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Psychopharmacology in the Emergency Room

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Pretest

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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. Severe depression
-

Pretest

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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
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Pretest

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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
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Pretest

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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

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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
-

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



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- 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



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



Outline



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



Treatment Principles



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- 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
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- ■ ■

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



-
- Standard tablets
 - Orally disintegrating tablets
 - Liquid concentrate



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
- Partial agonist-antagonist combinations lead 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 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
- Extrapiramidal side effects (EPS)
- Sedation



Haloperidol

■ ■ ■ --- Treatment Issues ---

- Multiple routes of administration
- 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
- No major drug-drug interactions



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
 - No 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
- Avoid use with other agents causing QTc prolongation

Ziprasidone

Short-term Side Effects

- Somnolence
- Nausea
- Akathisia
- qTc prolongation



Ziprasidone



Treatment Issues

- Moderately sedating
- No cardiac problems have been reported



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

■■■ 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 at least as effective as antipsychotics
- Benzodiazepines are highly sedating
- Lorazepam is the only IM benzodiazepine

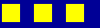
Treatment Selection for Psychotic Agitation

- 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).



Acute Dystonic Reaction



Acute Dystonic Reaction



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- 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)

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

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-

Pre- and Post-test Answers



1. c

2. b

3. d

4. b

5. e

