Buprenorphine/naloxone

~~Suboxone®~~-The basics and that's all!

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Faculty/Presenter Disclosure

- **Faculty:** Nicole Nakatsu

- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
  - **Speakers Bureau/Honoraria:** Fresenius Kabi
  - **Consulting Fees:** None
  - **Other:** None

Mitigating Potential Bias

- Fresenius Kabi, did not, at the time of the presentation produce any narcotics nor did they have any input on the content of the presentation.

Learning Objectives

- By the end of this session, participants will be able to
- Describe the pharmacology of buprenorphine/naloxone
- have a basic understanding of how to start a patient on buprenorphine/naloxone

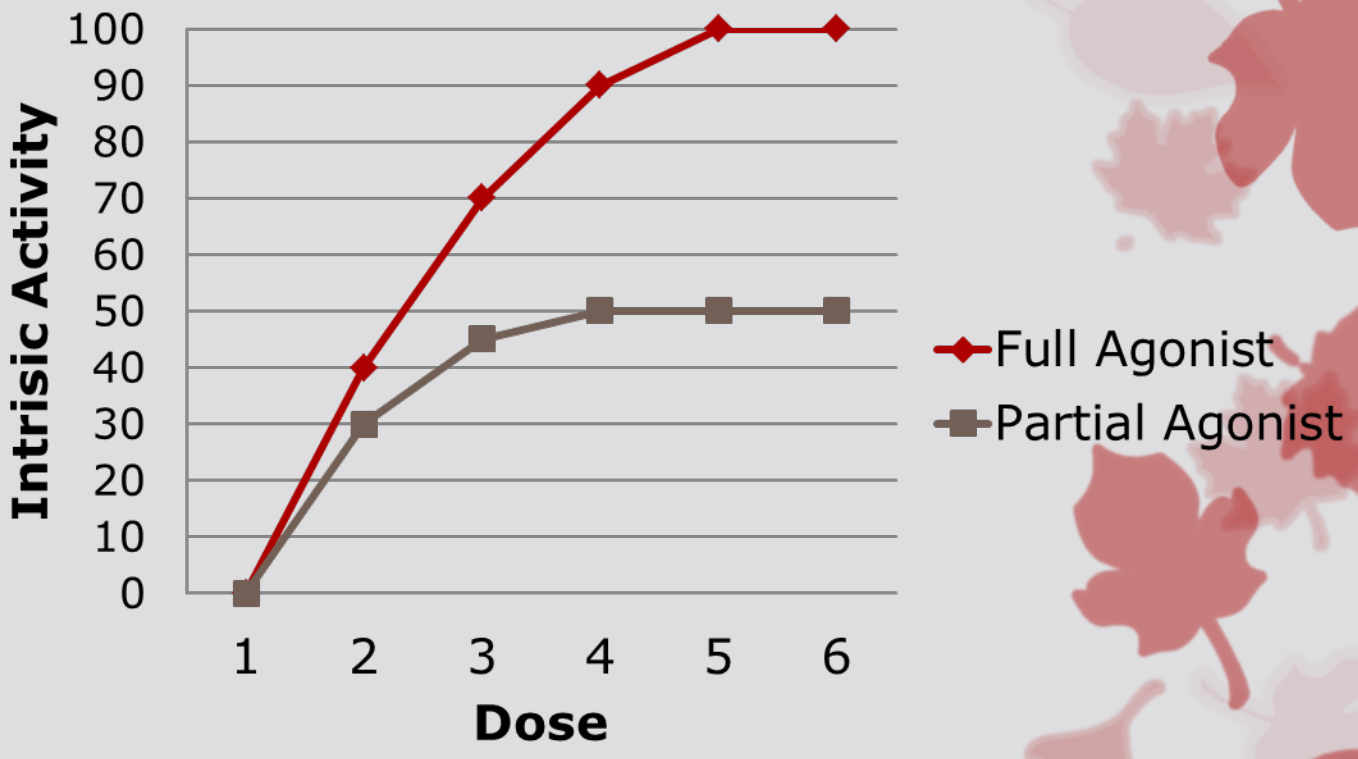
Buprenorphine/naloxone

- Opioid agonist treatment option for opioid-dependent patients
- Considered first line by the recently published “Management of opioid use disorders: a national clinical practice guideline” CMAJ

