Tips on using opioids during COVID-19

<u>These following terms are interchangeable:</u>

SA, Short Acting, IR Immediate Release, plain
LA Long Acting, CR Controlled Release, ER Extended Release, Contin

Opioids can be used for pain, help with sedation and **are one of the best medications** we have for shortness of breath/dyspnea/breathlessness and cough suppressant in the palliative care setting.

1. Start low but be prepared to titrate up quickly using PRNs

2. <u>Oral route</u>
   a) Start with short acting morphine or equivalent
   b) See Table 1 for starting doses and available formulations in Canada
   c) Using Table 1, start with a baseline dose of opioid on a regular basis; for example, morphine 5 mg PO q4h or hydromorphone 1 mg PO q4h.
      - When using tablets dosages should be in increments of ½ tablet strength as ¼ or 1/3 tablet is not feasible i.e. lowest morphine tablet=5 mg so lowest dose is 2.5 mg
      - If you need low doses or doses not easily divisible by the pill formation consider using a liquid formulation of the opioid i.e. morphine 1,5,10 mg/ml allows you to give 1 or 2 mg by syringe as opposed to a 5 mg tablet
   d) As well, use a breakthrough dose (see Section 4) of the same opioid up to every 1-hour prn to achieve desirable effect on pain or dyspnea
   e) If in the home setting a caregiver must keep track of all doses
   f) **Tip**: some pharmacies and homecare nurses can draw up prefilled syringes of medication solution for caregivers to just squirt into the mouth
   g) Most pain and breathlessness can be controlled with total daily doses of oral **Morphine equivalent to 50 mg/day or less**. If you have to keep increasing the dose, consider other modalities or consulting a palliative care physician.
   h) Every 2-3 days look at the total 24-hour consumption
      - If the 24-hour dose is predictable then you can add in a Long Acting (LA) version of the opioid **if the total daily dose is <u>≥</u> lowest LA dose.** Available on ODB:
        - Lowest morphine LA is 10 mg bid = 20 mg/day
        - Lowest hydromorphone LA is 3 mg = 6 mg/day
      - Take the total 24-hour dose, divide by 2 and use that as the Long Acting dose (Long acting is usually a q12 hour medication)
      - You will likely have to round up/down to the dose available in pill format as Long Acting medications are no longer long acting if broken
      - Keep the Short Acting around q1Hour for PRN pain/breathlessness
      - When reassessing the total daily dose add all the Short Acting and Long Acting opioid doses used in the last 24 hours and consider

increasing the long acting dose if it has increased to the next available dosage size

3. Non-oral route
    a) Once a patient cannot swallow the best route is to give the opioid subcutaneously (SQ)
    b) The SQ/IM route is typically 40-50% of the oral dose
    c) If there will only be 1-2 injections you can give the dose IM
    d) Any IV formulation of a medication can be given SQ or IM at the same dose
    e) For repeated dosages the best method is to run a SQ line, using a different line for each medication,
    f) There are special SQ lines such as Saf-T-Intima (https://www.youtube.com/watch?v=BpMUPQ21eEo) and Cleo line (https://www.youtube.com/watch?v=rXDMEzN6sgk) which can be set up by a homecare nurse but in an emergency, a regular butterfly placed SQ and taped in place will work
    g) Prime (fill the line first with the medication you are using until a few drops come out of the needle (this way when you inject a syringe at the port you are giving that exact dose)
    h) **Tip**: some pharmacies and homecare nurses can draw up prefilled single dose syringes. Caregivers can be taught to attach the syringe to the port to give a dose
    i) **Tip:** Pharmacies used by Home and Community care can often make opioids for SQ use in special concentrations starting at 1 mg/mL
        - Portable pumps (i.e. CADD pumps) might be available for home or hospital usage that allow you to order a continuous dose of a SQ opioid with a button that can be pushed for breakthrough dosing (http://www.mhcwcancer.ca/Providers/PalliativeToolbox/Documents/Subcutaneous%20Pain%20Pump%20Form.pdf)

4. Calculating break through doses

    a) For a patient already on a regular dose of an opioid the breakthrough dose is calculated at 10-20% of the total 24-hour dose (pick the dose that's easiest to dispense)
    b) For a starting patient who is opioid naïve the breakthrough dose can be the lowest formulation available (i.e. ½ lowest tablet strength)
    c) For the oral route, the breakthrough dose is repeated q1h prn and for SQ/IV every 30 minutes prn

5. Switching from one opioid to another

    a) You might have to switch if there is an allergic reaction (hives, angioedema not GI upset) or a drug shortage

b) Use Table 2 to determine what the equivalent dose of the alternate opioid is

c) Due to a concept called partial cross tolerance* **you must decrease the new medication dose by 25-50%**

* partial cross tolerance: when pharmacological tolerance develops to one opioid it will likely be conferred **in part** to another opioid **but not completely** due to differences in the molecular structure of each opioid, personal differences in opioid receptors and the variable binding to different opioid receptors. Therefore, the dose needs to be reduced.

