

# Treatment of Alcohol and Opiate Withdrawal

Renee Striker, Pharm.D., BCPS, BCPP  
Pharmacy Clinical Specialist  
Huron Hospital  
East Cleveland, Ohio

## Objectives

- Outline the diagnostic criteria for substance abuse and dependence
- Identify the signs and symptoms of alcohol and opiate withdrawal
- Discuss pharmacologic agents available for the management of alcohol and opiate withdrawal.

## Overview

- Epidemiology
- Diagnosis of Substance abuse and dependence
- Alcohol
  - Signs and Symptoms of withdrawal
  - Treatment of withdrawal
- Opiates
  - Signs and Symptoms of withdrawal
  - Treatment of withdrawal

## Epidemiology

- Alcohol
  - 23.3% binge drink
  - 6.9% heavy drinking (17.2 million)
- Heroin
  - 0.2 million in the US
- 2/3 male 1/3 female
- 1/3 of hospitalized psychiatric patients have a co-morbid substance related disorder (excluding nicotine)

www.oas.samhsa.gov 2008 data

## Diagnosis – Substance Abuse

- 1 or more of the following in a 12 month period
  - Failure to fulfill obligations at work, school, or home
  - Use in physically hazardous situations
  - Substance related legal problems
  - Continued use despite persistent or recurrent social or interpersonal problems

DSM-IV TR, 2000.

## Substance Dependence

- 3 of the following in a 12 month period
  - Tolerance
  - Withdrawal
  - Larger amounts or longer time than intended
  - Difficulty cutting down
  - Time spent drug seeking
  - Decreased activities
  - Use continued despite knowledge of persistent or recurrent physical or psychological problem

DSM-IV TR, 2000.

## CAGE Questions

- **C** - Have you ever felt the need to **CUT** down your drinking?
- **A** - Do you get **ANNOYED** when people criticize you about your drinking?
- **G** - Have you ever felt **GUILTY** about your drinking?
- **E** - Have you ever taken a morning **EYE-OPENER** to steady your nerves or get rid of a hangover?

## Clinical Issues

- Wernicke's Encephalopathy
- Seizure
- Delirium Tremens

## Wernicke's Encephalopathy

- Incidence in US – 0.8-2.8%, up to 12.5% in alcohol dependent population<sup>1</sup>
- CNS depression – mental sluggishness, restlessness, confusion, coma (rare)
- Ambulating difficulty – wide-based ataxic gait
- Ocular problems – horizontal nystagmus, pupillary abnormalities
- Autonomic regulation – hypothermia, hypotension

1. Thomson 2002

## Korsakoff's Psychosis

- Patients that do not recover from Wernicke's in 48-72 hours will progress
- Presentation – psychosis, anterograde amnesia, retrograde amnesia, confabulation, apathy, ataxia, tremors
- 25-50% do not recover

## Treatment and Prevention

- Parenteral (IM or IV) thiamine 100mg given before IV fluids containing dextrose
  - Banana Bags
    - Normal Saline 1 liter, thiamine 100mg, folic acid 2-5mg, multi-vitamins, +/- magnesium sulfate 2gm
- Glucose load may precipitate condition
- Continue thiamine 100mg daily

## Stages of alcohol withdrawal

- Stage 1 (6-8 hours)
  - moderate autonomic hyperactivity
- Stage 2 (24 hours)
  - auditory, visual, and tactile hallucinations, anxiety, tremor, continued autonomic hyperactivity
- Stage 3 (7-48 hours)
  - generalized seizures
- Stage 4 (3-5 days)
  - delirium tremens

## Treatment of Alcohol Withdrawal

- Who should be ordered an alcohol withdrawal protocol?
  - Anyone admitted intoxicated
  - With a detectable blood alcohol level
  - Those with positive CAGE questions
  - Patients that report daily consumption

## Treatment of Alcohol Withdrawal

- Benzodiazepines
  - Based on CIWA scale
- Treatment recommendations
  - CIWA > 8 symptoms may benefit treatment
  - CIWA ≥ 15, OR a history of withdrawal seizures, medication should be started
- CIWA monitoring Q1-4H PRN for score greater than 8, if score less than 8 CIWA Q4H X 1, then Q12H thereafter. Typically continued for 5-7 days.

