Management of Acute Agitation in the Adult Emergency Department

GENERAL INFORMATION

- This guideline describes the management of acute agitation in the Adult Emergency Department (ED). Refer to the separate guideline for managing acute agitation in the Pediatric ED. This guideline may be used for pediatric patients seen in the Adult ED, such as trauma patients, when appropriate.
- De-escalation should be attempted prior to medication management and physical restraint
- All attempts to avoid physical restraint should be considered prior to its use, and 2-point physical restraint is preferred to 4-point. If physical restraint is used, please follow current Departmental and UNMH guidelines AND try to minimize the time in physical restraint.
- Use preferred agents as listed below. Preferred agents show better clinical properties including quicker onset of action, greater effectiveness, and lower incidence of adverse effects. ¹
- Review prior medication administration (pre-hospital and in the ED) when selecting agents and dose.

ASSESSMENT AND MONITORING

- Use the Riker Sedation Agitation Scale (SAS) to determine the severity of agitation.
- RIKER Sedation-Agitation Scale (SAS)

#	Term	Descriptor
7	Dangerous Agitation	Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side-to-side
6	Very Agitated	Requiring restraints and frequent verbal reminding of limits, biting ETT
5	Agitated	Anxious or physically agitated, calms to verbal instructions
4	Calm and Cooperative	Calm, easily arousable, follows commands
3	Sedated	Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
2	Very Sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

- Patients receiving medication therapy should be placed on end-tidal pCO2 monitoring and cardiac telemetry.
- Document vital signs at least once an hour or more frequently, as clinically warranted.

SEVERELY AGITATED (SAS 7)

- Intravenous administration is preferred, when feasible. Unnecessary IM medication administration may increase agitation.
- Maximize the dosing of the first agent, allowing for the onset and effect of prior doses, before administering second agents.
- Adjust dosing for special populations (e.g., elderly, pre-hospital administered medications, etc.) as below.
- Use "Not-Preferred" agents have delayed onset of action and higher incidence of adverse effects and should only be used when preferred agents are unavailable such as due to medication shortage.
- Do not administer diphenhydramine as a prophylactic therapy for dystonic reaction.s²

	Medication	Dose	Soft Max	Onset ³	Duration	Patient Considerations
	Droperidol IM/IV	5 - 10 mg	20 mg	3-10 min	2-4 hours	EKG for doses greater than 20 mg after patient is calm/sedated ⁴
Preferred	Ketamine IM (100 mg/mL)	2 5 mg/kg 5 mg/kg 3-4	3-4 min	15-25 min (anesthetic effect)	Use appropriate concentration for route	
	Ketamine IV (10 mg/mL)	1 mg/kg	2 mg/kg	1 min	30-45 min	Emergence reactions may occur
	Midazolam IM	5 - 10 mg	30 mg	15 min	2 hours	Delayed onset IM
	Midazolam IV	5 mg		1-5 min	1-2 hours	Hypotension with larger doses
Secondary Options	Olanzapine IM/IV	10 mg	30 mg (including PO doses)	IM: 15 min IV: 5-10 min	15- 45 min (time to peak)	Separate from IV BZD by 1-2 hours to avoid excessive sedation / cardiorespiratory depression ⁵
Not	Haloperidol IM/IV	5 mg	10 mg	IM: 15 min IV: 20 min	2 hours	Greatest risk for EKG changes
Preferred	Lorazepam IM/IV	4 mg	20 mg	IM: 20-30 min IV: 15-20 min	6-8 hours	Erratic IM absorption

IM Ketamine Dosing^{6,7}

Use rounded dosing for ease of IM administration:

Range	Dose	Volume (100 mg/mL)
50-59 kg	150 mg	1.5 mL
60-79 kg	200 mg	2 mL
80-99 kg	250 mg	2.5 mL
≥100 kg	300 mg	3 mL

Special Populations

- Consider alcohol withdrawal as a concomitant or primary cause of agitation. Treat alcohol withdrawal using the phenobarbital/CIWA protocols first.
- <u>Trauma</u>: Consider pain management and the urgency for diagnostic studies prior to administering medications for agitation. Please also consider trauma as one of the possible (likely) factors in the cause of agitation.
- IM Midazolam Prehospital:
 - o Evaluate the dose and time from when the dose(s) were administered.
 - If the dose is within a range to control the agitation and the expected onset is likely to have time to act and the patient is still agitated, consider starting therapy from the "preferred" group.
 - If the dose is suboptimal or the therapy is unlikely to have taken affect, consider a reduced dose of a medication from the "preferred" group.
- Older Patients (65+ years)8:

- Reduce doses by ~50% in older patients (≥ 65 years of age).
- Prioritize droperidol or olanzapine in this population; other agents, however, may be appropriate given the clinical situation.
 Avoid benzodiazepines, if possible, given the risk for delirium, accumulation, and association with worse outcomes.

