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FAST FACTS AND CONCEPTS #86

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Background Methadone is an effective opioid analgesic for severe pain. Because of low cost (a month's supply may be US \$5-10) and apparent efficacy in complex pain syndromes, it is increasingly used as a first-line opioid. It is, in effect, a combination drug – part opioid and part NMDA receptor antagonist – although there is yet to be any evidence from controlled trials that it is a superior first-line analgesic to other opioids. Methods of dose conversion to methadone from other opioid analgesics that account for its dual action were discussed in Fast Fact # 75. A future Fast Fact will discuss different protocols for switching to methadone from other opioids. This Fast Fact will describe strategies for beginning methadone when the patient has not been taking a strong opioid. **Note:** due to its complex pharmacology, physicians unfamiliar with methadone are advised to seek consultation prior to initiating therapy (see Fast Fact #171).

Pharmacology Methadone is lipophilic, thus it takes time to develop tissue stores that maintain serum levels. There is enormous interindividual variation in how long this takes. After a single dose there is a short distribution phase (associated with acute pain relief) with a half-life of 2-3 hours and a slow elimination phase (half-life 15-60 hours). Dosing must account for the accumulation of drug over days. It is this accumulation that accounts for most therapeutic misadventures. Liver metabolites are inactive; therefore no dose reduction is required with renal failure. After steady-state is reached, about two-thirds of patients will get adequate pain relief with twice a day dosing. **Note:** a number of drugs will alter methadone metabolism, so there needs to be close follow-up and attention to the addition or subtraction of interacting medications.

There are several approaches to starting methadone for the treatment of pain. All take into account the long-half life of the drug that leads to drug accumulation over days. The following discussion presents approaches based on the literature and the author's clinical experiences.

Conservative Approach

- Begin fixed dose methadone 5 or 10 mg orally bid or tid for 4-7 days.
- If incomplete pain relief, increase the dose by 50% and continue for 4-7 days.
- Continue increasing dose every 4-7 days until stable pain relief achieved.
- Breakthrough pain: use an alternative short acting oral opioid with short half-life (e.g. morphine 10 mg) every 1 h PRN for breakthrough pain and to provide pain relief during titration phase. This dose too may need to be titrated based on efficacy.

Loading Dose Approach

- Load: Start methadone at fixed oral dose (e.g. 5 or 10 mg) q 4h **PRN only**.
- Calculate Maintenance: On day 8, calculate the total methadone dosage taken over the last 24 hour period and give that in scheduled, divided doses bid or tid. Give 10% of total daily methadone as PRN drug q1h for breakthrough pain. Instruct the patient to call you if they need to use more than 5 breakthrough doses per day. *Example:* if someone took a total of 45 mg methadone on day 7 they would be converted to 15 mg tid scheduled with 5 mg as the prn dose.

References

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