6. Managing Side effects

Counsel patients/caregivers in advance as much as possible about what they can expect and how to manage side effects. Most are transient and subside over time.

a) The most common side effect is constipation and can be prevented with encouraging fluids if possible and
   - Prescribe sennosides (Sennokot®) 1-2 tabs OD- bid or PEG Polyethylene Glycol 3350 (MiraLAX®, RestoraLAX® ½-2 capfuls in smallest amount of tolerable liquid or soft food (i.e. applesauce, pudding)

b) Nausea/vomiting, Sedation, Delirium/Confusion/Hallucinations
   - Lower the dose, skip doses, take with food (for nausea), tolerance usually develops after a few days
   - Trial of metoclopramide 10 mg PO/SQ q6h prn

c) Pruritus
   - Stop and switch to another opioid or pre-medicate with antihistamine or steroid if no time or not available

d) Urinary retention
   - Hold the dose and wait, place a catheter

e) Myoclonus/seizures, Agitation
   - Stop opioid switch (section 5) to another opioid. Decrease the equivalent dose of the second opioid by 30-50%.

f) Respiratory Depression
   - If Respiratory Rate greater than 8/min. Stop opioid and monitor vitals closely
   - If Respiratory Rate less than 8/min, use naloxone 0.4 mg sc/IM and seek help

Case example

A 62-year-old patient with diabetes and hypertension has COVID-19 and is short of breath when walking from a chair to the bed. You decide to start them on an opioid to help with breathlessness. What is your starting prescription?

Possible answer: Rx Hydromorphone 1 mg tablet
S: 0.5-1 tablet PO q 4h PRN Breathlessness
M: 20 tablets

Explanation: *Hydromorphone is chosen as it's the most tolerable for possible renal impairment (diabetic and hypertensive, see Table 1 notes) though any opioid is appropriate. It also has the advantage of being available in an IV formulation if needed in the future. Prescribe the hydromorphone as a number of tablets as opposed to duration of use.*

Four days later, you speak with the patient's partner. In the last 3 days the patient has taken 5-6 tablets a day and seems to be less breathless but is waking often in the night short of breath. What can you do now?

Possible answer: Switch to long acting preparation with breakthrough

Rx 1. Hydromorphone LA 3 mg
S: 1 tablet PO bid
M: 20 tablets
Rx 2. Hydromorphone SA 1 mg
S: 0.5-1 mg q 1 h PRN breakthrough symptoms
M: 20 tablets

Explanation: *Patient is taking 5-6x1 mg hydromorphone=5-6 mg hydromorphone total daily dose. The smallest LA version is a 3 mg tablet (info point 1.h, Table 1) so start at 3 mg hydromorphone LA bid. You can start with just giving the 3 mg hydromorphone LA pill at night time to give 12 hours of relief and use SA during the day. Breakthrough doses are calculated as 10-20% of total daily dose (info point 4.a) i.e. 10-20% of 5-6 mg = 0.5-1.2 mg. Breakthrough is dosed every hour orally (info point 4.c) as it's usually needed to help a pain or breathing crisis. Often only a few doses are needed then the patient settles down.*

The pharmacy calls you later that day. They have no more Hydromorphone LA 3 mg tablets or Hydromorphone SA in any dose. What do you do now?

Possible answer: Switch to another opioid

Rx 1. Morphine LA 15 mg
S: Start at 1 PO qhs then bid
M: 20 tablets

Rx 2. Morphine SA 5 mg
S: 1 tablet PO q4-6 h
M: 20 tablets

Explanation: *Patient was taking Hydromorphone LA 3 mg x2 for total daily dose of 6 mg. To convert hydromorphone to morphine multiply by 5 (Table 2) = 30 mg. Due to cross tolerance you need to decrease by 25-50% (info point 5.c) so total daily dose morphine to begin with should be 15-22.5 mg. As the patient needs a 12-hour medication overnight start with the smallest dose of the LA in the evening (15 mg) and use the SA during the day. If with their SA usage you feel they can tolerate the LA dose q12 h, you can subsequently increase Morphine LA to 15 mg PO bid for more consistent pain relief. You can include some breakthrough doses i.e. 5mg morphine SA q1 h PRN breathlessness if needed and not too complicated for the caregivers.*

A few days later the nurse calls that the patient was comfortable on Morphine LA 15 mg bid and taking 3-4 5 mg tablets for breakthrough pain but can no longer swallow. She feels there isn't much time left. What do you do now?

