Reza Daneshmand
MD Psychiatrist

Managing Buprenorphine Early Reactions

Pharmacology

Onset of effects	30–60 minutes
Peak clinical effects	1–4 hours
Duration of effects	8–12 hours at low dose (e.g. 2 mg)
	24–72 hours at high dose (e.g. >16 mg)

Property	Clinical implication
Produces opioid effects	Reduces cravings for heroin and enhances treatment retention.
Prevents or alleviates heroin withdrawal symptoms	Can be used for maintenance or withdrawal treatment.
Diminishes the effects of additional opioid use (e.g. heroin)	Diminishes psychological reinforcement of continued heroin use. May complicate attempts at analgesia with opioid agonists (e.g. morphine).
Long duration of action	Allows for once-a-day to three-times-a-week dosing.
Ceiling on dose response effect	Less sedating than full agonists (heroin, morphine or methadone). Buprenorphine doses above 12mg/day may not increase the opioid agonist effects, but will prolong the duration of action. Safer in overdose, as high doses in isolation rarely result in fatal respiratory depression.
Sublingual preparation	Safer in accidental overdose (e.g. in children) as poorly absorbed orally. More time involved in supervised dispensing.
Modified withdrawal precipitated by opioid antagonists.	Treatment with naltrexone can be commenced within 5–7 days of buprenorphine. May complicate management of opioid overdose requiring high naloxone doses.
Side effect profile similar to other opioids	Generally well tolerated, with most side effects transient.

Adverse Reactions

Adverse event	Proportion of patients reporting adverse event	Relation to dose
Headache	8.7 %	Appears unrelated to dose
Constipation	7.5 %	More common on higher doses
Insomnia	7.3 %	Appears unrelated to dose
Asthenia	6.1 %	Appears unrelated to dose
Somnolence	4.3 %	Appears unrelated to dose
Nausea	3.5 %	More common on doses > 8 mg
Dizziness	2.7 %	More common on higher doses
Sweating	2.7 %	Appears unrelated to dose

Adverse Reactions

- Withdrawal precipitated by buprenorphine dose
  - Occurs early in treatment (or after absence from treatment) when buprenorphine dose administered soon after opioid use
    - *Transient effect. Aim to prevent by patient education. Delay buprenorphine dose until patient experiencing opioid withdrawal Discourage use of on-top heroin.*

Adverse Reactions

- Withdrawal symptoms maximal before next dose
  - Dose too low
  - Changes in legal or illegal drugs that patient may be using
    - *Raise maintenance dose or review other drugs patient is taking*

Adverse Reactions

- Headache
  - Common in first week of buprenorphine treatment
  - Other causes of headache; those with migraine history are more prone
    - *Side effect is transient and generally mild. Consider aspirin or paracetamol, ibuprofen. Consider other causes*
    - *Taking the dose at bedtime may help. Splitting the dose is sometimes helpful.*

Adverse Reactions

- Constipation
  - All opioids do this. Will be made worse by lack of dietary fiber, fluid intake or exercise
    - *Treat with over-the-counter stool softeners; encourage fiber intake (fruit, cereals, vegetables), fluids; and regular exercise.*

Adverse Reactions

- Poor sleep, Insomnia
  - Dose too low and causing withdrawal at night
  - Dose too late at night, causing stimulation at time of peak effects
  - Other drugs
  - General anxiety, depression, history of insomnia
    - *Review maintenance dose and review other medications*
    - *Follow sleep hygiene recommendations*

Adverse Reactions

- Feeling drowsy after taking dose, Sedation
  - Dose too high
    - *Lower the maintenance dose and review other medications the patient may be taking*
    - *Patients should not become so relaxed that they "nod off" on buprenorphine.*
  - Other drug use (legal or illegal)
    - *Review use of sedative and other drugs affecting cognition*

Adverse Reactions

- Nausea
  - Common early in treatment, particularly if buprenorphine dose too high, and is sometimes related to the taste of the pills
    - *Side-effect usually transient (days). Avoid rapid dose increases. Consider dose-reduction if persistent*
    - *Try to get the pill to dissolve more quickly. Use mints, breath strips on tongue while medication under tongue*
    - *Split dosing.*

Adverse Reactions

- Taste Perversion
  - Sensitivity to the taste of the medicine
    - *Drink something before taking dose to increase saliva, and quicken absorption. OJ and Soda work well.*
    - *Break or crush tablet before putting under the tongue to quicken the process.*
    - *Do not put more than two large tablets under tongue at one time*

Adverse Reactions

- Vomiting
  - This side effect occurs very early on. When it happens, it is very difficult for the patient, and can jeopardize ability to stay on buprenorphine
    - *Distinguish between a side effect and withdrawal*
    - *Medical support is needed to assess and mange the causes of this symptom; may need antiemetic, hydration, …*
    - *It usually resolves, and is not a common side effect.*

Adverse Reactions

- Sweating
  - This symptom may be a side effect of the medication, or it may be due to withdrawal; It occurs less frequently at lower doses
    - *Distinguish between a side effect and withdrawal*
    - *Try splitting the dose to decrease sweating*

Adverse Reactions

- Pain
  - If this symptom begins during induction, the patient may have been sub-consciously self-medicating
    - *Evaluate the etiology of the pain*
    - *Determine the best treatment for the pain*

Adverse Reactions

- Anxiety
  - Comorbid anxiety may worsen during the treatment period and patient may abuse buprenorphine as a self-treatment for anxiety
    - *The patient should be seen by a psychiatrist and evaluated to avoid relapse.*
    - *The patient should avoid benzodiazepines if at all possible and if there is a history of abuse.*

Adverse Reactions

- Lowered sex drive
  - More common with a high dose
  - Cause by many other psychological factors
    - *Review dose*
    - *May resolve; if it doesn't resolve, seek medical support*
    - *Consider treatment of psychiatric comorbidities*

Adverse Reactions

- Weight gain, particularly for women
  - Fluid retention caused by opioids; more likely on high doses
    - *Lower dose*
  - Eating more while in treatment; high salt intake
    - *Reduce fat and salt in diet, exercise regime*

Adverse Reactions

- Rash, Hives, Pruritus
  - This may be an allergic reaction
    - *In this instance, treatment may need to be discontinued*
    - *Seek medical provider attention*

Adverse Reactions

- Amenorrhea or oligomenorrhoea
  - All opioids can do this
  - May be related to lifestyle stressors, poor diet, and general poor health
    - *Periods may return after cessation of heroin use, or following withdrawal from opioids*
    - *Address other causes*

Adverse Reactions

- Increase liver enzymes
  - This should be carefully monitored for patients with HIV and HCV.
    - *Obtain baseline LFTs as well as Hepatitis B, and C serology's.*
    - *Check levels frequently during treatment.*

Adverse Reactions

- Dental problems
  - All opioids reduce saliva flow
  - Poor diet, dental hygiene
    - *Encourage oral hygiene, dental floss and use of sugar free gum.*
    - *Dental check-up. Reduce intake of sugary drinks and sweet food*