## Comparison of Benzodiazepines

Drug	Half-life	Equivalencies	Active metabolite	Metabolism pathway
Chlordiazepoxide (Librium)	>100 hours	50	desmethyldiazepam	oxidation
Diazepam (Valium)	>100 hours	10	desmethyldiazepam	oxidation
Lorazepam (Ativan)	10-20 hours	1.5-2	none	conjugation

## Dosing strategies

- Scheduled Dosing
  - Chlordiazepoxide (Librium) 50mg Q2-4H
  - Diazepam (Valium) 5-10mg Q2-4H
  - Lorazepam (Ativan) 1-2mg Q2-4H
- PRN Dosing and taper
  - Give PRNs x 24 hours, calculate daily requirement then taper over 3-5 days
- Daily maximum dose is equivalent to chlordiazepoxide 600mg

## PRN only regimens

- Lorazepam 2mg Q4H PRN CIWA-A ≥ 10 and HR ≥ 100 bpm or SBP ≥ 140
- Lorazepam 1mg Q2H PRN CIWA-A ≥ 6 but less than 9, or lorazepam 2mg Q2H PRN CIWA-A ≥ 9 or HR ≥ 100 bpm
- Diazepam 5-10mg Q4H PRN CIWA-A ≥ 8 or HR ≥ 100 bpm

## Fixed vs. Symptom Triggered Dosing

- Fixed dosing
  - Chlordiazepoxide 100mg Q6H x 4 doses
  - 50mg Q8H x 3 doses
  - 25-100mg Q1H PRN CIWA-A ≥ 8
- Symptom triggered
  - 25-100mg Q1H PRN CIWA-A ≥ 8
- No difference in symptom severity, withdrawal seizures or delirium tremens rate
- Symptom triggered decreased duration of treatment and quantity of medication received

## Fixed vs. Symptom Triggered Dosing

- Fixed dosing
  - Oxazepam 30mg q6h x 4 doses
  - Oxazepam 15mg q6h x 8 doses
  - With PRN dosing 30 minutes after dose
- Symptom triggered
  - Oxazepam 15mg Q6H PRN CIWA-Ar 8-15
  - Oxazepam 30mg Q6H PRN CIWA-Ar >15
- Symptom Triggered group
  - Decreased duration of treatment, quantity of medication, and side effects. 1 seizure reported. No difference in comfort

Daepfen et.al. Arch Intern Med  
2002;162:117-1121

## Special Considerations

- Elderly
- Hepatic dysfunction
- COPD
- Severe withdrawal symptoms

## Management of Patients that Develop Delirium Tremens

- Benzodiazepine Regimens
  - Diazepam – 5mg IV repeat in 5-10 minutes, 3<sup>rd</sup> and 4<sup>th</sup> dose if needed give 10mg Q5-10 minutes, the 20mg if 5<sup>th</sup> dose is needed.
    - Then 5-20mg every hour to achieve somnolence
  - Lorazepam – 1-4mg IV Q5-15 minutes or 1-4mg IM every 30-60 minutes until calm
    - Then 1-4mg every hour to maintain somnolence
- Neuroleptic Regimens
  - Haloperidol 0.5-5mg Q4H PRN agitation not controlled by sedative agent

Mayo-Smith 2004

## Other Therapies

- Anticonvulsants
  - Carbamazepine (Tegretol)
    - Mild to moderate withdrawal, outpatients, short term 7 days, no interaction with alcohol, NO prevention DT's
  - Phenytoin (Dilantin)
    - Not effective in preventing withdrawal seizure
  - Valproate (Depakote) – limited data
- Antihypertensives
- Antipsychotics

## Resources and Recommended Readings for Students

- Kosten RK, O'Connor PG. Management of Drug and Alcohol Withdrawal. N Engl J Med. 2003;348:1786-1795.
- Mayo-Smith MF, et.al. Pharmacological Management of Alcohol Withdrawal. JAMA. 1997;278:144-151.
- Kenna GA, et.al. Pharmacotherapy, pharmacogenomics, and the future of alcohol dependence treatment, Part 1. Am J Health-Syst Pharm. 2004;61:2272-9.
- [www.aa.org](http://www.aa.org)
- [www.oas.samhsa.gov](http://www.oas.samhsa.gov)
- [www.psychiatryonline.org](http://www.psychiatryonline.org). Practice Guidelines – Treatment of Patients with Substance Use Disorders.

## Protocol and Policy Recommendations

- Include monitoring parameters with medication administration
- Collaborate with nursing and physician groups
  - Identify barriers and levels of experience
- Include options for patients that are NPO
- Include recommendations for when a patient needs an increased level of care

## Opiates



## Opioid Withdrawal Symptoms

- Early (6-12 hours) – anxiety, rhinorrhea, lacrimation, sweating, yawning
- Other symptoms – mydriasis, restlessness, irritability, anorexia, shaking, chills, profuse sweating, pilomotor activity, nausea, vomiting, myalgias, diarrhea
- Peak is ~ 72 hours, may last 7-10days

## Opiate Detoxification

- Clonidine
- Methadone
- Buprenorphine
- Buprenorphine/naloxone
- Tramadol
- General Anesthesia

## Clonidine

- Off label use
- No federal restrictions
- Dosing
  - Scheduled - 0.1-0.2mg TID
  - PRN - 0.1mg Q2H PRN withdrawal symptoms
- Disadvantages
  - Hypotension, sedation
  - Withdrawal symptoms not treated
    - Insomnia, muscle aches, drug cravings, distress/anxiety

## Methadone

- Approved for opioid withdrawal and maintenance
- Control Schedule II product
- Inpatient or Specially licensed outpatient facility
- Ohio State Board of Pharmacy Law
  - Acute therapy for patients admitted for a reason other than opiate withdrawal – CFR title 21, 1306.07
  - Maintenance Therapy – ORC 3719.61

