Psychopharmacology in the Emergency Room

Michael D. Jibson, M.D., Ph.D.
Associate Professor of Psychiatry
University of Michigan
Pretest

1. Appropriate target symptoms for emergency room medication treatment include all of the following except:
   a. Psychotic agitation
   b. Suicidal ideation
   c. Alcohol withdrawal
   d. Acute anxiety
   e. Acute dystonic reaction
2. Which medication is available for intramuscular (IM) injection?
   a. Alprazolam (Xanax)
   b. Chlordiazepoxide (Librium)
   c. Clonazepam (Klonopin)
   d. Diazepam (Valium; Dizac)
   e. Lorazepam (Ativan)
3. Advantages of haloperidol (Haldol) over atypical antipsychotics for intramuscular (IM) injection for acute agitation include which of the following?

a. Low risk of side effects  
b. Low cost  
c. FDA approval for acute agitation  
d. Efficacy for alcohol withdrawal  
e. Superior efficacy for acute agitation
4. One day after an extended drinking binge, a 35-year-old man is seen in the ER with acute agitation, diaphoresis, and auditory hallucinations. Which of the following treatments is most appropriate:

a. Nonpharmacologic washout
b. Olanzapine (Zyprexa) 5 mg IM
c. Lorazepam (Ativan) 2 mg IM
d. Quetiapine 25 mg PO
e. Triazolam (Halcion) 0.25 mg IM
5. A 23-year-old woman is placed on a court order and receives a single dose of haloperidol (Haldol) PO, the next morning she appears rigid, with her head turned to the side and her eyes looking upward. This most likely represents:

a. An acute dystonic reaction
b. Acute onset catatonia
c. Tardive dyskinesia
d. Akathisia
e. Malingering
Major Teaching Points

- Pharmacologic interventions in the emergency room are limited to specific situations and target symptoms
- Patient and staff safety are the highest priorities
- Treatment selection is based on:
  - target symptoms
  - underlying pathology
  - preferred route of administration
Outline

- Target Symptoms for ER Treatment
- Acute Agitation
  - Evaluation
  - Treatment
    - Antipsychotic Medications
      - IM and PO options
    - Benzodiazepines
- Acute Anxiety
- Alcohol Withdrawal
- Acute Dystonic Reactions
Emergency Pharmacology

Likely to benefit from emergency medications

- Psychotic agitation
- Acute anxiety
- Alcohol/sedative/hypnotic withdrawal
- Acute dystonic reaction
Emergency Pharmacology

Unlikely to benefit from emergency medications

- Major depression
- Suicidality
- Other drug withdrawal
Evaluation and Treatment of Acute Agitation
Agitation

Acute state of

- Anxiety
- Heightened arousal
- Increased motor activity
Agitation

May include

- Lack of cooperation
- Attempts to elope
- Hostility
- Aggression
Agitation

May be caused by

- Drug or alcohol intoxication
- Alcohol or sedative withdrawal
- Personality disorders
- Mood disorders
- Psychotic disorders
- Delirium
- Hypoxia
- Cognitive impairment
Agitation

May occur in conjunction with psychosis

- Mania
- Disturbing content of delusions or hallucinations
- Thought disorganization
- Intrusion of law enforcement or mental health workers
- Akathisia
Agitation

May include aggression related to

- More severe pathology
- Persecutory delusions
- Thought disorganization
- Command hallucinations
Treatment

Goals

- Maintain patient and staff safety
- Identify and address underlying pathology
  - Reduce psychosis
  - Reduce mania
  - Improve cognition
  - Treat medical problems
Treatment

Essential Resources

- Adequate staff
- Verbal de-escalation
- Medication
- Room seclusion
- Physical restraints
Treatment

Medications

- Antipsychotics
  - Oral
  - Injectable
- Benzodiazepines
  - Oral
  - Injectable
Injectable Antipsychotic Medications

- Haloperidol (Haldol)
- Olanzapine (Zyprexa)
- Ziprasidone (Geodon)
Haloperidol

Dosing (intramuscular or intravenous injection)

