Opioid Overdose Best Practices Guideline

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Key Points

- Patients with opioid overdose die from respiratory depression
- Ultra potent opioids like fentanyl are increasingly responsible for overdose presentations in BC
- Naloxone should initially be dosed cautiously to prevent precipitating withdrawal
- High doses of naloxone may be required for higher potency opiates such as fentanyl
- All patients who present with opioid overdose should be offered follow up with addictions services and provided with information regarding take home naloxone and safer drug practices.

In 2016 there were 914 illicit drug overdose deaths in BC, the highest rate ever, and fentanyl was detected in 60% . In response to this epidemic these new guidelines were written to reflect both the high potency and unknown duration of action of fentanyl in overdose.

A. General description:

Opioids are substances that are active at the opioid receptors in the CNS. They are most commonly prescribed to relieve pain but are also infrequently used as cough suppressants and antidiarrheal agents. Opioid agonist therapy with methadone and buprenorphine is used to treat opioid use disorder. Heroin has historically been the most common causative agent in opioid overdose; however, prescription opioids and potent synthetic opioids such as fentanyl are increasingly common in overdose.

Toxic dose: Toxicity varies with the patient's age, past medical history, route of administration, presence of additional drugs such as ethanol or benzodiazepines, degree of tolerance and potency of the opioid. Fentanyl, which is increasingly common in BC, is roughly 100 times more potent than morphine and 25 to 70 times more potent than heroin.

B: Typical signs and symptoms:

Opioid toxicity presents as sedation, miosis and progresses to **r*espiratory depression, coma and death.*** People who inject drugs may have cutaneous signs of drug use such as "track marks." Some opioids, including methadone and loperamide, cause QT prolongation and predispose patients to ventricular dysrhythmias such as torsades de pointes. Fentanyl may induce chest wall rigidity, which is a contributing factor to respiratory arrest. Significant opioid overdose can also lead to acute lung injury and non-cardiogenic pulmonary edema.

Note: The possibility of other ingestions such as ASA and acetaminophen must be considered in the context of opioid overdose due the ubiquity and abuse of ASA and acetaminophen opioid combination products.

C. Expected course:

Onset of symptoms: Symptoms develop rapidly following IV injection or insufflation. Peak effect typically occurs within 1 hour of ingesting regular-release products or crushed/adulterated sustained-release tablets. Symptoms may be significantly delayed with massive ingestion and sustained-release products. Absorption may be delayed up to 24 hours with ingested fentanyl patches.

Duration of action: The duration of action depends on dose, ongoing absorption and the half-life of the opioid. The duration of action of any drug in overdose can be significantly longer than seen with therapeutic dosing.

Short/moderate half-life (2-4 hours): heroin, morphine, hydrocodone, hydromorphone, oxycodone, meperidine, and fentanyl*.

Long half-life (>12 hours): buprenorphine, methadone. Oral extended-release preparations of shorter half-life opioids may have durations of action similar to longer half-life opioids.

Note that the duration of action of fentanyl may exceed 24 hours in overdose.

D. Making the diagnosis:

The diagnosis of opioid overdose is made clinically based on the typical toxidrome, history of drug use, paraphernalia found with the patient, and response to naloxone.

Laboratory testing

1. Acetaminophen and salicylate drug levels should be obtained on all patients with suspected intentional overdose or overdose of unknown substance.
2. Toxicology testing can be obtained if there is diagnostic uncertainty

Rapid urine fentanyl testing may help guide therapy in patients who do not initially respond to lower doses of naloxone (< 1mg).

Note: *Urine drug screens may be of limited value**.** Not all urine drug screens test for fentanyl or other synthetic opioids so they may produce negative results despite the presence of an opioid. There is also the possibility of false positive results. Finally, drug tests may remain positive for days following opioid use and therefore may not reflect the cause of the patient's current symptoms.*

Comprehensive drug screening is available from the provincial toxicology laboratory, however the turnaround time for results is prolonged (days to weeks) and is not of benefit in the acute setting. It may be of diagnostic benefit for ongoing management of admitted patients

E. Recommended treatment:

Treatment involves supportive care and the administration of the antidote naloxone (box).

1. Do not induce vomiting
2. Provide supplemental oxygen with assisted ventilations as required
3. Consider administering activated charcoal if the opioid was **ingested** within 1-2 hours and there is no concern for aspiration.
4. Administer naloxone if indicated
5. Protect airway as needed
6. Hypotension typically responds to IV fluids
7. Perform a chest X-ray in patients with suspected acute lung injury
8. Obtain an EKG to rule out significant QT prolongation or other dysrhythmias if methadone or loperamide is suspected
9. Call the poison centre if there are any management or diagnostic questions

Start with low doses of naloxone to avoid inducing withdrawal. Patients with acute withdrawal are difficult to manage and may leave medical care prematurely and reuse opiates at a higher dose to overcome the effect of naloxone. Much higher doses of naloxone may be required for overdoses involving ultra-potent opioids like fentanyl and therefore naloxone dosing should be escalated aggressively in patients who do not initially respond.

Indications for naloxone: Respiratory rate < 10 /min OR saturation < 92% on room air, inability of patient to protect their airway OR fentanyl induced chest wall rigidity.
Routes of administration: IV/IO preferred. IM/SC if IV/IO access is not available.
Initial dose: Adults: 0.1 mg IV/IO or 0.4 mg IM if no IV/IO
Pediatrics: 0.1 mg/kg IV/IO/IM of body weight

Subsequent dosing: If there is an insufficient response to the initial dose, subsequent doses should be administered every 2 minutes (3 minutes if IM) according to the following schedule: 0.4 mg, 0.4 mg, 2 mg, 4 mg, and then 10 mg as a final dose if there is a high clinical suspicion of opioid intoxication. If there is no response after this dosing regimen, alternate causes for symptoms should be sought.

