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Psychopharmacology in the Emergency Room

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Pretest

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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
-

Pretest

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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)
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Pretest

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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
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Pretest

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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
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Pretest

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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



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- 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



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- 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
- Extrapiramidal 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



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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
- 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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 - d. Akathisia
 - e. Malingering
- _____ ■■■

Pre- and Post-Test Answer Key



1. b

2. e

3. b

4. c

5. a

