Introduction

The DSM-5 defines psychomotor agitation as an excessive motor activity associated with a feeling of inner tension.\(^1\) Aggression may not be the key feature of agitation, but when severe, agitation can lead to violence.\(^2\) Acute agitation in patients with psychiatric disorders, such as schizophrenia and mood disorders, is common and can occur in any clinical setting, including emergency departments (ED), outpatient psychiatric settings, and inpatient hospitalizations.\(^3\) In the United States, around 1.7 million ED visits every year involve symptoms of agitation,\(^4\) and approximately 10% of patients treated by psychiatric emergency services are at risk of becoming agitated or violent.\(^5\)

In a survey among psychiatry residents, 36% reported being assaulted by patients during training; however, only a third of those residents reported being adequately trained in managing possibly violent patients.\(^6\) Educational activities are essential to improve the ability of psychiatrists to manage symptoms of agitation effectively and to reduce the risks of physical injury to themselves and their patients. In this article, we highlight the available recommendations regarding the assessment and management of agitation in psychiatry.

Etiology and Differential Diagnosis

The differential diagnosis of agitation is wide and includes both medical and psychiatric conditions.\(^7\) As a general rule, causes of agitation can be divided into three major categories: a general medical condition (infections, metabolic derangements, brain disorders, systemic organ failure, etc), substance (alcohol or other drugs of abuse) intoxication or withdrawal, or a primary psychiatric illness (psychosis, manic episode, agitated depression, anxiety disorder, personality disorder, etc).\(^8\)

To narrow the differential diagnosis, the initial steps in the assessment of agitation symptoms should include attempts to obtain vital signs, medical and psychiatric history, and general assessment of the patient’s behavior.\(^8\) In a patient without a known history of a psychiatric disorder, acute agitation should be considered to be secondary to a general medical condition until proven otherwise.\(^3\)
Aggression Risk Assessment

Avoiding escalation of agitation into violence relies on the identification of individuals at risk. Research into this area is limited; however, several variables, including a history of violent behaviors, nonvoluntary admission, extended length of hospital stay, impulsiveness, hostility, and aggressive speech are commonly associated with violence in psychiatric settings.\(^9\)

Several objective assessment scales have been developed to help clinicians estimate the risk of aggression or violence in agitated patients with psychiatric disorders.\(^3\) Generally, these tools evaluate a number of demographic, behavioral, and clinical variables to predict violent behaviors:

- **The Brøset Violence Checklist (BVC)**, a 6-item checklist that can be used to help predict imminent violent behavior within the next 24 hours in inpatient psychiatric settings.\(^10\)

- **The Historical, Clinical, Risk Management-20 (HCR-20)**, a 20-item assessment tool that can help predict the potential for aggression or violence in patients undergoing acute episodes of a major psychiatric disorder.\(^11\)

- **The McNiel-Binder Violence Screening Checklist (VSC)**, a 5-item scale designed to assess the risk for aggression or violence in patients with psychiatric disorders who were recently admitted to short-term inpatient units.\(^12\)

Management

Studies examining the best methods for management of agitation are limited. The available literature, which is largely based on recommendations and expert consensus, has classified four methods for managing symptoms of agitation: environmental modifications, verbal de-escalation techniques, physical restraints, and pharmacological interventions.\(^13\)

**Environmental Modifications.** Clinicians cannot de-escalate the situation if they don’t feel safe. The primary initial concern of management is to ensure the safety of the agitated patient, the medical team, and all other persons in the nearby environment.\(^14\) To decrease the likelihood of violence, several environmental modifications by healthcare providers are recommended; for example, removal of any items that could be potentially thrown, avoiding extremely loud or uncomfortable physical environment, and ensuring access to exits for both the patient and staff.\(^3,\(^15\)
**Verbal De-escalation.** Noncoercive techniques such as verbal de-escalation should be usually attempted before physical restraints or medications are used, especially in agitated but cooperative patients. The American Association for Emergency Psychiatry De-escalation Workgroup recommends that all medical staff should be trained in verbal de-escalation techniques. The workgroup has also outlined 10 key recommendations for verbal de-escalation:

1. Respect the patient’s and your personal space and maintain a safe distance
2. Avoid any direct or indirect provocation
3. Establish the identity of one person who will be verbally interacting with the patient
4. Choose simple and concise language and persistently repeat your message to the patient
5. Identify the needs, wants, and feelings of the patient
6. Be an active listener and show interest in the patient’s standpoint
7. Try to find points to agree about with the patient or agree to disagree
8. Reasonably and respectfully establish the working conditions (eg, violence cannot be tolerated) and gently teach the patient how to stay in control
9. Propose alternatives to violence and provide hope
10. To alleviate the traumatic nature of any involuntary intervention and to prevent future escalation, debrief the patient and staff after the intervention

If verbal de-escalation fails and agitation symptoms escalate to aggression, the use of physical restraints and medications may be considered; however, if only minor violent behaviors occur (eg, punching the wall), the medical staff may attempt to continue the verbal de-escalation while increasing the consequences of violating the working conditions.

**Physical Restraints.** The use of restraints or seclusion may have deleterious psychologic and physical effects on the patient and the medical team; therefore, restraints are never indicated for convenience or punishment. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) mandated in 2000 that physical restraints or seclusion can only be used in an emergency when other noncoercive attempts to manage agitation have failed and there is imminent risk of harm to a patient or others.

