

Pain, opioids and substance misuse

Pain Research Summit
Discussion
Jodie Trafton

Opioid Prescribing

- Opioid prescribing for chronic pain is prevalent (~10% of all prescriptions in US)
- Use of opiates for chronic pain treatment is increasing

Up 73% for morphine, 400% for oxycodone (1997-2002)¹

Opioid Misuse

- Abuse of prescription opioids is increasing more than all other drugs of abuse
 - For example: According to the NSDUH, in 2002, 2.5 million Americans reported using prescription opioids for non-medical purposes for the first time. In 1990, this number was 537,000. Notably, 55% were female and 56% were over 18.
- Risk of opiate abuse/addiction associated with pain treatment is not known
 - Range from 1% to 50% across studies

Opioid Effectiveness

- There is little research on the long-term effectiveness of opioid medications for chronic pain, or the most effective methods for prescribing.
- There is substantial variation in clinical practice.

Martell meta-analysis

- Examined effectiveness and misuse in trials of opioid medications for chronic back pain
 - Weak evidence for short term (less than 16 weeks) efficacy of opioids,
 - No studies of long-term efficacy.
 - Substance use disorders are common in patients with chronic back pain receiving opioids, and aberrant medication-taking behaviors occur in up to 24% of patients.

Risk factors for opioid misuse, lack of opioid effectiveness, and pain chronicity

- Data is weak, but suggests that co-morbid psychological problems, particularly anxiety, PTSD, depression, substance use disorders, and personality disorders, are associated with poor outcomes on chronic opioid therapy

Such psychological problems are prevalent in OIF/OEF veterans

■ Karen Seal

■ Study population: Veterans of OEF/OIF seen at a VA facility and included in the national VA “OEF/OIF Roster” database

■ Time frame: From 9/30/01 (invasion of Afghanistan) through 12/31/05

■ MH Disorders OEF/OIF Veterans (N=103,788)

PTSD	13,205 (13%)
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Anxiety	6,267 (6%)
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Depression	5,405 (5%)
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Substance use disorders	4,878 (5%)
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Other psychiatric disorders	12,447 (12%)
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Big Questions

- Do opioids effectively reduce chronic pain? If so, do they improve functioning and quality of life?
- For what populations are opioid effective?
- Do opioids amplify chronic pain?
- How do we define and identify problematic opioid use in chronic pain patients? What behaviors are actually associated with poor outcomes?
- Can we predict who will have problems with opioid use?
- Does pain and/or opioid use increase substance use problems? What are effective and appropriate pain and addiction treatments for patients with co-occurring chronic pain and substance use disorders?

Summary

Overall about 28% of patients had significant medication abuse problems over the 12 month study leading to discontinuation

On two measures of pain (worst pain and relief from medications) the adequate relief group showed a small but significantly greater improvement

There were no group differences in disability

Patients with highest morphine amounts showed greater total relief in the tolerable pain group

Age-related difference in opioid efficacy

- Pam Pierce Palmer (UCSF)
- Compared dose escalation in chronic pain patients at a multidisciplinary pain clinic (11 prescribers) by retrospective record review
 - Age 50 and under (young)
 - Age 60 and older (old)

Characteristics

- Similar pain history: ~ 8 years
- All received multidisciplinary care eventually including long-acting opioids
- Similar time on opioids in clinic: 27 months
- Examined VAS at initial visit, before starting long-acting opioids, and at discharge to primary care management

Results

- Significant reduction in pain score from initial visit to prior to starting opioids in both groups

- Time to opioids: Young: 3.9 +/- 0.6 months, Old: 6.9 +/- 1.1 months

	Baseline VAS	Pre-opioid VAS
Young	8.4	6.2
Old	8.3	6.9

Opioids only reduced pain in Old

- Improvement in VAS from prior to starting opioids to discharge to primary care

	Pre-opioid VAS	Discharge VAS
Young	6.2	6.1
Old	6.9	5.6

Dose escalation was much higher in young:

27 mg morphine eq/month versus 12 mg/month

Young had a 640% increase in daily opioid dose, from 49.3 mg/day to 365.4 mg/day over an average of 26.4 months

For what populations are opioids effective?

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Do opioids amplify chronic pain?

- Prospective study of opioid induced hyperalgesia in 6 chronic pain patients initiating opioid therapy
- Larry Chu (Stanford)
- Patients tested before starting opioid therapy and 1 month after opioid start. Patients were tested shortly after skipping their morning morphine dose.

Patients developed significant hyperalgesia to cold pressor pain after 1 month of oral morphine therapy ($P < .01$).

Cold pressor pain tolerance dropped by about 24% (from 28.0 +/- 13.7 to 19.8 +/- 6.0 seconds).

