

Emergency Department Clinical Guidelines

ED/CCT Agitation Guidelines

Clinical Context and Purpose

To establish an evidence-based guideline for evaluating and managing acutely agitated patients in an efficient manner with the aim of achieving and maintaining the highest level of quality and safety for patients and staff.

Background

Acute agitation is a common emergency department presentation. In managing the acutely agitated patient, safety, for both the patient and staff, is the primary goal while facilitating efficient and thorough evaluation.

Verbal de-escalation:

Verbal de-escalation is important even in the critically ill patient, but the time spent on this must be balanced with the potential harm of delaying care. In the critically ill this step should be utilized if a patient is cooperative making this generally safer than pharmacological management; however, in cases when emergent and/or urgent facilitation of care is needed, quickly moving towards immediate pharmacological management is reasonable. For patients who have been assessed to be non-critical, additional time and care can be utilized at the EP's discretion where it is judged to be safe. Pharmacological management for agitation has its own potential for harm and could delay the overall disposition of a patient, while delayed care could additionally be harmful, the risks and benefits of each action must be carefully weighed.

Whenever **physical restraints** are employed, follow KCHC hospital policy and procedures for appropriateness of use, monitoring and reassessment, and documentation guidelines.

Medication choices:

There are a large number of potential agents that can be used for the pharmacological management of acute agitation. Single agents may be used rather than combination medications though combination therapy does have specific benefits and a potential role in management of the agitated patient. Benefits of single agents include the following:

1. More predictable medication onset and half-life
2. Allows for better ease of providing additional medications for additional effects
3. Reduces medication interactions
4. Reduces potential over-sedation
5. Makes dosing and administration simpler

For the acutely agitated patient there are three main drug classes that are utilized from an intramuscular route of administration; benzodiazepines, antipsychotics, and ketamine. Of note there are black box warnings for antipsychotics administered via the IV route, but both ketamine and benzodiazepines can be given through the IV route. For intravenous administration other

Emergency Department Clinical Guidelines

medications such as etomidate and propofol can be considered in the appropriate clinical setting (see flow sheet).

Benzodiazepines:

The advantage of benzodiazepines is multifactorial. Benzodiazepines are pure GABA-A receptor agonists, which increase channel opening frequency, increasing chloride influx and leading to reduced neuronal excitability. This pure single receptor action of benzodiazepines is highly advantageous as they are less likely to cause other side-effects or interactions with other medications, substances, or exposures. Further, benzodiazepines are the preferred treatment for multiple common causes of acute agitation in the emergency department including, sympathomimetic overdose, seizures, PCP intoxication, and alcohol withdrawal, among other. Benzodiazepines also have a highly preferential side-effect profile, they are unlikely to cause acute psychosis, they have minimal effects on heart rate or blood pressure, and other than a relative contraindication in elderly populations, the only major risk factor is respiratory depression, but this may occur in cases of polysubstance exposure such as with opioids, ethanol, or other sedatives such as antipsychotics. When choosing a benzodiazepine, there are three main options that are available in an IV/IM formulation: midazolam, lorazepam, and diazepam.

Midazolam is a preferred agent due to its fast absorption through the IM route (5-10 minutes), with a short duration of effect compared with other benzodiazepines. Lorazepam is another benzodiazepine that has relatively good absorption via the IM route (15-30 minutes), and has a longer duration of effect than midazolam, 14h vs 3h. Diazepam, the third medication choice has an even longer half-life of over 30 hours, has an unreliable onset of action as an IM medication, but has a rapid onset of action when given IV, with a peak effect of less than 5 minutes, with a long duration of effect with active metabolites. Midazolam has a similar rapid onset to peak effect, but has a much shorter duration of effect.

Antipsychotics:

The antipsychotic agents are predominantly anti D2 agents. However, these medications have a number of other receptors that they interact with including but not limited to other dopaminergic receptors and HAM (histamine, adrenergic, and muscarinic receptors). Furthermore, blocking of D2 receptors can cause a number of symptoms including EPS (extra-pyramidal side effects), and NMS (neuroleptic malignant syndrome, though usually not due to acute administration). Many patients are chronically on these medications or even on depo preparations. Haldol in doses of 2.5mg or 5mg are mainstays of treatment for acutely psychotic and agitated patients. However, haloperidol's time of onset is about an hour or longer, and can last for >8 hours. Haloperidol's long history of use has proven it to be extremely safe in the ED and it is widely available. Alternative antipsychotics are olanzapine which has been shown to generally be safe with a quicker onset, <30 minutes, and shorter half-life. All antipsychotics can be given PO, but carry black box warnings for IV administration due to QTc prolongation, though multiple studies have shown that QTc prolongation to the point of causing torsades de pointes is rare. Generally speaking use antipsychotics in patients with underlying psychiatric illness and non-compliance with meds or in the elderly (to avoid risk of benzodiazepine-induced delirium). When using antipsychotics for sedation, olanzapine has more rapid onset, but haloperidol can be considered another safe alternative. For advanced age, or frail appearance the IM doses are reduced. The medications can be given PO as well in cooperative patients, but their onset is slower.