Physical restraints should be used carefully and humanely as a last resort. Ideally, the institution would have a protocol and training programs in place to guide the staff in how to properly apply physical restraints.
Once verbal de-escalation fails, the interviewer should leave the examination room and call for assistance from the restraint team. After the patient is physically restrained, efforts for verbal de-escalation should resume, and medications to calm the patient should be administered. It is also essential that all patients in restraint be monitored to prevent complications.

**Pharmacological Interventions.** Three classes of medications are generally used to manage acute agitation: benzodiazepines, first generation (typical) antipsychotics, and second generation (atypical) antipsychotics. Effective drugs are usually fast acting and can be given orally or intramuscularly (IM). Intravenous (IV) formulations might be difficult to administer because of the need for an IV line access.

1. **Benzodiazepines**
   Benzodiazepines modulate γ-aminobutyric acid (GABA) neurotransmission. They are recommended for agitation due to substance intoxication or withdrawal and when there is no specific treatment for the psychiatric disorder causing agitation (eg, personality disorder).

   - *Lorazepam* acts rapidly and has a short half-life. It can be administered IV or IM at 0.5 to 2 mg. In a double-blind prospective trial, lorazepam (2 mg IM) was as effective as haloperidol (5 mg IM) in reducing psychotic disruptive behavior and resulted in significantly less extrapyramidal symptoms.

   - *Midazolam* is usually given at 2.5 to 5 mg IV or IM. It has a significantly shorter time to onset of sedation than lorazepam (5 to 15 minutes versus 1 to 1.5 hours), but a shorter duration of action (1 to 2 hours versus 8 to 10 hours). In a randomized double-blind trial, midazolam (5 mg IV) provided a more rapid sedation of severely agitated patients than lorazepam (2 mg IM) or haloperidol (5 mg IM) with no difference in sedation efficacy.

   Patients who are agitated but cooperative may be given lorazepam or midazolam orally at the same doses mentioned above. Because of increased risk for respiratory depression, clinicians must be vigilant in monitoring the respiratory function of patients treated with benzodiazepines. Excessive sedation is another significant concern.

2. **First generation (typical) antipsychotics**
   Typical antipsychotics have been used as the mainstay treatment for agitation for many years. Due to its known efficacy, haloperidol has been typically used as first-line therapy and is usually the comparator drug against which new medications for agitation are evaluated.
Typical antipsychotics are believed to reduce agitation through inhibition of dopaminergic transmission.\textsuperscript{28}

- \textit{Haloperidol} can be given IM, IV or orally at 2.5 to 10 mg and its onset of action is within 15 to 60 minutes. The dose should be adjusted in the elderly.\textsuperscript{29}

- \textit{Droperidol} has a shorter half-life than Haloperidol and can be given IM or IV at 2.5 to 5 mg. Its onset of action ranges from 15 to 30 minutes.\textsuperscript{30}

The most common adverse effects of typical antipsychotics are extrapyramidal symptoms, which may be prophylactically prevented or treated with anticholinergics.\textsuperscript{22} Because of their potential to induce quinidine-like QT prolongation that may result in fatal cardiac arrhythmias (torsades de pointes), haloperidol and droperidol were given the so-called black box warnings from the FDA.\textsuperscript{31} If possible, typical antipsychotic drugs should be avoided in cases of alcohol or benzodiazepine withdrawal, seizures, and in pregnant patients.\textsuperscript{13}

Benzodiazepines and typical antipsychotics can be given as combination therapies to sedate highly agitated patients. Commonly used combinations include lorazepam (2 mg IV or IM) with haloperidol (5 mg IM or IV) or midazolam (5 mg IV or IM) with droperidol (5 mg IV or IM).\textsuperscript{32,33}

3. \textbf{Second generation (atypical) antipsychotics}

Experience with atypical antipsychotics to control agitation is growing. These drugs act on serotonergic and dopaminergic receptors and cause less extrapyramidal adverse effects than typical antipsychotics.\textsuperscript{34} Some consensus guidelines recommend atypical antipsychotics as first-line therapy for acute agitation in schizophrenia.\textsuperscript{8}

- \textit{Olanzapine} can be given IM (2.5 to 10 mg) or orally (5 to 20 mg) and has an onset of action of 15 to 45 minutes.\textsuperscript{35} Randomized double-blind trials have shown efficacy and safety of IM olanzapine in treating agitation due to acute mania\textsuperscript{36} or schizophrenia.\textsuperscript{37} Parenteral benzodiazepines should be avoided in patients receiving IM olanzapine because of increased risk for hypotension.\textsuperscript{14}

- \textit{Risperidone} is not available in a fast-acting IM formulation, but can be given orally (1 to 2 mg) and controls agitation secondary to psychosis rapidly.\textsuperscript{38}
• **Ziprasidone** is available in oral and IM formulations and is typically administered IM at 10 to 20 mg.\(^{14}\) Caution is warranted when given to patients with renal disease because its excipient cyclodextrin is cleared by renal filtration. Cyclodextrin accumulation may be toxic to the liver and kidneys.\(^{14}\)

Atypical antipsychotics also increase the risk for QT prolongation to some degree. Ziprasidone carries a higher risk than other typical and atypical antipsychotics and is contraindicated in patients with known history of QT prolongation or recent myocardial infarction.\(^{39}\)

**Conclusion**

Agitation is a common scenario in clinical psychiatry. To prevent violence, clinicians are encouraged to use noncoercive measures (environmental modifications, verbal de-escalation, and oral medications) to calm agitated patients. Physical restraints and rapid sedation with benzodiazepines or antipsychotics may be necessary in highly agitated or violent patients.

**References**


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