

---

■ ■ ■

# Psychopharmacology in the Emergency Room

Michael D. Jibson, M.D., Ph.D.

Professor of Psychiatry

University of Michigan

---

■ ■ ■

# Author Disclosure

- Over the past 3 years, I have received \$5000-10,000 per year from the AstraZeneca speakers bureau for promotional programs on quetiapine.

# Learning Objectives

---

- Identify the goals and limitations of emergency room medication treatment
  - Recognize the symptoms, underlying causes, and treatments of acute agitation
  - Understand the advantages and disadvantages of oral and injectable administration of medications for acute agitation
-

# Learning Objectives



- 
- Recognized the advantages and disadvantages of the different antipsychotics for acute agitation
  - List the characteristics of lorazepam for treatment of acute agitation or acute anxiety
  - Identify the symptoms of and treatments for acute dystonia



# Outline



- 
- Appropriate targets for emergency room medication
  - Acute agitation
    - Clinical description
    - Underlying causes
    - Goals of treatment
    - Medications
      - PO antipsychotics
      - IM antipsychotics
      - Benzodiazepines
    - Treatment selection



# Outline



- 
- Acute anxiety
    - Diagnosis
    - Treatment
  - Acute dystonic reactions
    - Diagnosis
    - Risk factors
    - Treatment



# Pretest

- 
1. Which of the following conditions is **LEAST** likely to benefit from emergency room medication?
- a. Acute anxiety
  - b. Acute agitation
  - c. Acute suicidality
  - d. Chronic hallucinations
  - e. Alcohol withdrawal
-

# Pretest

- \_\_\_\_\_
2. Which of the following is the most important goal of emergency room medication treatment?
- a. Rapid diagnosis of underlying disorder
  - b. Establishment of patient and staff safety
  - c. Rapid control of psychotic symptoms
  - d. Reduction of suicidal ideation
  - e. Disposition to appropriate follow-up care
- \_\_\_\_\_ ■■■



# Pretest

- 
3. Compared to standard tablets of antipsychotics, orally disintegrating tablets have which of the following advantages?
- a. More rapid onset of action
  - b. Greater bioavailability
  - c. Significant transmucosal (eg, sublingual) absorption
  - d. Greater ease of administration
  - e. More appropriate dose strengths
-

# Pretest

- 
4. Compared to haloperidol, injectable atypical antipsychotics have which of the following advantages?
- a. Greater efficacy
  - b. Better EPS profile
  - c. Greater cost-effectiveness
  - d. More rapid onset of action
  - e. Greater convenience of administration
-

# Pretest

- 
5. Benzodiazepines are identical to one another in which of the following characteristics?
- a. Onset of action
  - b. Route of administration
  - c. Route of metabolism
  - d. Duration of action
  - e. Clinical efficacy
-

# Treatment Principles



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



# 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



# Oral Antipsychotics

---

## Preferred Option

---

- Orally disintegrating tablets

## Alternative Options

---

- Standard tablets
- Liquid concentrate
- Sublingual tablets





# Oral Antipsychotics

---

- Standard tablets
  - Most antipsychotics are available
  - Easy to check
- Liquid concentrate
  - Many antipsychotics are available
  - Difficult to administer
- Sublingual tablets
  - Only asenapine (Saphris) is available
  - No data on use for acute agitation



# Oral Antipsychotics

---

## Orally Disintegrating Tablets

---

- Easy to administer
- Noninvasive
- Hard to “cheek”
- NOT absorbed transmucosally
- Same pharmacokinetics as standard tablets



# Oral Antipsychotics

---

## Orally Disintegrating Tablets

---

- Aripiprazole (Abilify Discmelt)
- Olanzapine (Zyprexa Zydis)
- Risperidone (Risperdal M-Tab)



# Aripiprazole

---

## Dosing (disintegrating tablets)

---

- 10-15 mg q 2 hrs
- Average dose: 20 mg/day
- Maximum recommended dose: 30 mg/day
- Supplied in 10 mg and 15 mg tablets

# Aripiprazole

---

## Pharmacokinetics (oral)

---

- 3-5 hr to peak concentration
- 75-hr elimination half-time
- No significant drug interactions
- Pharmacokinetics are identical to standard tablet

# Aripiprazole

---

## Short-term Side Effects

---

- Nausea/vomiting
- Akathisia
- Insomnia



# Aripiprazole

## ■■■ --- Treatment Issues ---

- Nonsedating
- The combination of a partial agonist with an antagonist (ie, all other antipsychotics) leads to unpredictable receptor activities

# Risperidone

---

## Dosing (disintegrating tablets)

---

- 1-2 mg q 30 min - 2 hrs
- Average dose: 4 mg/day
- Maximum recommended dose: 6 mg/day
- Supplied in 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg tablets



# Risperidone



---

## Pharmacokinetics (oral)

---

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



# Risperidone

---

## Short-term Side Effects

---

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



# Risperidone



---

## Treatment Issues

---

- Higher risk of EPS
- Intermediate level of sedation



# Olanzapine

---

## Dosing (disintegrating tablets)

---

- 5-10 mg q 30 min - 2 hrs
- Average dose: 10 mg/day
- Maximum recommended dose: 20 mg/day
- Supplied as 5 mg, 10 mg, 15 mg, and 20 mg tablets



