Tramadol & Tapentadol

Dual Analgesic Mechanisms

Fb/Nurse-Info

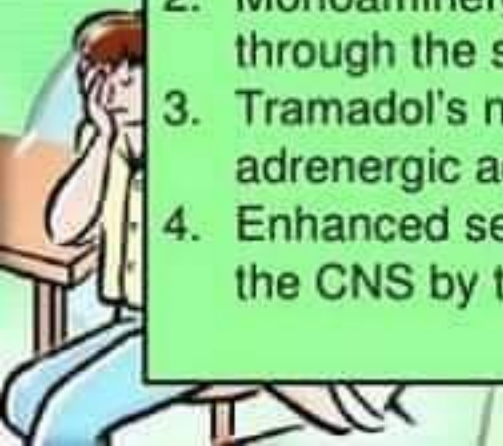
Tramadol

Opioid Activity

1. Tramadol produces antinociception via predominantly, a mu-opioid receptor mechanism.
2. No respiratory depression, sedation, or constipation, as observed with other opiates.
3. No analgesic tolerance
4. No psychological dependence or euphoric effects in long-term clinical trials

Monoaminergic Activity

1. Noradrenergic and serotonergic neurons originate in the brainstem and terminate in the dorsal horn of the spinal cord
2. Monoaminergic pathway modulates the spinal processing of nociception through the section of norepinephrine and serotonin
3. Tramadol's novel mechanism of analgesic action is partially due to its adrenergic action and
4. Enhanced secretion of serotonin and inhibits the reuptake of serotonin in the CNS by tramadol.



Tramadol

CYP2D6 Pathway

1. Tramadol is a racemic mixture of a (+)- and a (-)-enantiomer.
2. + enantiomer is selective agonist of mu-opiate receptors and preferentially inhibits serotonin reuptake.
3. -ve enantiomer mainly inhibits noradrenaline reuptake
4. Tramadol is a prodrug that requires transformation by the cytochrome P450 complex to the metabolically active **O-desmethyl-tramadol.**
5. The parent molecule also produced analgesia via a monoaminergic action

Tramadol

Efficacy

1. Effective and well-tolerated analgesic in all 3 forms of administration.(PO,IV,PR)
2. Onset of analgesia is within 30 minutes
3. Duration of action from 3 to 7 hours
4. Drowsiness is the most frequent side effect
5. No adverse effects were observed in the parturient after labor or in the newborn when given for Labour pain relief

Tramadol

Adverse Events

Dependence

1. Withdrawal symptoms after abrupt discontinuation or reduction of dose.
2. hallucinations, paranoia, extreme anxiety, panic attacks, confusion, and unusual sensory experiences can occur in rare cases

Serotonin Syndrome

1. Minor possibility of this exists with both tramadol and tapentadol
2. Avoid concurrent administration of SSRI's or selective-norepinephrine reuptake inhibitors, triptans, or tricyclic antidepressants

Tapentadol

1. FDA approved tapentadol hydrochloride in 2008
2. for oral treatment of moderate-to-severe acute pain in patients older than 18 years

Centrally acting analgesic with 2 mechanisms of action in a single molecule: mu-opioid agonism and norepinephrine reuptake inhibition

Major Difference

Tramadol	Tapentadol
racemic mixture of a (+)- and a (-)-enantiomer	nonracemic compound
Has active metabolites	has no active metabolites
Tramadol is a prodrug that requires transformation by the cytochrome P450 complex	No such thing is required
O-desmethyl-tramadol (the metabolite) is actually the active form	Tapentadol itself is the active form
Poor metabolizer will not show adequate response to therapy	No such problem with Tapentadol

Tapentadol is as effective as oxycodone or morphine, with a lower incidence of gastrointestinal adverse side effects

Tapentadol

Pharmacokinetics

1. Oral absorption of tapentadol is rapid
2. Is present in the serum in the form of conjugated metabolites
3. Excretion was exclusively renal (99%: 69% conjugates; 27% other metabolites; 3% in unchanged form)