The heat pain threshold did not change significantly between sessions.

Opioid tolerance was evident within 1 month

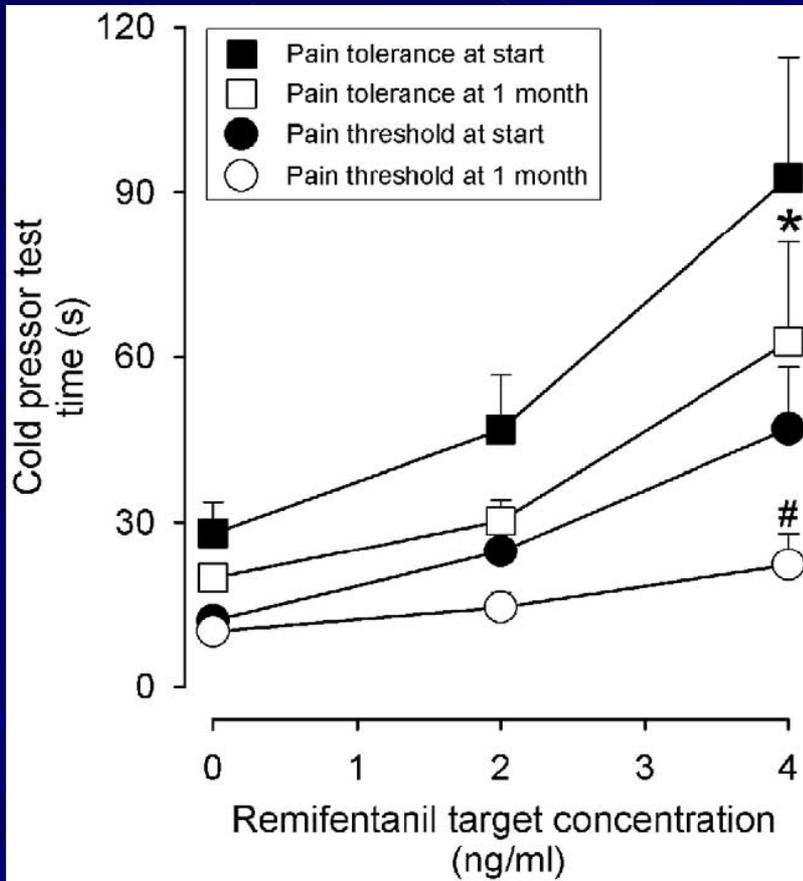


Figure 2. The remifentanyl target plasma concentration versus analgesic response relationship was determined before and 1 month after initiating chronic oral morphine therapy in 6 patients with chronic low back pain. Analgesic effects were quantified with aid of the cold pressor pain test. The potency of remifentanyl for increasing the experimental pain threshold (time to first pain) and pain tolerance (time to intolerable pain) was significantly decreased after 1 month of oral morphine therapy, indicating the development of analgesic tolerance (mean \pm standard error of the mean). Decreased potency was reflected statistically by a flattening of the slope or a right shift of individual plasma concentration versus analgesic response relationships (paired *t* test: #pain threshold, *P* .03; *pain tolerance, *P* .01).

How do we define and identify problematic opioid use in chronic pain patients? What behaviors are actually associated with poor outcomes?

■ Bruce Naliboff

- Prescription Drug Use Questionnaire
 - Interview and self-report version

■ Robert Jamison

- Current Opioid Misuse Measure

Copies of measures included in references.

Decision-support

- **ATHENA-Opioid Therapy**
 - A computerized decision support system based on VA/DOD clinical practice guideline for opioid therapy for chronic pain and linked to VistA
 - Provides individualized recommendations, tools, and reminders to help primary care physicians optimize analgesia and reduce misuse

Screen shot

ATHENA Opioid Therapy for Chronic Non-Cancer Pain

testcase,athena
0008 Jan 02,1925

Feedback for researchers

A. Summary Assessment Orders: Urinary Drug Screens/Meds/Consults Education & Agreements Documentation

Summary [Back to Summary](#)

Cautions B.
Bipolar Disorder
Age >=65 years

D. C.

Opioids Allergies Problems Labs Vitals

Drug	Daily Dose	Start	End
Hydrocodone...	10	08/15/2007	10/14/2007
Oxycodone	10	01/09/2007	03/10/2007

E.

Treatment CheckList

- Conducted Pain Assessment
- Ordered a Urine Drug Screen
- Educated Patient to Call Ahead for Refills (7-10 days Before Running Out)
- Had Patient Sign Pain Management Agreement
- Documented Pain Assessment, UDS, Patient Education Pain Management Agreement

Treatment Options

Use caution in employing opioids in the elderly. Slow initiation and titration schedules are appropriate. Short-acting opioids may be preferable in this age group.