Emergency Department Clinical Guidelines

Ketamine:

Ketamine is becoming a more common choice for managing acute agitation in both the emergency department and in the pre-hospital setting. Ketamine is an NMDA receptor antagonist, and has analgesic, amnesic, and sedation effects. Ketamine has been shown to cause both hypo- and hypertension, and can potentially cause respiratory depression and laryngospasm. Due to Ketamine's favorable time of onset, ability for patients to generally protect their airway with spontaneous ventilation and relatively short half-life many have proposed and explored its use for managing the acutely agitated patient. Its time of onset should be heavily weighed against its risk profile. Further ketamine has a number of contraindications, hypertension, other conditions causing elevated ICP such as ICHs, emergence reactions, worsening of psychiatric symptoms or precipitating psychiatric symptoms especially with lower doses. It is reasonable to consider using ketamine in the setting where there is a need to intubate the patient and either IV access is not possible or there is a contraindication to propofol or etomidate. If ketamine is used in settings that an intubation isn't planned, the patient must be very closely monitored and kept in the CCT. If ketamine is being used as an IM medication the recommended dose is 3-5mg/kg, which can be dosed with the 500mg/10ml and the 500mg/5ml formulations, and IV can be dosed as 1-2mg/kg.

Combination Therapy:

The evidence of combination therapy is limited, and generally the comparators/control are antipsychotics alone, rather than compared to benzodiazepines alone. However, it is reasonable to consider using combination therapies when there is a concern that a patient is more likely to be over sedated by a benzodiazepine, when a longer period of sedation is required, there is a concern for a psychiatric component to the patient's agitation, or to avoid benzodiazepine precipitated delirium in geriatric patients. Of note there is an FDA black box warning for combining olanzapine with midazolam. Extra precaution should be used when using a combination of drugs for managing the acutely agitated patient. One commonly used combination that is reasonable to use is midazolam and haloperidol taking advantage of the faster onset of midazolam and longer action of haloperidol.

Post Pharmacological Management Care:

After an acutely agitated patient is managed with pharmacological agents, it is extremely important to start and/or continue evaluating for the causes of their agitation and the reason necessitating their presentation to the emergency department, all while ensuring patient and staff safety. All patients should be placed in a gown, have their vital signs measured including a point of care dextrose level, an ECG should be obtained, IV access should be established with labs drawn for an appropriate workup for acute agitation, and indicated imaging should be performed. Many patients presenting for agitation will require a psychiatric evaluation and will potentially require a psychiatric admission, if labs are indicated it is often expeditious to send labs required for a CPEP transfer, including but not necessarily limited to antiepileptic drugs (if a patient is believed to be on medications with levels that are available via the laboratory), ethanol, APAP, and salicylates. A serum ethanol concentration can also be useful in identifying a potential cause for agitation, and to better understand the possible time course for the patient if their agitation and presentation is due to alcohol intoxication. All patients who are managed

Emergency Department Clinical Guidelines

pharmacologically should be placed on a monitor, preferably equipped with end tidal CO₂ detection via a nasal cannula.

Any patient to be cleared to the main adult emergency department should be adequately monitored, not requiring any airway maneuvers, or painful stimuli to achieve spontaneous ventilation or airway protection; they should be hemodynamically stable, and no longer a threat to themselves or others. If any advanced airway maneuvers are necessary (including but not limited to a jaw thrust, airway positioning, sternal rub, or other means of improving airway protection and respiratory status), then the patient should be kept in the CCT and not cleared to the main adult emergency department. If a patient is hypoxic, patients can be placed on oxygen, but oxygen therapy is not routinely indicated during the care of the agitated patient, (hypoxia should appropriately be evaluated). One potential cause for agitation is hypoxia; if a patient is hypoxic, but to the treating physician's determination has adequate respirations and is protecting their airway without any obstruction, then the patient should be evaluated for the cause of hypoxia, and not simply placed on oxygen. Some patients are hypoxic due to inadequate ventilation, and as such oxygenation alone may not address the underlying problem. End tidal CO₂, should be used to monitor the patient with poor ventilation.

