IV Oxycodone: An alternative to IV Morphine for post-operative PCA use?

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Acknowledgements

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What am I going to talk about?

- Pharmacology – only a little bit
- Clinical Trials – IV Morphine vs IV Oxycodone PCA for acute post-operative pain
- Recommended dosage and administration of IV Oxycodone
Oxycodone: Basic Pharmacology

**Chemical name:**
- 4,5alpha-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride

**Molecular formula:**
- $\text{C}_{18}\text{H}_{21}\text{NO}_4\cdot\text{HCl}$

**Molecular weight:**
- 351.83
Oxycodone: Basic Pharmacology

- **Structural formula:**

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![Structural formula of Oxycodone](image-url)
Oxycodone: Basic Pharmacology

**Description:**
- White, crystalline odourless powder
- Freely soluble in water
- Sparingly soluble in ethanol
- Nearly insoluble in ether
Oxycodone: Basic Pharmacology

**Actions:**

- Principal therapeutic action is **analgesia**
  - The inability to feel pain while still conscious (from the Greek *an-*, without + *algesis*, sense of pain).

- Full opioid agonist

- No antagonist properties

- Similar to Morphine in its action
Oxycodone: Basic Pharmacology

**Actions:**

- Affinity for mu, kappa and delta opiate receptors in the brain and spinal cord
  - Kappa-opiate receptors are widely distributed in visceral organs

- Other actions involve:
  - CNS: respiratory depression, sedative, miosis
  - CVS: histamine release, pruritus
  - SM: constipation, urinary retentions
Oxycodone: Basic Pharmacology

**Pharmacokinetics:**

**Absorption**

- Equivalent availability by all parenteral routes when administered as a single bolus dose or continuous infusion over 8 hrs
  - Tmax for S/C administration is 0.25-0.5 hrs (considerable inter-individual variability)
- Following absorption, it’s distributed throughout the entire body
  - Cmax for S/C bolus is lower than for IV bolus
Oxycodone: Basic Pharmacology

**Distribution**

- ~45% plasma bound

- Plasma concentrations
  - minimally affected by age (15% > elderly)
  - in those with mild to severe hepatic dysfunction
    - Oxycodone / Noroxycodone: Higher
    - Oxymorphone: Lower
Oxycodone: Basic Pharmacology

Metabolism

• Site:
  - intestines / liver

• Forms:
  - noroxycodone (CYP 3A4)
  - oxymorphone (CYP 2D6)
  - conjugated glucuronides

• Contribution of metabolites to analgesic effect is insignificant
  - oxymorphone has some analgesic activity but present in plasma in low concentrations
Oxycodone: Basic Pharmacology

- **CYP 2D6**
  - Oxycodone is N-demethylated by CYP2D6 to its active metabolite oxymorphone
  - Expressed as 2 phenotypes (genetic polymorphism)
    - Extensive metabolisers:
    - Poor metabolisers:
      - ~10% Caucasian population
      - May have increased plasma concentrations of oxycodone because of decreased oxidation by CYP 26D

- **Q: so what does this mean?**
  - **A: lower dosage may be needed**
Oxycodone: Basic Pharmacology

Elimination

• Half life: 3hrs

• Half life *may* be increased with mild to severe hepatic or renal dysfunction
  – Considerable inter-individual variability
  – Administration doesn’t result in significant levels of active metabolites, but plasma concentrations in this group may be increased
Ok, enough pharmacology...
A bit about clinical trials…..

IV Morphine vs IV Oxycodone PCA in the post-operative period É..

É. How do the two compare regarding analgesic efficacy?
What I found in the literature...

  Silvasti M, Rosenberg P, Seppälä T, Svartling N, Pitkänen M

“Comparison of analgesic efficacy of oxycodone and morphine in postoperative intravenous patient-controlled analgesia”
BACKGROUND: Morphine has been the standard opioid in patient-controlled analgesia (PCA). Oxycodone, the analgesic potency of which in IV administration has been suggested to be slightly greater than that of morphine, has not yet been studied for its efficacy in PCA.

METHODS: 50 patients, undergoing a plastic reconstruction of the breast or a major operation of the vertebrae, such as lumbar spinal fusion, used PCA for postoperative pain. Patients were randomized to receive either morphine 45 microg/kg or oxycodone 30 microg/kg as IV bolus doses. Patients were assessed for pain with a visual analogue scale (VAS) and side effects at 3, 9 and 24 h. Venous blood samples for the measurement of plasma concentration of oxycodone and that of morphine and its metabolites were taken.

RESULTS: In this study patients needed, on average, the same amount of oxycodone and morphine in the recovery room and on the ward. There was no difference in the quality of analgesia (VAS) or incidence of side effects, such as nausea, vomiting, pruritus and urinary retention. The plasma concentrations of morphine-6-glucuronide showed that this metabolite might contribute to the analgesia resulting from morphine administration.

CONCLUSION: The same dose of IV oxycodone and morphine administered by PCA pump was needed for immediate postoperative analgesia. The two drugs appear to be equipotent.
But wait....there's more!

The last knives you'll ever need.
Other stuff I found in the literature...


- Looked at comparing safety and efficacy of PCA IV oxycodone vs IV morphine for acute post-operative pain
  - Randomised, double blind, parallel group study
  - ITT / safety populations: 133 patients (117 completed)
  - 56 patients oxycodone: 61 patients morphine

- Findings
  - No significant difference in median drug use
  - 69mg (12 to 336mg) oxycodone : 54mg (7 to 212mg) morphine
  - In the per-patient protocol and in the ITT population
  - Common adverse drug reactions were all known opioid SEs, but respiratory depression was uncommon
Recommended dosage & administration
IV Oxycodone

- I’m gonna hand ball this one to Spiro from..