ORC - Ohio Revised Code, CFR - Code of Federal Regulations

## Methadone

- Management of acutely hospitalized patients
  - Methadone 20mg once, evaluate patient for withdrawal symptoms between 2-4 hours later for additional dosing.
  - If needed give additional 5-10mg
  - Dose should not exceed 40mg the first day
  - Continue dose for 2-3 days and then decrease each daily dose by ~ 20%
- Efficacy
  - Superior to clonidine for relief of withdrawal symptoms

## Inpatient Implications

- Patients hospitalized for non-opiate withdrawal diagnosis, may be continued on methadone therapy.
- Cleveland Area Methadone Treatment Facilities
  - Cleveland Treatment Center
    - 216-861-4246
  - Community Action Against Addiction
    - 216-881-0765
  - Veterans Affairs Medical Center Drug Dependence Treatment Program
    - 440-526-3030 or 216-791-3800
  - Community Drug Board Inc, Community Health Center, Akron OH
    - 330-434-4141

## Buprenorphine

- Buprenorphine (Subutex) off-label
- Buprenorphine/naloxone (Suboxone) off-label
- Partial opioid agonist/antagonist
- Inpatient or outpatient use with certified prescriber
- Dosing – 4 - 24mg per day scheduled or PRN with CINA scale
- Administer sublingually



## Buprenorphine injection

- Buprenorphine
  - Day 1 - 0.4mg SQ/IM every 6 hours
  - Day 2 – 0.3mg SQ/IM every 6 hours
  - Day 3 - 0.2mg SQ/IM every 6 hours
  - Day 4 - 0.1mg SQ/IM every 6 hours
- Other regimens start at 0.6mg

## Comparison Studies

- Buprenorphine vs. clonidine
  - Treatment of withdrawal symptoms – favors buprenorphine<sup>1-4</sup>
  - Treatment completion – favors buprenorphine<sup>2,4,7</sup>
- Buprenorphine vs. methadone
  - Completion of withdrawal treatment – no difference<sup>8-11</sup>

1. Linteris 2002, 2. Nigam 1993, 3. O'Connor, 4. Ling 2005, 5. Cheskin 1994, 6. Collins 2005, 7. Ponzivsky 2006, 8. Bickel 1998, 9. Petitjean 2002, 10. Seifert 2002, 11. Steinmann 2008

## Pharmacy Law Implications

- Buprenorphine injection
  - FDA indicated for moderate to severe pain treatment
  - May be used off-label without restriction
- Buprenorphine +/- naloxone tablets
  - Have specific indications for opiate dependence maintenance therapy
  - Requires prescriber certification
  - CFR Title 21 1306.04 & 1301.28 **do not** allow for use of oral buprenorphine by prescribers that are not certified

CFR – Code of Federal Regulations

## Tramadol

- Tramadol (Ultram) taper (off-label use)
- Binds to  $\mu$  receptors and alters perception and response to pain
- Non-controlled product

## Tramadol

- Protocol 1<sup>1</sup>
  - 100mg Q4H x 6 doses
  - 100mg Q6H x 4 doses
  - 50mg Q6H x 4 doses
  - 50mg Q8H x 3 doses
- Protocol 2<sup>2</sup>
  - 100mg Q4H x 6 doses
  - 100mg Q6H x 4 doses
  - 100mg Q8H x 3 doses
  - 50mg Q6H x 4 doses
  - 50mg Q8H x 3 doses
  - 50mg Q12H x 2 doses

1. Tamaskar 2003, 2. Sobey 2003

## Comparison Studies

- Tramadol vs. Buprenorphine<sup>1,2</sup>
  - No difference in LOS, withdrawal symptoms, tramadol with lower AMA rate (20% vs. 7%<sup>1</sup>, 44% vs. 29%<sup>2</sup>)
- Tramadol vs. clonidine<sup>3</sup>
  - Tramadol with less withdrawal symptoms and lower AMA rate (day 4: 41% vs. 12%, day 8: 63% vs. 20%)
- Tramadol vs. methadone<sup>4</sup>
  - Tramadol with lower side effect rate, similar dropout rate (39% vs. 33%)

1. Tamaskar 2003, 2. Threlkeld 2006, 3. Sobey 2003, 4. Salehi 2006

## Other agents

- Hydroxyzine
- Ibuprofen
- Dicyclomine
- Ondansetron, Prochlorperazine, Promethazine

## Resources and Recommended Readings for Students

- Kosten RK, O'Connor PG. Management of Drug and Alcohol Withdrawal. N Engl J Med. 2003;348:1786-1795.
- [www.na.org](http://www.na.org)
- [www.oas.samhsa.gov](http://www.oas.samhsa.gov)
- [www.psychiatryonline.org](http://www.psychiatryonline.org) Practice Guidelines – Treatment of Patients with substance use disorders.