Close monitoring of opioid therapy in this patient is necessary.

- Opioids may alter symptoms of mania and depression and should only be used when the benefits outweigh the risks.

OPTION: INCREASE DOSE OF SHORT-ACTING OPIOID.

OPTION: SWITCH TO LONG-ACTING DRUG.

OPTION: DISCONTINUE OPIOID THERAPY.

Validation of medical record-based risk assessment

- Current ATHENA-OT recommendations are based upon expert consensus
- Hard to operationalize risk factors suggested in the literature
 - How many ER visits?
 - How many different prescribers?
 - History of alcohol problems? Tobacco?
- Conducting interview assessments with 100 patients with recent opioid prescriptions which we will use to develop more specific algorithms for medical record based assessment of risks associated with opioid use.

Example tool: Conversion calculator

ATHENA Opioid Therapy for Chronic Non-Cancer Pain

Feedback for researchers

Summary Assessment **Orders: Urinary Drug Screens/Meds/Consults** Education & Agreements Documentation

Opioid Conversion Calculator [Back to Summary](#)

Please select the presently used opioid, the new opioid to switch to, enter the present dose and cross tolerance reduction percentage, then press calculate to obtain the equivalent dose for the new opioid.

Converting From: To:

Present Daily Dose (mg/day OR mcg/h Fentanyl only):

Reduction for incomplete cross tolerance (%):

Equivalent Daily Dose:
12.0 mg of Methadone
(for 120 mg of Morphine at 0 % reduction)

WARNING: When switching to methadone, the VA guideline recommends a dose no greater than 5 mg q 8 hrs (15 mg/day), and suggest consulting a specialist. Disregard the calculated equivalent dose if this limit is exceeded.

Does pain and/or opioid use increase substance use problems? What are effective and appropriate pain and addiction treatments for patients with co-occurring chronic pain and substance use disorders?

- Methadone-maintained patients
- Before treatment, chronic pain was associated with greater misuse of potentially analgesic drugs (benzos, alcohol to intoxication, opioid meds, marijuana).
- But chronic pain did not affect drug use outcomes following methadone maintenance treatment

Associations between alcohol use and functional status in pain patients

Steven K. Dobscha MD^{1,2}, Katharine Bradley MD MPH^x, Kathryn C. Dickinson MPH¹, Eun Sul Lee PhD^x, Michael Lasarev MS^x, and Bentson McFarland MD MPH^x

Background: Relatively little is known about the prevalence and functional impact of alcohol misuse among patients with chronic pain, and published studies have shown mixed results.

Objectives: To examine associations among alcohol screening scores and functional status in veterans receiving treatment for chronic pain in Veterans Affairs (VA) facilities.

Design: Cross-sectional analysis of data from the national VA Survey of the Health Experiences of Patients (SHEP) for fiscal year (FY) 2005.

Subjects: 255,522 veterans treated in VA ambulatory clinics in FY 2005.

Measures: Alcohol Use Disorders Identification Test (AUDIT-C), Veterans Short-Form Health Survey (VSF-12) Physical Component Score (PCS) and Mental Component Score (MCS), Medical Outcomes Study Depression Questionnaire (MOSDQ).

Results: Patients who received treatment for chronic pain were younger, more often non-white, and had significantly lower PCS and MCS as compared to veterans who did not receive pain treatment. Depression symptoms were over twice as prevalent among patients receiving pain treatment. The prevalence of alcohol misuse (AUDIT-C > 3 for men and > 2 for women) was not significantly higher among people receiving pain treatment. In adjusted models, AUDIT-C scores were associated with small increases in PCS and MCS except for at the lowest and highest levels of alcohol consumption. Depression symptoms were a stronger predictor of MCS than was receiving treatment for chronic pain or AUDIT-C score.

Conclusions: Self-reported alcohol misuse is not more common among veterans who receive treatment for chronic pain. Our results are consistent with other recent studies showing that modest levels of alcohol do not adversely affect functional status, and indicate that this relationship does not appear to be different for patients receiving pain treatment.

Research needs & Possible ideas for collaboration

- Prospective multisite study of opioid misuse following prescription for pain
- Multisite study comparing long-term effectiveness of various strategies of opioid prescribing. Placebo comparison? Sub-populations? Aggressive treatment? Primary care?
- Multisite study of continuation versus cessation of long-term opioid therapy in primary care patients with chronic pain
- Prospective study of safety and efficacy of opioid prescribing in patients with existing SUDs
- Study of safety and efficacy of Suboxone for treatment of chronic pain in patients at risk of misuse/overdose