widely recognized as a world authority on the treatment of chronic pain with opioids. Here is what he has to say on the subject in *Substance Abuse: A Comprehensive Textbook* ed. 3, Lowinson, Joyce H., ed., Williams & Wilkins Co, 1997:

Once an opioid and route of administration are selected, the dose should be increased until adequate analgesia occurs or intolerable and unmanageable side effects supervene. **There is no ceiling effect to the analgesia provided by the pure agonist opioid drugs and the maximal dose is immaterial as long as the patient attains a favorable balance between analgesia and side effects.** This implies that the opioid responsiveness of a specific pain can only be ascertained by dose escalation to limiting side effects. In clinical practice, the range of opioid doses required by patients is enormous. **Doses equivalent to more than 35 g morphine per day have been reported** in highly tolerant patients with refractory cancer pain.
- P. 573,

This therapy remains controversial and prescribers cannot be assured that those in the regulatory community will not initiate an investigation, or even issue a sanction, because of bias against the approach and without regard for the details of the case.
- P. 582

Concern about regulatory scrutiny is understandable, and **it is likely that dose escalation is sometimes withheld solely in response to perceived risk of sanctions.**
- P. 584

CHRONIC PAIN AND OPIOIDS: DEBUNKING THE MYTHS

Comments/Opinions
Frank B. Fisher, MD
frankbfisher@earthlink.net
510-233-3490
Or webmaster@cpmission.com