How to Manage Acute Agitation in the Medical Setting

Objective:

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 (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, 2)
- Having staff available as a “show of force”
- Close observation
- Decrease sensorial stimulation

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 (3, 4):
  - Underlying cause of agitation should drive choice of medication
  - Ease of preparation/administration
  - Rapid onset of action: IV > IM > PO
  - Sufficient duration of effect
  - Low risk of adverse reactions or drug interactions

Box 1: De-escalation techniques (1, 2)

- 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
- Offer choices
- 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
• Medication algorithm for pharmacologic treatment of acute agitation based on the American Association for Emergency Psychiatry (3) and the World Federation of Societies of Biological Psychiatry (WFSBP) Expert Consensus (1):
  (see Table 1 for medication details)
  o 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 of haloperidol due to increased risk of EPS in delirious patients) or IV (with caution)
    ▪ Avoid BZD
  o 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
    ▪ Parenteral BZD if unable to give PO: lorazepam 1-2 mg IM or IV
  o Agitation due to CNS depressant (e.g., acute EtOH intoxication)
    ▪ Oral haloperidol 2-10 mg
    ▪ If unable to give PO, parenteral haloperidol 2-10 mg IM
    ▪ Avoid BZD
  o 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 10 mg IM* or haloperidol 5-10 mg IM or IV (with caution)
    ▪ If antipsychotic alone is not sufficient, add lorazepam 1-2 mg PO or IM
  o 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

Prolonged QTc: Utilize BZD if appropriate; if antipsychotic is necessary preference given to aripiprazole (see Table 1)

Step 4: Learn how to manage agitation in special populations

• Acute Agitation in Pregnancy
  o The same initial steps for assessment and de-escalation (Steps 1 and 2) should be used in pregnant patients (1,5) as in non-pregnant patients.
  o Given the lack of evidence on the effectiveness of pharmacologic interventions in pregnant women, verbal interventions should be utilized whenever possible (1).
  o If medication is required, the minimal effective dose should be utilized: 1) for mild to moderate cases of agitation, oral or intramuscular diphenhydramine 25-50 mg may
suffice; 2) for severe agitation, haloperidol is the medication of choice, oral or parenteral 2-5 mg (4-5).

- Elderly Patients
  - Agitation in elderly patients 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 (4).
  - 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 in the elderly (6).
  - In agitation related to dementia first choice risperidone 0.5 mg, second choice aripiprazole 2.5 mg or quetiapine 25 mg; lower doses recommended in frail patients (7).

### Table 1: Medications Commonly Used in the Management of Acute Agitation (1, 4)

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Medication</th>
<th>Dosing</th>
<th>Side Effects/Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine</td>
<td>Alprazolam</td>
<td>Only available PO</td>
<td>• Paradoxical reactions can be seen in character-disordered patients and can worsen symptoms in the elderly</td>
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<td></td>
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<td>Initial dose is 0.5-4 mg/day</td>
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<td></td>
<td>Diazepam</td>
<td>PO, IM, IV</td>
<td>• Calming/sedating effect with rapid onset</td>
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<td></td>
<td>Start at 5 mg</td>
<td>• Use cautiously with elderly patients because of the long half-life</td>
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<tr>
<td></td>
<td>Lorazepam</td>
<td>PO, SL, IM, IV</td>
<td>• No active metabolites; therefore, there is a small risk of drug accumulation</td>
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<td></td>
<td></td>
<td>Start at 1 mg, moderate half-life (10-20 hr)</td>
<td>• Metabolized only via glucuronidation; therefore, it can be used in most patients with impaired hepatic function</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Drug of choice within this class due to moderately long half-life</td>
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<tr>
<td>Typical antipsychotics</td>
<td>Haloperidol</td>
<td>PO, IM, IV</td>
<td>• High-potency neuroleptic with favorable side-effect profile and cardiopulmonary safety.</td>
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<td></td>
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<td>‘IV formulation is not FDA approved</td>
<td>• IV form less likely to cause EPS</td>
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<td></td>
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<td></td>
<td>• ECG monitoring needed to assess torsades de pointes or QTc prolongation</td>
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<td></td>
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<td>• Risk of NMS increases in patients who are poorly hydrated, restrained, and kept in poorly aerated rooms while given large doses of antipsychotics</td>
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<td></td>
<td>• Frequent vital sign checks and testing for muscular rigidity are recommended</td>
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<td></td>
<td></td>
<td></td>
<td>• Can cause hypotension</td>
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<tr>
<td>Atypical antipsychotics</td>
<td>Risperidone</td>
<td>PO, orally disintegrating tablet (OTD)</td>
<td>• No IM form is available</td>
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<td></td>
<td></td>
<td>Starting dose 0.5-2 mg acutely</td>
<td>• Offers calming effect with treatment of underlying condition</td>
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<td></td>
<td></td>
<td></td>
<td>• Orthostatic hypotension with reflex tachycardia</td>
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<td></td>
<td>• Increased risk of stroke in the elderly with CVD</td>
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<tr>
<td></td>
<td>Olanzapine</td>
<td>PO, OTD, IM;</td>
<td>• Useful in patients with poor reaction to haloperidol</td>
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<td></td>
<td></td>
<td>Starting dose 2.5-5 mg, max 30 mg/24 hr with doses 2-4 hours apart</td>
<td>• Calming medication with treatment of underlying disorder</td>
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<td></td>
<td></td>
<td></td>
<td>• Avoid IM combination with lorazepam</td>
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<td></td>
<td></td>
<td>• Increased risk of stroke in the elderly with CVD</td>
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<td></td>
<td>Zaprasidone</td>
<td>PO, IM</td>
<td>• Use caution in patients with preexisting QT prolongation</td>
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<td></td>
<td>Max of 40 mg/24 hr of IM formulation</td>
<td>• Less sedating medication; therefore, good choice if desire tranquillization without sedation</td>
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<td></td>
<td>Aripiprazole</td>
<td>PO, OTD</td>
<td>• Akathisia risk</td>
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<td>Starting PO dose 5-10 mg, max 30 mg/day (currently IM formulation only for extended-release maintenance therapy)</td>
<td>• Less sedating than other medications</td>
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<td>• Increased risk of stroke in the elderly</td>
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<td>• Good choice for patients with QT interval prolongation</td>
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<td>Combinations</td>
<td>Haloperidol, lorazepam, diphenhydramine, or benztropine</td>
<td>5 mg IM, 2 mg IM, 50 mg IM, 1 mg IM</td>
<td>• Most commonly used in the acute setting</td>
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<td>• Young athletic men are at increased risk for dystonia</td>
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<td>• Akathisia must be considered if agitation increases after administration</td>
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References:


