ACLP How To Guide: Acute Agitation

How to Manage Acute Agitation in the Medical Setting

Learning Objectives:

1) To identify different sources of agitation.
2) To become familiar with the stepwise approach to manage acute agitation.
3) To know the different types of pharmacological interventions for the management of acute agitation in the medical setting.

Step 1: Assess situation and cause of agitation

- Delirium (make sure underlying medical cause is being addressed)
- Intoxication or withdrawal (central nervous system [CNS] stimulant vs depressant)
- Primary psychiatric disorder (e.g., psychosis, mania)
- Undetermined cause

Step 2: Attempt to de-escalate and utilize non-pharmacological interventions

- Clearing the room: removing dangerous objects and reducing external stimuli
- Verbal de-escalation (see Box 1) (1-3)
- Having staff available as a "show of force"
- Close observation
- Decrease sensorial stimulation

Box 1: De-escalation techniques (1-3)

- Respect personal space
- Do not be provocative
- Calm, concise conversation: use gentle, relaxed, assured tone; answer calmly, maintaining firm attitude
- Identify wants and feelings
- Active listening; paraphrase what patient says
- Set clear limits; agree or agree to disagree
- Offer choices and optimism
- Redirect conversation when disruptive/provocative questions are asked
- If facing imminent violence:
    - Make clear violence is not acceptable
    - Propose resolution through dialogue
    - Offer pharmacological treatment
    - Inform patient you may rely on physical restraint, if necessary

Step 3: If non-pharmacological interventions fail, medication is now required.

- The goal of psychopharmacologic treatment of acute agitation is **rapid tranquilization** *not* total sleep induction.
- Pharmacologic considerations (4,5):
    - Underlying cause of agitation should drive choice of medication
    - Ease of preparation/administration
    - Rapid onset of action: IV > IM > PO
    - Sufficient duration of effect

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- Low risk of adverse reactions or drug interactions

- Medication algorithm for pharmacologic treatment of acute agitation based on the American Association of Emergency Psychiatry (2) and the World Federation of Societies of Biological Psychiatry (WFSBP) Expert Consensus (1): (see Table 1 for medication details)
    1. Agitation associated with delirium [**not** due to benzodiazepine (BZD) or alcohol (EtOH) withdrawal]
        - Oral antipsychotic: first choice, atypical (e.g., risperidone 2 mg, olanzapine 5-10 mg), or second choice, typical (e.g., haloperidol 2-5 mg)
        - If unable to give PO, parenteral antipsychotic: olanzapine 10 mg IM* or haloperidol 5 mg IM (use lowest effective dose due to increased risk of EPS in delirious patients) or 2.5 mg IV (twice as potent, use with caution)
        - Avoid BZD
    2. Agitation due to EtOH or BZD ***withdrawal*** or CNS stimulant intoxication (e.g., amphetamines, synthetic cannabinoids)
        - Oral BZD: lorazepam 1-2 mg, diazepam 5-10 mg
        - Parental BZD if unable to give PO: lorazepam 1-2 mg IM or IV
    3. Agitation due to CNS depressant (e.g., acute EtOH ***intoxication***)
        - Oral haloperidol 2-10 mg
        - If unable to give PO, parenteral 2-10 mg IM or 1-5 mg IV
        - Avoid BZD
    4. Agitation associated with psychosis/mania due to known psychiatric disorder
        - Oral antipsychotic: first choice, atypical (e.g., risperidone 2 mg, olanzapine 5-10 mg), or second choice, typical (e.g., haloperidol 2-5 mg)
        - If unable to give PO, parenteral antipsychotic: olanzapine 5-10 mg IM* or haloperidol 5 mg IM or 2.5 mg IV (with caution)
        - If antipsychotic alone is not sufficient, add lorazepam 1-2 mg PO/IM/IV
    5. Agitation due to undetermined cause
        - No evidence of psychosis, treat as number 2 above
        - If evidence of psychosis, treat as number 4 above

*IM olanzapine should NOT be administered with BZDs or CNS depressants given reports of excessive sedation and cardiorespiratory depression (FDA warning; however, evidence of the safety of this combination exists (6)).

