Dosing and Titrating Opioids

Clinician Outreach and Communication Activity (COCA) Call
August 17, 2016
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Planners have reviewed content to ensure there is no bias.

This presentation will not include any discussion of the unlabeled use of a product or products under investigational use.
Objectives

At the conclusion of this session, the participant will be able to:

- Describe the evidence for the association between opioid dosage and opioid therapy benefits and harms.
- Compare and contrast immediate release and extended-release/long-acting opioid formulations.
- Identify methods for calculating morphine milligram equivalent dosage.
- List the steps for titrating opioids to specific dosage thresholds.
- Identify best practices for opioid tapering and discontinuation.
## Guideline for Prescribing Opioids for Chronic Pain Call Series

Listen to recordings from previous calls

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Deborah Dowell, MD, MPH
Senior Medical Advisor
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention
TODAY’S PRESENTER

Mark Sullivan, MD, PhD
Professor, Psychiatry and Behavioral Sciences
Anesthesiology and Pain Medicine
Bioethics and Humanities
University of Washington
Disclaimer

The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.
CDC Guideline for Prescribing Opioids for Chronic Pain:

Dosing and Titration of Opioids

Deborah Dowell, MD, MPH

August 17, 2016
CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Deborah Dowell, Tamara Haegerich, and Roger Chou

CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Published online March 15, 2016
Evidence does not support safety of ER/LA opioids relative to immediate-release opioids

• Did not find evidence that ER/LA opioids are more effective or safer than immediate-release opioids

• Higher overdose risk initiating treatment with ER/LA opioids than with immediate-release opioids

• Disproportionate numbers of overdose deaths associated with methadone
Use immediate-release opioids when starting

- When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

(Recommendation category A: Evidence type: 4)

Additional cautions for
- Methadone
- Transdermal fentanyl
- Immediate-release opioids combined with ER/LA opioids
Higher dosages add risk without clear benefit

- Benefits of high-dose opioids for chronic pain not established
- RCT*: no difference in pain, function between
  - Liberal dose escalation (average 52 MME)
  - Maintenance of current dosage (average 40 MME)
- Opioid use associated with dose-dependent increased risk of serious harms, including fatal and nonfatal overdose

Dosages at or above 50 MME/day increase risks for overdose by at least 2x the risk at <20 MME/day.
Overdose risk increases with opioid dosage

Odds Ratio or Hazard Ratio for Overdose Relative to 1 to <20 MME

- Bohnert 2011 (fatal overdose)
- Dunn 2010 (overdose)
- Gomes 2011 (fatal overdose)
- Zedler 2014 (overdose)
Higher opioid dosages associated with opioid use disorder

Use caution at any dose and avoid increasing to high dosages

- When opioids are started, clinicians should prescribe the lowest effective dosage.
- Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

(Recommendation category A: Evidence type: 3)
What about patients already taking high dosages?

- Offer the opportunity to reevaluate continuation of high-dosage opioids in light of recent evidence

- For patients who agree to taper opioids to lower dosages, collaborate on a tapering plan
Calculate MME

1. **Determine** the total daily amount of each opioid the patient takes.

2. **Convert** each to MMEs—multiply the dose for each opioid by the conversion factor. *(see table)*

3. **Add** them together.
CAUTION: Do **not** use to convert one opioid to another

<table>
<thead>
<tr>
<th>OPIOID</th>
<th>CONVERSION FACTOR</th>
</tr>
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<tbody>
<tr>
<td>Codeine</td>
<td>0.15</td>
</tr>
<tr>
<td>Fentanyl transdermal (in mcg/hr)</td>
<td>2.4</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
</tr>
<tr>
<td>1-20 mg/day</td>
<td>4</td>
</tr>
<tr>
<td>21-40 mg/day</td>
<td>8</td>
</tr>
<tr>
<td>41-60 mg/day</td>
<td>10</td>
</tr>
<tr>
<td>≥ 61-80 mg/day</td>
<td>12</td>
</tr>
<tr>
<td>Morphine</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1.5</td>
</tr>
<tr>
<td>Oxymorphonone</td>
<td>3</td>
</tr>
</tbody>
</table>
Offer a taper if opioids cause harm or are not helping

- Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.
- Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently.
- If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

(Recommendation category A: Evidence type: 4)
Taper slowly enough to minimize withdrawal

- 10% per week is a reasonable starting point
- Some patients do better with slower tapers - 10%/month
- Consider more rapid taper when needed for safety
- Access appropriate expertise during pregnancy
- Optimize pain management and support
  - Anticipate hyperalgesia immediately after tapering
  - Over the long term, most patients report improved function without worse pain
New Resource

Available under the Clinical Tools section of our Guideline resources: http://www.cdc.gov/drugoverdose/prescribing/resources.html
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CDC Guideline for Prescribing Opioids for Chronic Pain

DOSING AND TITRATION OF OPIOIDS

JANE BALLANTYNE, MD, FRCA*
MARK SULLIVAN, MD, PHD*#

University of Washington
*Anesthesiology and Pain Medicine
#Psychiatry and Behavioral Science
#Bioethics and Humanities
Ms. Brown is 67 years old and has spinal stenosis
She has had steadily worsening symptoms of leg pain, lower back pain, leg numbness and tingling, and difficulty walking
She now finds it difficult to start moving and ambulating in the mornings
She is motivated to get as well as she can without medication, and has been doing aqua aerobics and graded exercise under the supervision of therapists
She has tried amitriptyline, gabapentin, and tramadol, but none of these helped
Her clinician suggested a trial of low dose strong opioid
She agreed
WHICH OPIOID?

• Choose something simple with simple pharmacokinetics and pharmacodynamics

• This makes the treatment much safer and easier to manage by patients

• Do not use any of the long acting opioids when starting opioid therapy in an opioid naïve patient

• Long acting opioids include ER/LA opioids, methadone and transdermal fentanyl (fentanyl patches)
When starting opioids for chronic pain, prescribe IR not ER/LA opioids

- Choose predictable pharmacology to minimize overdose risk
- In general, avoid IR combined with ER/LA opioids
- Methadone should not be the first choice for an ER/LA opioid
  - Only providers familiar with methadone’s unique risk and who are prepared to educate and closely monitor their patients should consider prescribing it for pain.
- Only consider prescribing transdermal fentanyl if familiar with the dosing and absorption properties and prepared to educate patients about its use.

From the supporting text for Recommendation #4 from the CDC Guideline for Prescribing Opioids for Chronic Pain. Recommendation category: A; Evidence type: 4
WHY NOT START WITH LONG ACTING OPIOIDS?

- Dosage forms for ER/LA and transdermal fentanyl are too high for opioid naïve patients, especially elderly patients.

- Most patients prefer taking opioids as needed and not round the clock.

- Most patients find it easier to control their usage if they are taking opioid as needed and not round the clock.

- Overall doses tend to be much lower if IR opioids are taken intermittently and no opioid is taken round the clock.
IS THERE A ROLE FOR LONG-ACTING OPIOIDS?

• Yes, but not at the start of treatment

• Yes, when treating end-of-life pain and some long-term pain conditions

• Yes, when the patient has difficulty controlling usage (e.g. has a substance use disorder)

• Never in conjunction with IR opioids except during palliative or end-of-life pain care
WHY NOT METHADONE?

- Methadone has very complicated pharmacokinetics

- There are possible cardiac effects including QT prolongation

- There are many drug interactions

- Clearance is idiosyncratic, unpredictable and usually delayed

- Methadone is hard to get off

- Methadone should be reserved for specialists, cancer pain or addiction treatment
WHY NOT TRANSDERMAL FENTANYL?

• Even the lowest dose is too high for start of therapy

• Absorption can be unreliable

• Heat (e.g. hot showers or baths) can release medication suddenly leading to overdose

• Cannot provide intermittent or as needed doses
2.5 mg oxycodone (1/2 tablet) every 4 hours as needed
When opioids are started, prescribe the lowest effective dose

- Use caution when prescribing opioids at any dosage
- Carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day
- Avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

(Recommendation category: A; Evidence type: 3)
AT FOLLOW-UP: MS. BROWN

- She returned to the clinic the following week and reported no improvement but tolerating opioid well and taking it 4 times daily

- Her dose was increased to try and get an effect

- After 2 further dose increases, she stabilized at 5 mg 4 hrly as needed, up to times daily
Re-evaluate benefits and harms of opioids, and continue therapy only as a deliberate decision

• Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.
• Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently.
• If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

(Recommendation category: A; Evidence type: 4)
• At her 3 month follow up she came with her daughter who said her mother was drowsy all the time, and getting out and about even less that before.