• 5 mg q 30 min - q 2 hr

• Average dose: 10 mg/day

• Maximum recommended dose: 20-30 mg/day
Haloperidol

Short-term Side Effects

- Akathisia
- Acute dystonia
- Extrapyramidal side effects (EPS)
- Sedation
Haloperidol

Treatment Issues

• Advantages
  • Well-established efficacy
  • Multiple routes of administration
  • Low cost
• Disadvantages
  • High risk of side effects
  • Requires treatment transition
Olanzapine

Pharmacokinetics (injectable)

- 15-30 min time to peak concentration
- 30-hr elimination half-time
- No major drug-drug interactions
Olanzapine

Dosing (intramuscular injection)

• 10 mg q 30 min - 2 hrs
• Average dose: 20 mg/day
• Maximum recommended dose: 30 mg/day
Olanzapine

Short-term Side Effects

• Sedation
• Orthostatic hypotension
• Anticholinergic effects
• Akathisia
Olanzapine

Treatment Issues

• Advantages
  • FDA approved for agitation
  • Low risk of EPS
  • Sedation

• Disadvantages
  • High cost
Ziprasidone

Pharmacokinetics (injectable)

- 1-hr time to peak concentration
- 2.5-hr elimination half-time
- Serum levels decreased by carbamazepine
Ziprasidone

Dosing (intramuscular injection)

- Common dose range: 10-40 mg/day q 4 hr
- Average dose: 20 mg/injection
- Maximum recommended dose: 40 mg/day
- Available in 20 mg vials
Ziprasidone

Short-term Side Effects

- Somnolence
- Nausea
- Akathisia
- qTc prolongation
Ziprasidone

Treatment Issues

- Advantages
  - FDA approved for agitation
  - Low EPS
- Disadvantages
  - High cost
Disintegrating Tablets

- Olanzapine (Zyprexa Zydis)
- Risperidone (Risperdal M-Tab)
Olanzapine

Pharmacokinetics (oral)

- 5-hr time to peak concentration
- 30-hr elimination half-time
- No major drug-drug interactions
- Pharmacokinetics are identical to coated tablets
Olanzapine

Dosing (disintegrating tablets)

- 5-10 mg q 30 min - 2 hrs
- Average dose: 10 mg/day
- Maximum recommended dose: 20 mg/day
- Dosing is the same as coated tablets
Olanzapine

Treatment Issues

• Advantages
  • Requires minimal patient cooperation
  • Assures clinician of patient compliance

• Disadvantages
  • High cost
Risperidone

Pharmacokinetics (oral)

- 1.5-hr time to peak concentration
- 20-hr elimination half-time
- No significant drug interactions
- Pharmacokinetics are identical to standard tablets
Risperidone

Dosing (disintegrating tablets)

• 2 mg q 1-2 hrs
• Average dose: 4 mg/day
• Maximum recommended dose: 6 mg/day
• Dosing is the same as standard tablets
Risperidone

Short-term Side Effects

- Sedation
- Orthostatic hypotension
- Akathisia
- EPS (dose-dependent)
Risperidone

Treatment Issues

- **Advantages**
  - Requires minimal patient cooperation
  - Assures clinician of patient compliance
- **Disadvantages**
  - High cost
Standard Tablets

- Aripiprazole (Abilify)
- Quetiapine (Seroquel)
- Ziprasidone (Geodon)
Aripiprazole

Pharmacokinetics

• 3-5 hr time to peak concentration
• 75 hr elimination half-time
• No major drug interactions
  • Serum levels modestly affected by carbamazepine and fluvoxamine
Aripiprazole

Dosing

- Common dose range: 10-20 mg/day
- Average dose: 15 mg/day
- Maximum recommended dose: 30 mg/day
- Once daily dosing
Aripiprazole

Side Effects

- Headache
- Nausea/vomiting
- Insomnia
- EPS
- Somnolence
- Lightheadedness
- Akathisia
Aripiprazole

Treatment Issues

- Advantages
  - Favorable side effect profile
  - Long serum half-life
- Disadvantages
  - Minimal clinical experience for agitation
Quetiapine

Pharmacokinetics

- 1.5-hr time to peak concentration
- 6-7-hr elimination half-time
- No major drug interactions
  - Serum levels modestly affected by carbamazepine and fluvoxamine
Quetiapine