# Olanzapine

---

## ■ ■ ■ Pharmacokinetics (oral)

---

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

# Olanzapine



---

## Treatment Issues

---

- More sedating
- More anticholinergic



# Injectable Antipsychotics

---

## ■ ■ ■ Intramuscular Injection

- Ensured administration
- Rapid absorption
- Difficult to administer
- Invasive

# Injectable Antipsychotic Medications

---

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





# Haloperidol

## ■■■ Dosing (intramuscular or intravenous injection)

- 5-10 mg q 30 min - q 2 hr
- Average dose: 10 mg/day
- Maximum recommended dose: 20-30 mg/day

# Haloperidol

## ■■■ --- Pharmacokinetics (IM or IV injection) ---

- IV: 20-30 min to peak concentration
- IM: 30-45 min to peak concentration
- 20-hr elimination half-time
- No major drug-drug interactions

# Haloperidol

---

## Short-term Side Effects

---

- Akathisia
  - Acute dystonia
  - Extrapyramidal side effects (EPS)
  - Sedation
  - QT prolongation (IV administration only)
-

# Haloperidol

---

## Treatment Issues

---

- Multiple routes of administration (IM, IV)
- Low cost
- High risk of side effects
- May require treatment transition



# Aripiprazole

---

## Dosing (intramuscular injection)

---

- 9.75 mg q 2 hrs
- Average dose: 19.5 mg/day
- Maximum recommended dose: 30 mg/day
- Available in 9.75 mg vials



# Aripiprazole

---

## Pharmacokinetics (injectable)

---

- 1-3 hr to peak concentration
- 75-hr elimination half-time
- No major drug-drug interactions

# Aripiprazole

---

## Short-term Side Effects

---

- Nausea/vomiting
- Headache
- Mild sedation



# Aripiprazole

## ■ ■ ■ Treatment Issues

- Less sedation
- May be administered concurrently with BZDs
- Partial agonist-antagonist combinations lead to unpredictable receptor activities



# Olanzapine

---

## Dosing (intramuscular injection)

---

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



# Olanzapine

---

## Pharmacokinetics (injectable)

---

- 15-45 min to peak concentration
- 30-hr elimination half-time
- Possible interaction with BZDs



# Olanzapine

---

## Short-term Side Effects

---

- Sedation
- Orthostatic hypotension
- Anticholinergic effects
- Akathisia



# Olanzapine

## Treatment Issues

- More sedating
- Unclear if safe with BZDs
  - No controlled studies of safety
  - Few published case reports of problems
  - Some expert guidelines recommend a 1-hr delay between the medications to avoid cardiorespiratory depression

# 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

---

## ■ ■ ■ Pharmacokinetics (injectable)

---

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

# Ziprasidone

## Short-term Side Effects

- Somnolence
- Nausea
- Akathisia
- QT prolongation

# Ziprasidone

## Treatment Issues

- Moderately sedating
- No cardiac problems have been reported  
but
- Avoid use with other agents causing QT  
prolongation



# 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, Valium)
  - Lorazepam (Ativan)
-

# Lorazepam

## ■■■ Dosing (oral, intramuscular, intravenous)

- 1-2 mg q 30 min - 2 hr
- Average dose: 2-4 mg/day
- Maximum recommended dose: 12 mg/day

# Lorazepam

---

## ■ ■ ■ Pharmacokinetics (Oral)

---

- 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



---

## Pharmacokinetics (IM or IV injection)

---

- 30 min to peak concentration
- 16 hr serum half-time



# Lorazepam

## Side Effects

- Sedation
- Disinhibition
- Delirium
- Respiratory depression

# Lorazepam

## ■ ■ ■ --- Treatment Issues

- Highly sedating
- Generally well tolerated
- May cause respiratory depression when given IV
- May cause delirium or disinhibition



# 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 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).



# 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
- Highest incidence is at trough drug level
- May be isolated to specific regions of the body
  - Oculogyric crisis (extraocular muscles)
  - Torticollis (neck)
  - Laryngospasm (throat/larynx) – may be life threatening

# 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



# Post-test

- 
1. Which of the following conditions is **LEAST** likely to benefit from emergency room medication?
- a. Acute anxiety
  - b. Acute agitation
  - c. Acute suicidality
  - d. Chronic hallucinations
  - e. Alcohol withdrawal
-

# Post-test

- 
2. Which of the following is the most important goal of emergency room medication treatment?
- a. Rapid diagnosis of underlying disorder
  - b. Establishment of patient and staff safety
  - c. Rapid control of psychotic symptoms
  - d. Reduction of suicidal ideation
  - e. Disposition to appropriate follow-up care
-

# Post-test

- 
3. Compared to standard tablets of antipsychotics, orally disintegrating tablets have which of the following advantages?
- a. More rapid onset of action
  - b. Greater bioavailability
  - c. Significant transmucosal (eg, sublingual) absorption
  - d. Greater ease of administration
  - e. More appropriate dose strengths
-

# Post-test

- 
4. Compared to haloperidol, injectable atypical antipsychotics have which of the following advantages?
- a. Greater efficacy
  - b. Better EPS profile
  - c. Greater cost-effectiveness
  - d. More rapid onset of action
  - e. Greater convenience of administration
-

# Post-test

- 
5. Benzodiazepines are identical to one another in which of the following characteristics?
- a. Onset of action
  - b. Route of administration
  - c. Route of metabolism
  - d. Duration of action
  - e. Clinical efficacy
-



# Pre- and Post-test Answers



1. c

2. b

3. d

4. b

5. e