• The decision was made to taper her off the opioid.
HOW TO DO A STRAIGHTFORWARD TAPER

• Do not try to taper too quickly, even for someone who hasn’t been on opioids for very long

• A reasonable regime would be:
  10% reduction per week until off

• Warn about possible withdrawal symptoms and be prepared to treat withdrawal if it occurs
Mr. Casey is a 55 year-old self-employed truck driver who has had back pain for 7 years, starting with a back sprain injury.

He initially had a disc protrusion but that has resolved and he now has an MRI consistent with age and a normal exam.

He has been treated with opioids since the initial sprain injury.

His current regime is 30 mg oxycontin 3 times daily with 30 mg oxycodone 6 times daily as needed (MME 405).
CASE OF MR. CASEY CONTINUED:

• He has tried other medical and non medical treatments but says none of them work

• He works night to try and make up for time lost during painful episodes

• He doesn’t remember what it’s like to sleep well

• His wife of 18 years recently asked him to leave because he is dragging down the family

• He is convinced that opioids are the only thing that enable to work
WHAT ARE YOU GOING TO DO?

• His opioid dose is higher than currently recommended

• His function is poor and his life is in tatters

• He is almost certainly dependent on opioids

• It will be hard to persuade him to taper and hard to achieve a taper

• He will need a lot of ancillary help if he is going to improve
Re-evaluate benefits and harms of opioids, and continue therapy only as a deliberate decision

- Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.
- Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently.
- If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

(Recommendation category: A; Evidence type: 4)
1. Spend time convincing the patient that tapering is the right thing to do (This may take more than one visit)

2. Taper slowly **e.g. 10% reduction per month**

3. Be prepared to stop and give it a rest for a while if it gets difficult

4. As long as the trend is downwards, the amount of time it takes doesn’t matter

5. Never go up
6. If surgery or trauma intervene, always go back to the pre-event dose ASAP.

7. If it is necessary or desirable to do a rapid taper, buprenorphine is a useful tool.

8. Buprenorphine is a useful tool anyway.

GET BUPRENORPHINE TRAINING
• **Work with patients to taper opioids down or off when**
  - no sustained clinically meaningful improvement in pain and function
  - opioid dosages >50 MME/day without evidence of benefit
  - concurrent benzodiazepines that can’t be tapered off
  - patients request dosage reduction or discontinuation
  - patients experience overdose, other serious adverse events, warning signs.

• **Taper slowly enough to minimize opioid withdrawal**
  - A decrease of 10% per week is a reasonable starting point

• **Access appropriate expertise for tapering during pregnancy**

• **Optimize nonopioid pain management and psychosocial support**
• Start with lowest effective dosage and increase by the smallest practical amount.

• If total opioid dosage >50 MME/day
  o reassess pain, function, and treatment
  o increase frequency of follow-up; and
  o consider offering naloxone.

• Avoid increasing opioid dosages to >90 MME/day.

• If escalating dosage requirements
  o discuss other pain therapies with the patient
  o consider working with the patient to taper opioids down or off
  o consider consulting a pain specialist.
IF PATIENT IS ALREADY RECEIVING A HIGH DOSAGE

- Offer established patients already taking >90 MME/day the opportunity to re-evaluate their continued use of high opioid dosages in light of recent evidence regarding the association of opioid dosage and overdose risk.

- For patients who agree to taper opioids to lower dosages, collaborate with the patient on a tapering plan.
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  - “Click” the Q&A tab at the top left of the webinar tool bar
  - “Click” in the white space
  - “Type” your question
  - “Click” ask

- **On the Phone**
  - Press Star (*) 1 to enter the queue
  - State your name
  - Listen for the operator to call your name
  - State your organization and then ask your question
Thank you for joining!

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Atlanta, Georgia
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What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

http://emergency.cdc.gov/coca/calls/2016/callinfo_081716.asp
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