Combination Therapy

- Avoid combination therapy as a default response; combination therapy has significantly higher risk of adverse effects.
- Do not use Diphenhydramine + Haloperidol + Lorazepam ("B52"): Evidence suggests poorer outcomes and delayed agitation control with this combination⁹
- IV/IM Olanzapine + IV Benzodiazepine: There may be an increased risk of adverse effects with this combination, especially within 1 hour of concomitant administration. Monitor for adverse effects (excessive sedation / cardiorespiratory depression).
- Droperidol + Midazolam: Consider addition of midazolam as adjunct only after reaching the maximum dose of droperidol.^{10–13}

MODERATE AGITATION (SAS 6)

- Do not use ketamine for moderate agitation.
- IV administration is preferred over IM therapy for moderate agitation if parenteral administration is required.
- Preferred agents are similar to those for severe agitation. Smaller doses will generally be sufficient.
- Use a patients home medication regiment when patients can tolerate oral therapy.

MILD AGITATION (SAS 5)

- Patients with mild agitation should be managed with oral therapy, if necessary.
- Administer home medication therapy, when possible.

REFERENCES

- Hatten BW, Bonney C, Dunne RB, et al. ACEP Task Force Report on Hyperactive Delirium with Severe Agitation in Emergency Settings. Accessed January 31, 2023. https://www.acep.org/globalassets/new-pdfs/education/acep-task-force-report-on-hyperactive-delirium-final.pdf
- 2. Jeffers T, Darling B, Edwards C, Vadiei N. Efficacy of Combination Haloperidol, Lorazepam, and Diphenhydramine vs. Combination Haloperidol and Lorazepam in the Treatment of Acute Agitation: A Multicenter Retrospective Cohort Study. *J Emerg Med*. 2022;62(4):516-523. doi:10.1016/j.jemermed.2022.01.009
- 3. Lexicomp. Accessed January 31, 2023. https://online.lexi.com/lco/action/home
- 4. Cole JB, Lee SC, Martel ML, Smith SW, Biros MH, Miner JR. The Incidence of QT Prolongation and Torsades des Pointes in Patients Receiving Droperidol in an Urban Emergency Department. West J Emerg Med. 2020;21(4):728-736. doi:10.5811/westjem.2020.4.47036
- 5. Williams AM. Coadministration of intramuscular olanzapine and benzodiazepines in agitated patients with mental illness. *Ment Health Clin*. 2018;8(5):208-213. doi:10.9740/mhc.2018.09.208
- 6. Li M, Martinelli AN, Oliver WD, Wilkerson RG. Evaluation of Ketamine for Excited Delirium Syndrome in the Adult Emergency Department. *J Emerg Med*. Published online November 14, 2019:S0736-4679(19)30802-9. doi:10.1016/j.jemermed.2019.09.019

- 7. O'Brien ME, Fuh L, Raja AS, White BA, Yun BJ, Hayes BD. Reduced-dose intramuscular ketamine for severe agitation in an academic emergency department. *Clin Toxicol (Phila)*. 2020;58(4):294-298. doi:10.1080/15563650.2019.1643468
- 8. Shenvi C, Kennedy M, Austin CA, Wilson MP, Gerardi M, Schneider S. Managing Delirium and Agitation in the Older Emergency Department Patient: The ADEPT Tool. *Annals of Emergency Medicine*. 2020;75(2):136-145. doi:10.1016/j.annemergmed.2019.07.023
- 9. Thiemann P, Roy D, Huecker M, et al. Prospective study of haloperidol plus lorazepam versus droperidol plus midazolam for the treatment of acute agitation in the emergency department. *Am J Emerg Med*. 2022;55:76-81. doi:10.1016/j.ajem.2022.02.042
- 10. Yap CYL, Taylor DM, Knott JC, et al. Intravenous midazolam-droperidol combination, droperidol or olanzapine monotherapy for methamphetamine-related acute agitation: subgroup analysis of a randomized controlled trial. *Addiction*. 2017;112(7):1262-1269. doi:10.1111/add.13780
- 11. Chan EW, Taylor DM, Knott JC, Phillips GA, Castle DJ, Kong DCM. Intravenous droperidol or olanzapine as an adjunct to midazolam for the acutely agitated patient: a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Ann Emerg Med*. 2013;61(1):72-81. doi:10.1016/j.annemergmed.2012.07.118
- 12. Taylor DM, Yap CYL, Knott JC, et al. Midazolam-Droperidol, Droperidol, or Olanzapine for Acute Agitation: A Randomized Clinical Trial. *Ann Emerg Med*. 2017;69(3):318-326.e1. doi:10.1016/j.annemergmed.2016.07.033
- 13. Isbister GK, Calver LA, Page CB, Stokes B, Bryant JL, Downes MA. Randomized controlled trial of intramuscular droperidol versus midazolam for violence and acute behavioral disturbance: the DORM study. *Ann Emerg Med.* 2010;56(4):392-401.e1. doi:10.1016/j.annemergmed.2010.05.037