Dosing

- 25-100 mg q 1-2 hrs
- Average dose: 50 mg/day
- Maximum recommended dose: 200 mg/day
Quetiapine

Side Effects

• Sedation
• Orthostatic hypotension
• Akathisia
Quetiapine

Treatment Issues

- Advantages
  - Lowest EPS risk
  - Rapid onset of action
  - Highly sedating

- Disadvantages
  - High risk of hypotension
Ziprasidone

Pharmacokinetics (oral)

• 6-8-hr time to peak concentration
• 7-hr elimination half-time
• No major drug interactions
  • Serum levels decreased by carbamazepine
Ziprasidone

Dosing

• 20-40 mg q 1-2 hrs
• Average dose: 40-80 mg/day
• Maximum recommended dose: 80 mg/day
Ziprasidone

Side Effects

- Somnolence
- Nausea
- Akathisia
- Rash
- qTc prolongation
Ziprasidone

Treatment Issues

- Advantages
  - Favorable side effect profile
- Disadvantages
  - Limited clinical experience
Benzodiazepines

- Alprazolam (Xanax)
- Chlordiazepoxide (Librium)
- Clonazepam (Klonopin)
- Clorazepate (Tranxene)
- Diazepam (Valium, Dizac)
- Estazolam (ProSom)
- Flurazepam (Dalmane)
- Halazepam (Paxipam)
- Lorazepam (Ativan)
- Midazolam (Versed)
- Oxazepam (Serax)
- Prazepam (Centrax)
- Quazepam (Doral)
- Temazepam (Restoril)
- Triazolam (Halcion)
Benzodiazepines

Differ in
- Potency
- Onset of action
- Duration of action
- Route of administration
- Metabolic pathways

Are identical in
- Efficacy
- Clinical activity
- Pharmacologic activity
Benzodiazepines

Intramuscular

- Lorazepam (Ativan)

Intravenous

- Chlordiazepoxide (Librium)
- Diazepam (Dizac)
- Lorazepam (Ativan)
Lorazepam

Pharmacokinetics

- Available for IM or IV injection
- 30 min to onset of action
- 2 hr to peak concentration
- 16 hr serum half-time
- No active metabolites
- Metabolism not affected by liver dysfunction
Lorazepam

Dosing (oral, intramuscular, intravenous)

- 1-2 mg q 30 min - 2 hr
- Average dose: 2-4 mg/day
- Maximum recommended dose: 8 mg/day
Lorazepam

Side Effects

- Sedation
- Disinhibition
- Delirium
- Respiratory depression
Lorazepam

Treatment Issues

- **Advantages**
  - Rapid onset
  - Reduces agitation, anxiety, and akathisia
  - IM, IV, and PO formulations
  - Favorable side effect profile

- **Disadvantages**
  - None
Treatment Selection for Psychotic Agitation

- FDA studies do not include highly agitated, involuntary patients
- Few studies compare available drugs
- Published studies are small, uncontrolled, and retrospective
Treatment Selection for Psychotic Agitation

Antipsychotics

- All antipsychotics appear comparable in efficacy
- Differences in onset of action have not been demonstrated
- Side effect profiles differ, but are rarely important in the acute phase
- Mode of administration differs
Treatment Selection for Psychotic Agitation

Benzodiazepines

• In the short term, benzodiazepines appear at least as effective as antipsychotics
• Benzodiazepines are highly sedating
• Lorazepam is the only IM benzodiazepine
Treatment Selection for Psychotic Agitation

- Antipsychotics are essential to treat underlying psychosis or mania
- Antipsychotics may have longer duration of action
- The combination of antipsychotics and benzodiazepines appears more effective than either one alone (but only one major study)
Evaluation and Treatment of Acute Anxiety
Acute Anxiety

Differential Diagnosis

• Panic attack
• Generalized anxiety
• Adjustment disorder
• Posttraumatic stress disorder (PTSD)
• Medical conditions
• Drug intoxication or withdrawal
Acute Anxiety