Prolonged QTc: Utilize BZD if appropriate; if antipsychotic is necessary preference given to aripiprazole

Step 4: Learn how to manage agitation in special populations

- Acute agitation in pregnancy
    - The same initial steps for assessment and de-escalation (Steps 1 and 2) should be used in pregnant patients (1,7) as in non-pregnant patients.
    - Given the lack of evidence on the effectiveness of pharmacologic interventions in pregnant women, verbal interventions should be utilized whenever possible (1).
    - If medication is required, the minimal effective dose should be utilized:
        - For mild to moderate cases of agitation, oral or IM diphenhydramine 25-50 mg may suffice.
        - For severe agitation, haloperidol is the medication of choice, oral or IM 2-5 mg

(5, 7).

- Older adults
  - Agitation in older adults in the hospital setting should be presumed to be delirium until proven otherwise if the mental status is altered (1).
  - Initially try all non-pharmacological strategies (5).
  - Cautious use of antipsychotics is recommended: start with low doses (e.g., risperidone 0.5 mg) and slowly titrate with small increments; monitor closely for signs of confusion or over-sedation.
  - Expert Consensus Guidelines on Using Antipsychotics in Older Patients give preference to risperidone for treating delirium (8).
  - In agitation related to dementia, first choice is risperidone 0.5 mg, second choice is aripiprazole 2.5 mg or quetiapine 25 mg; lower doses recommended for frail patients (9).

Table 1: Medications Commonly Used in the Management of Acute Agitation (1,5)

Medication Class	Medication	Dosing	Side Effects/Considerations
Benzodiazepines	Alprazolam	Only available PO Initial dose is 0.5-4 mg/day	• Paradoxical reactions can be seen in character-disordered patients and can worsen symptoms in older adults
	Diazepam	PO, IM, IV Start at 5 mg	• Calming/sedating effect with rapid onset • Use cautiously with older adults because of long half-life
	Lorazepam	PO, SL, IM, IV Start at 1 mg Moderate half-life (10-20 hours)	• No active metabolites; therefore, there is small risk of drug accumulation • Metabolized only via glucuronidation; therefore, it can be used in most patients with impaired hepatic function • Drug of choice within this class due to moderately long half-life
Typical antipsychotics	Haloperidol	PO, IM, IV* Start at 5-10 mg PO/IM Or 2-5 mg IV* *IV formulation is not FDA approved	• High-potency neuroleptic with favorable side-effect profile and cardiopulmonary safety • IV form less likely to cause EPS • ECG monitoring needed to assess for QTc prolongation or torsades de pointes (higher risk with IV) • Risk of neuroleptic malignant syndrome increases in patients who are poorly hydrated, restrained, and kept in poorly aerated rooms while given large doses of antipsychotics • Frequent vital sign checks and testing for muscular rigidity are recommended • Can cause hypotension
Atypical antipsychotics	Risperidone	PO, ODT Starting dose 0.5-2 mg acutely	• No IM form is available • Orthostatic hypotension with reflex tachycardia • Increased risk of stroke in older adults with cardiovascular disease
	Olanzapine	PO, ODT, IM Starting dose 2.5-5 mg, max 30 mg/24 hours with doses 2-4 hours apart	• Useful in patients with poor reaction to haloperidol • Avoid IM combinations with lorazepam* • Increased risk of stroke in older adults with cardiovascular disease
	Ziprasidone	PO, IM Starting 10-20 mg Max of 40 mg/24 hours if using IM	• Use caution in patients with preexisting QT prolongation • Less sedating medication; therefore, good choice if desire tranquilization without sedation
	Aripiprazole	PO, ODT Starting PO dose 5-10 mg, max 30 mg/day (currently IM formulation only for extended-release maintenance therapy)	• Akathisia risk • Less sedating than other medications • Increase risk of stroke in older adults • Good choice for patients with QT prolongation
Combinations	Haloperidol + lorazepam + diphenhydramine OR benztropine	5 mg IM + 2 mg IM + 50 mg IM OR 1 mg IM	• Most commonly used in the acute setting • Young athletic men are at increased risk for dystonia – mitigated by the third agent in this combination • Akathisia must be considered if agitation increases after administration

(PO = by mouth, IM = intramuscular, IV = intravenous, SL = sublingual, ODT = oral disintegrating tablet)

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