Goals of naloxone therapy: RR ≥ 10/min, GCS > 10, protecting airway, no acute withdrawal symptoms precipitated.

The requirement for repeat dosing following reversal should be anticipated following large overdoses or ingestion of long-acting products because the duration of action of naloxone is shorter than that of most opioids.

Naloxone infusion:
Consider infusion if there is recurrence of symptoms following initial successful reversal with naloxone.
Dose: Following a naloxone bolus sufficient to reverse opioid effect, administer 0.4-0.8mg/hr titrated to clinical effect. For infants, administer 0.04-0.16 mg/kg/hr.
Alternatively administer two-thirds of the initial effective bolus dose per hour to keep the patient alert.
Note: Common formulation is 4 mg in 250 mL of D5W (16mg/L) run at 0.4-0.8 mg/hr (25-50 mL/hr).

There is no role for the administration of flumazenil in the setting of opioid overdose.

Observation
Asymptomatic patients who have injected, smoked or insufflated an opiate and have NOT received any naloxone**:** Monitor for 2 hours.
Asymptomatic patients who have ingested opiate and have NOT received any naloxone**:**
Monitor for 4 hours following regular release opioids and 12 hours following ingestion of sustained release opioids or methadone*. Catastrophic delayed onset of symptoms has been reported in the setting of sustained release opioid ingestion. Assume it is a sustained release preparation if the substance is not known with certainty.*

Symptomatic patients:
Lower risk patients: Observe for a minimum of ***2 hours*** following naloxone administration.
Lower risk definition:
1. Did not require more than 0.9 mg naloxone for reversal, AND
2. Opioid smoked, insufflated or injected **(not ingested),** AND
3. Did not require repeat doses or infusion of naloxone following initial reversal

Higher risk patients: Observe for a minimum of ***6 hours*** following last dose of naloxone
Higher risk definition:
1. Oral overdose, OR
2. More than 0.9 mg of naloxone required for reversal

Naloxone infusion: Observe for at least ***12 hours*** after naloxone infusion has been stopped.

Special cases:
Methadone overdose: Observe for a minimum of 12 hours following any overdose AND at least 12 hours following the last naloxone dose or discontinuation of naloxone infusion.
Buprenorphine: The management of buprenorphine overdose can be complex. After administering naloxone as per dosing guidelines (above), the poison centre should be called to guide further management in all cases.
Pediatric opioid exposure: Prolonged opioid toxicity may occur. Initiate naloxone as per dosing recommended above if indicated. The poison centre should be contacted to guide management in all cases.
Fentanyl patch ingestion: Initiate naloxone as per dosing recommended above if indicated. The poison centre should be contacted to guide management in all cases.
Opiate packers and stuffers (ingestion of opiates for the purposes of concealment): Initiate naloxone as per dosing recommended above if indicated. The poison centre should be contacted to guide management in all cases.

Patients wishing to leave prematurely:
Ensure that the patient understands the risks associated with leaving prior to the completion of the observation period and encourage them to stay. Avoid antagonistic interactions that may prevent the patient from seeking medical treatment in the future.

F. Criteria to consider discharge:
Consider discharge when the patient is awake, alert, has normal vital signs (including a normal oxygen saturation on room air) and can mobilize as usual after the requisite observation period. Patients must meet these criteria without verbal or physical stimulation.

G. Criteria for hospital admission
1. Comorbidities requiring admission
2. Acute lung injury
3. Consider admission to a high acuity unit (step up) or intensive care if naloxone infusion is required.

H. Criteria for transfer to another facility
1. Unable to complete toxicological blood work (i.e. acetaminophen or salicylate) if exposure to additional substances is suspected
2. Patient requires more intensive care than is available at the current facility.

Take home naloxone: Offer the patient take home naloxone (if available) and or provide the patient with information on how it can be obtained. Teaching regarding overdose prevention and recognition as well as response training should be offered to the patient as well as to their family and friends if present.

Opioid Agonist Therapy: Provide referral to community addiction treatment and information on opioid agonist therapy (Suboxone® (buprenorphine) or methadone).

Addictions referral: For all cases, consider consultation with an addiction medicine specialist to assist with long-term treatment planning available through the RACE line (www.raceconnect.ca) Monday-Friday 8am-5pm.

Recommended further information

1. Boyer EW. Management of opioid analgesic overdose. New Engl J Med. 2012;367:146-55.
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4. Adams AP, Pybus DA. Delayed respiratory depression after use of fentanyl during anaesthesia. Br Med J. 1978;6108: 278-279.
5. Burns G, DeRienz R, Baker DD, et al. Could chest wall rigidity be a factor in rapid death from illicit fentanyl abuse? Clin Toxicol. 2016;54:420-423.
6. Harm reduction and take home naloxone information. Available from: http://towardtheheart.com/naloxone. Accessed November 2016.
7. Kent DA, editor. Poison management manual. 5th ed. Vancouver: British Columbia Drug and Poison Information Centre; 2015.

Prepared by: Jesse Godwin MD, Andrew Kestler MD, Chris DeWitt MD, Roy Purssell MD. Nov 23, 2016
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