PART II: EQUIANALGESIC DOSING

Alternative Routes of Administration

- In general, the oral route is the least invasive, most convenient route for administering opioids on a routine basis
- However, selected patients may benefit from other routes of administration if:
    - Oral intake is not possible due to:
        - Vomiting
        - Dysphagia
        - Esophageal obstruction
    - Oral intake causes uncontrollable adverse effects such as:
        - Nausea
        - Drowsiness
        - Confusion
- Alternate routes of administration include the following:
    - Enteral feeding tubes
    - Transmucosal
    - Rectal
    - Transdermal
    - Parenteral
    - Intraspinal

Enteral feeding tubes

- Provide alternatives for bypassing gastroesophageal obstructions
- Deliver the medications to the stomach or upper intestine where the medications behave pharmacologically as though they had been ingested orally

Transmucosal

- Transmucosal (buccal mucosal) administration of more concentrated immediate-release liquid preparations provides an alternative similar to that provided by enteral feeding tubes
- This route is particularly effective for:
    - The patient who is unable to swallow
    - Patients who are dying
- Oral transmucosal fentanyl citrate is a new formulation of fentanyl in a candy matrix on a stick
    - Approved for the treatment of breakthrough pain
    - To date, experience with the formulation is very limited (US only)

Rectal

- Rectal administration of immediate or extended-release rectal preparations behave pharmacologically like related oral preparations
- This route may be very effective if oral intake is suddenly not possible
- Many patients do not like this route for continuous administration

Transdermal

- Transdermal patches present an effective alternative route of administration for patients receiving stable routine opioid dosing
- Transdermal patches currently only manufactured containing fentanyl

- They behave quite differently from other extended-release formulations
    - Steady-state equilibrium is established between the medication in the patch, a subdermal pool that develops, and the patient's circulation
    - On average, best possible pain control is achieved within 1 dosing interval (i.e., 3 days) with peak effect at about 24 hours
    - The effect usually lasts for 48 to 72 hours before the patch needs to be changed
- Care must be taken to ensure that patches:
    - Adhere to the patient's skin (avoid hairy areas)
    - Do not lift off with bathing or sweating

Parenteral

- Parenteral administration using injection or infusion can be very useful in selected patients
- When renal function is normal:
    - Provide routine parenteral bolus doses every 3 hours
    - Adjust the dose every 12 to 24 hours (once steady state is reached)

- If a parenteral route will be used for some time, continuous infusions may:
    - Produce a more constant plasma level
    - Reduce the risk of adverse effects
    - Be better tolerated by the patient
    - Require less intervention by professional staff

- Patient-controlled analgesia has been shown to be:
    - Effective
    - Well tolerated by patients

- Parenteral administration options, all of which require effectively the same dosages, include:
    - Subcutaneous
    - Intravenous
    - Intramuscluar

Subcutaneous

- All opioids available for parenteral use may be administered subcutaneously
- Subcutaneous administration helps avoid:
    - Discomfort associated with searching for an IV site
    - Risk of serious infection
- Either 25- or 27-gauge needles can be used for both bolus dosing and infusions
    - The needles can be left in place for 7 days or more as long as there is no sign of infection or local irritation
    - Family members can be taught to change them

Intravenous

- Intravenous infusions may be preferable if intravenous access is:
    - Already established
    - In use for other medications
- If intravenous access is not already established and in use, subcutaneous administration may be preferable in order to reduce:
    - Discomfort associated with searching for an IV site
    - Risk of serious infection

Intramuscluar

- Intramuscular injections are not recommended

- Intermittent subcutaneous doses are:
    - Much less painful
    - Equally effective

Intraspinal

- Options for intraspinal opioid administration include:
    - Epidural
    - Intrathecal
- Intraspinal administration may be useful in selected patients who have:
    - Pain in the lower part of their body
    - Pain that is poorly responsive to routine systemic opioid therapy
- A specialist who is knowledgeable about their specific indications and pharmacology, and who is skilled in their delivery, is usually required to administer them

Bolus Effect

- As the total dose of opioid to the bloodstream increases, some patients may experience:
    - Drowsiness ½ to 1 hour after ingestion of a dose of medication (as the plasma level peaks)
    - Pain just before the next dose is due (as the plasma level falls)
- This syndrome, known as the "bolus effect," can only be resolved by reducing swings in the plasma concentration after each dose by switching to:
    - Extended-release formulation (oral, rectal, or transdermal) or
    - Continuous parenteral infusion

Changing Opioids: Converting To or From Transdermal Patches

- When converting to or from transdermal fentanyl patches, published data suggest that a 25-mg patch is equivalent to 45 to 135 mg of oral morphine per 24 hours
- However, clinical experience suggests that most patients will use the lower end of the range of morphine doses (i.e., for most patients, 25 mg is about equivalent to 45 to 60 mg of oral morphine per 24 hrs)

Opioid Cross-Tolerance

- While pharmacologic tolerance may develop to the opioid in use, tolerance may not be as marked relative to other opioids
- Incomplete cross-tolerance is likely due to subtle differences in:
    - The molecular structure of each opioid
    - The way each interacts with the patient's opioid receptors

- Consequently, when switching opioids, there may be differences between published equianalgesic doses of different opioids and the effective ratio for a given patient
- Start with 50% to 75% of the published equianalgesic dose of the new opioid to compensate for incomplete cross-tolerance and individual variation, particularly if the patient has controlled pain
    - If the patient has moderate to severe pain, do not reduce the dose as much
    - If the patient has had adverse effects, reduce the dose more

- An important exception is methadone, which appears to have higher than expected potency during chronic dosing (compared with published equianalgesic doses for acute dosing)
    - Start with 10% to 25% of the published equianalgesic dose
    - Titrate appropriately to achieve pain control

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