Treatment

- Benzodiazepines provide optimal short-term treatment for anxiety and panic symptoms.
- Benzodiazepines may be used as an interim treatment during titration of other medications for anxiety (e.g., SSRIs, SNRIs).
Evaluation and Treatment of Alcohol/Sedative/Hypnotic Withdrawal
Alcohol/Sedative/Hypnotic Withdrawal

- Benzodiazepines are the preferred treatment for alcohol and sedative/hypnotic withdrawal
Alcohol/Sedative/Hypnotic Withdrawal

Monitor Vital Signs and Physical Symptoms

- Systolic blood pressure >140-160
- Diastolic blood pressure >90-100
- Heart rate >100-110
- >2 beats of clonus
- Diaphoresis
- Tremulousness
- Agitation
Alcohol/Sedative/Hypnotic Withdrawal

Long-acting Benzodiazepines

- Chlordiazepoxide (Librium)
  - 25-50 mg PO or IV q30 min – 2 hrs
- Diazepam (Valium, Dizac)
  - 5-10 mg PO or IV q30 min – 2 hrs
Alcohol/Sedative/Hypnotic Withdrawal

Long-acting Benzodiazepines

- **Advantages**
  - Continuous relief of symptoms
  - Ease of administration
  - Self-taper after acute phase

- **Disadvantages**
  - Poor clearance with hepatic dysfunction
Alcohol/Sedative/Hypnotic Withdrawal

Short-acting Benzodiazepines

• Lorazepam (Ativan)
  • 1-2 mg PO, IM, IV q 30 min – 2 hrs
Alcohol/Sedative/Hypnotic Withdrawal

Short-acting Benzodiazepines

• Advantages
  • Unimpaired clearance with hepatic dysfunction
  • Multiple routes of administration

• Disadvantages
  • Continuous monitoring required to avoid resurgence of symptoms
Acute Dystonic Reaction
Acute Dystonic Reaction

• Intense muscle cramps as side effect of antipsychotic medications

• Highest risk with high potency first generation antipsychotics (e.g., haloperidol, thiothixene, fluphenazine)

• Not specific to any one medication
Acute Dystonic Reaction

- Most common early in treatment or shortly after a dose increase
- May be isolated to specific regions of the body
  - Oculogyric crisis (extraocular muscles)
  - Torticollis (neck)
  - Laryngospasm (throat/larynx)
Acute Dystonic Reaction

Treatment

• Benztropine (Cogentin)
  • 2 mg IM q 15-30 min up to 8 mg/day
• Diphenhydramine (Benadryl)
  • 50 mg IM q 15-30 min up to 200 mg/day
1. Appropriate target symptoms for emergency room medication treatment include all of the following except:
   a. Psychotic agitation
   b. Suicidal ideation
   c. Alcohol withdrawal
   d. Acute anxiety
   e. Acute dystonic reaction
2. Which medication is available for intramuscular (IM) injection?

a. Alprazolam (Xanax)
b. Chlordiazepoxide (Librium)
c. Clonazepam (Klonopin)
d. Diazepam (Valium; Dizac)
e. Lorazepam (Ativan)
3. Advantages of haloperidol (Haldol) over atypical antipsychotics for intramuscular (IM) injection for acute agitation include which of the following?

a. Low risk of side effects
b. Low cost
c. FDA approval for acute agitation
d. Efficacy for alcohol withdrawal
e. Superior efficacy for acute agitation
4. One day after an extended drinking binge, a 35-year-old man is seen in the ER with acute agitation, diaphoresis, and auditory hallucinations. Which of the following treatments is most appropriate:

a. Nonpharmacologic washout
b. Olanzapine (Zyprexa) 5 mg IM
c. Lorazepam (Ativan) 2 mg IM
d. Quetiapine 25 mg PO
e. Triazolam (Halcion) 0.25 mg IM
5. A 23-year-old woman is placed on a court order and receives a single dose of haloperidol (Haldol) PO, the next morning she appears rigid, with her head turned to the side and her eyes looking upward. This most likely represents:

a. An acute dystonic reaction
b. Acute onset catatonia
c. Tardive dyskinesia
d. Akathisia
e. Malingering
Pre- and Post-Test Answer Key

1. b
2. e
3. b
4. c
5. a