Possible answer: Switch to SQ injections, if possible by SQ line

Rx Morphine IV preparation 2 mg/mL
S: 0.5 mg (0.25 cc) SQ q 30 minutes PRN breathlessness/pain
M: 10 vials

Explanation: *The patient is entering end of life and likely there is not enough time to order a continuous pump. There is no long acting version of an IV formulation so convert all doses to short acting and give every 30 minutes as needed (info point 4.c). Patient was taking morphine LA 15mg x 2=30 mg + 3-4 Morphine SA 5 mg =15/20 mg for a total daily dose of 45-50 mg morphine. SQ dose is 40-50% of oral dose (info point 2.b) i.e. 18-25 mg/day. Q30 minute dose would be 18-25/48 (i.e. 24 hours x 2) = 0.37-0.52. For ease of dosing 0.5 mg is chosen to start.*

Table 1 Common opioid doses and formulations for COVID-19

Opioid	Useful Dosage Forms	Starting Dose for Breathlessness	Starting Dose for pain	Notes
Codeine SA/IR	• Tab: 15, 30 mg • Syrup: 5 mg/mL • Tab: 8, 15, 30, 60 mg with Acetaminophen 300 mg and caffeine 15 mg (except T#4) Tylenol® #1/2/3/4 • Tab: 15, 30 mg with Acetylsalicylic acid 375 mg	15-30mg PO q4-6h	30 mg PO q4-6h	8mg combined with ASA/acetaminophen available behind the counter No SQ/IV form
Codeine LA/CR/Contin	• Tab: 50, 100, 150, 200 mg	Start with IR	50 mg PO q 12 h	
Hydromorphone SA/IR	• Tab: 1, 2, 4, 8 mg • Syrup: 1 mg/mL • IV: 2, 10 mg/ml	0.5-1 mg PO q 4h	1 mg PO q4-6h	Best for renal disease For small doses use syrup
Hydromorphone LA/CR/Contin/PR	• CR: 3, 4.5, 6, 12, 18, 24, 30 mg • PR (daily): 4, 8, 16, 32 mg	Start with IR	• CR: 3 mg PO q 12 h • PR:4 mg PO q 24 h	
Morphine SA/IR	• Oral solution: 1, 5, 10, 20, 50 mg/mL • Tab: 5, 10, 20, 25, 30, 50 mg • IV: 1, 2, 5, 10, 15 mg/ml	2.5 -5mg PO q4h	5 mg PO q4h	For small doses use elixir
Morphine CR, Contin/ER	• Tab: 15, 30, 60, 100, 200 mg • Cap (12 h): 10, 15, 30, 60, 100, 200 mg • Cap (24 h): 10, 20, 50, 100 mg	Start with IR	• CR:10–15 mg PO q 12 h • ER:10 mg PO q 24 h	
Oxycodone SA/IR	• Tab: 5, 10, 20 mg • Tab: 5 mg with acetylsalicylic acid or acetaminophen 325 mg • Tab: 2.5 mg with acetaminophen 325 mg	2.5-5mg PO q4h	5mg PO q 6h	No IV/SQ form
Oxycodone LA/Contin/Neo	• Tab: 5, 10, 15, 20, 30, 40, 60, 80 mg	Start with IR	• 10 mg PO q 12 h	

Legend: cap = capsule, CR = controlled release, ER = extended release, g = gram, h = hour, IR = immediate release, IV= intravenous, LA= Long acting, mg = milligram, mL = milliliter, PO = Per os, by mouth PR = prolonged release, prn = as needed, q = every, SA= Short acting, SQ=subcutaneous, tab = tablet

Table 2 Opioid Conversion and Equianalgesic Table

Opioid	Equivalent Dose compared to Morphine 10 mg PO	Drug: Morphine Oral Dose Ratio	To convert **to** oral morphine equivalent, multiply by:	To convert **from** oral morphine, multiply by:	50 MED equivalent dose
Codeine	60-100	6-10:1	0.15 (0.1-0.2)	6.67	334 mg/d
Hydromorphone	2	1:5	5.0	0.2	10 mg/d
Morphine	10	1:1	1.0	1	50mg/d
Oxycodone	5-6.5	1:1.5-2	1.5	0.667	33 mg/d

Adapted from 2017Canadian guideline for Opioids for Chronic Non-Cancer Pain
http://nationalpaincentre.mcmaster.ca/documents/Opioid%20GL%20for%20CMAJ_01may2017.pdf

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