Buprenorphine-MOA

- Partial opioid agonist
- Low intrinsic activity at the μ-opioid receptor-ceiling effect
- Very high affinity for the μ-opioid receptor (will displace morphine, methadone, other full agonists)
- Slow dissociation from the μ-opioid receptor
- Antagonist at the kappa opioid receptor

Full Agonist vs Partial Agonist



Buprenorphine

- Considered safer in overdose than methadone
- Generally less side effects
- May not fully prevent withdrawal symptoms in heavy opioid users
- Less withdrawal on discontinuation
- Less adverse effects or attenuated adverse effects (less sedation, less constipating)

Buprenorphine

- Onset of action 30-60 minutes
- Peak effects 1-4 hours
- Duration of action is dose dependent (4 hours to 3 days)
- Reaches steady state in 3-7 days

Buprenorphine

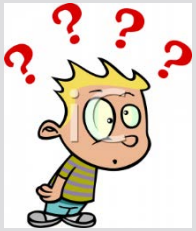
- Extensive first pass metabolism
- Metabolized by CYP450 3A4 to active metabolite nor-buprenorphine and glucuronidated
- Mainly eliminated in the feces

Drug Interactions

- Monoamine Oxidase inhibitors (MAOIs)
- Strong 3A4 inducers/inhibitors
- Other sedating drugs
- Blocks analgesic effects of full opioid agonists-pain management can be difficult.
- Benzos-combination produces additive respiratory depression-no plateau
- Can prolong QT interval

Buprenorphine/Naloxone

- Buprenorphine
  - Partial μ-opioid agonist
- Naloxone
  - Pure antagonist to *μ* (mu) and *κ* (kappa) opioid receptors



Buprenorphine/naloxone

- SL administration
- Buprenorphine has good SL bioavailability (30-55%) but low PO bioavailability (very high first pass metabolism)
- The purpose of associating buprenorphine with naloxone is to prevent inappropriate IV usage
  - Rapid binding **precipitates a rapid opioid-withdrawal syndrome** when naloxone injected
- Naloxone has low SL or PO bioavailability

Observed dosing

- Dissolution time: 2-10 minutes
  - Becomes a pulpy mass

Dosing

- Usual daily dose: 4 to 16 mg
- Maximum dose: **24 mg/day** (Canadian monograph)
- When initiating buprenorphine the person must be in opioid withdrawal
- Will cause precipitated withdrawal in a person who has taken a full opioid agonist and is physically dependent on opioids

Precipitated Withdrawal?

- Partial agonist with stronger binding to μ opioid receptors than other opioids and other opioid antagonists
- Prevents other opioids from attaching to μ opioid receptors and displaces other opioids with weaker affinities for the μ receptors (morphine, methadone, heroin, oxycodone)
  - **Effects from full opioid agonist are replaced by lesser effects of partial agonists**
- Clinicians need to determine the **correct timing and dosage** of buprenorphine/naloxone according to the patient's **last dose of opioid**

Clinical Opiate Withdrawal Scale (COWS)

Flow-sheet for measuring symptoms over a period of time during buprenorphine induction.

For each item, write in the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date: _____

Buprenorphine induction:

Enter scores at time zero, 30min after first dose, 2 h after first dose, etc.

Times: _____ _____ _____ _____

Resting Pulse Rate: (record beats per minute) *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120				
Sweating: *over past ½ hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face				
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds				
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible				
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/ muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present				

Initiating Suboxone Treatment

- Assess patient for withdrawal using the COWS scale
  - if withdrawal is moderate: start with 2 mg dose
  - if withdrawal is severe: can start with 4 mg dose
- A second dose can be given after 4 hours
- Day 2 give the total dose for day 1 plus another increase if needed
- Dose can be adjusted daily
  - A stable dose can be reached within 3-4 days

Questions?

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