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## **Pain Treatment with Opioids: Achieving the Minimal Effective and the Minimal Interacting Dose**

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### **Abstract**

Appropriate and successful management of pain with opioid analgesics is based on tailoring pharmacologic treatment to the individual and identifying the minimal effective dose at which pain is controlled with minimal adverse effects. Morphine and morphine-like-agonists exhibit similar pharmacodynamic profiles, but substantially different receptor affinities and pharmacokinetic properties, which dictate the dosage, route and regimen required to achieve analgesic effect.

Opioids exhibit differences in drug elimination resulting in marked variations in the plasma half-life value. Although fentanyl is more potent than morphine, with a shorter duration of action than parenteral morphine, its oral bioavailability is poor and it is administered transdermally. Morphine, with a short half-life and a time to steady-state plasma concentrations of 10-12 hours is better suited than transdermal fentanyl for initial opioid therapy and for the treatment of unstable pain, which requires a fluctuating opioid dose. International guidelines recommend normal-release morphine for initial optimization of individual dose because its pharmacokinetics allow 'real-time' dose regimen changes and rapid identification of the dose required for pain control.

Once an effective normal-release morphine dosage is achieved, other administration routes, formulations and opioids can be considered as required. Despite guidelines advocating that transdermal fentanyl should only be used in patients who are shown to be tolerant to strong opioid therapy, in Italy and other European countries, controlled-release or transdermal opioids

are often used when starting opioid therapy. Opioids are associated with a wide range of adverse reactions, but these can be minimized with careful drug titration and maintenance.

A major challenge with pain control is polypharmacy and the risk of pharmacokinetic or pharmacodynamic drug-drug interactions. Prevention and management of interactions rely on careful and timely adjustment of drug regimens involved, according to the severity of the effect. Dose titration is the key to successful therapy initiation with strong opioids in patients with moderate-to-severe pain. It is the only way to establish the optimal and minimal effective dose and provides the best protection against adverse effects. Committed physicians should adhere to guidelines on the appropriate use of opioids in all patients, particularly those with a high risk of adverse reactions.

### Special Announcements:

#### Save the Date!

**August 28–29, 2010:** TNA's 8th National Conference  
Celebrating our 20th Anniversary at The Mayo Clinic Rochester, MN

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