Documentation:

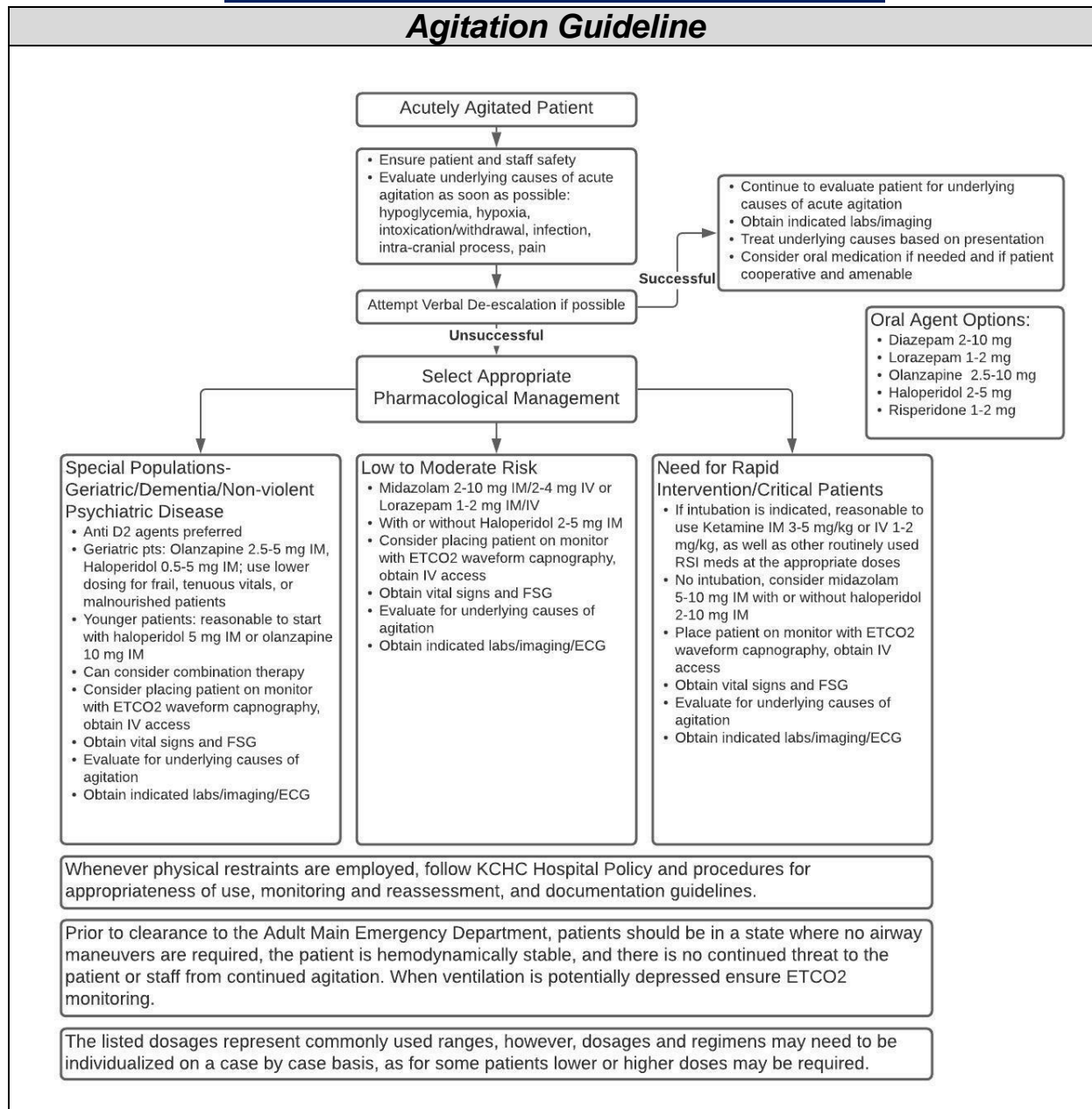
For patients being cleared to the Main Adult emergency department from CCT, a progress note should address all steps the CCT team took to manage the patient's agitation, the rationale for use of pharmacological agents, and a reasonable differential and plan for the patient indicating appropriateness for continued evaluation in the Main Adult emergency department.

Handoffs:

This is particularly important for patients being cleared from the CCT to the Main Adult ED. There should be an adequate verbal nursing and physician handoff per the CCT Clearance Guidelines. Hand-offs can be given to the attendings on both sides of the adult ED if the patient hasn't been placed already. If the patient has already been placed in a bed, the handoff should be given to a provider if assigned or to the attending on that side of the ED. In regards to bed placement, the patients require monitoring, so they should not be brought over to the main ED until a monitored bed is available. Nursing should additionally give their own handoff.

Emergency Department Clinical Guidelines

Agitation Guideline



Resources/References

1. O'Connor L, Rebesco M, Robinson C, et al. Outcomes of Prehospital Chemical Sedation With Ketamine Versus Haloperidol and Benzodiazepine or Physical Restraint Only. *Prehospital Emerg Care*. 2019;23(2):201-209. doi:10.1080/10903127.2018.1501445
2. Breier A, Meehan K, Birkett M, et al. A double-blind, placebo-controlled dose-response comparison of intramuscular olanzapine and haloperidol in the treatment of acute agitation in schizophrenia. *Arch Gen Psychiatry*. 2002;59(5):441-448. doi:10.1001/archpsyc.59.5.441

Emergency Department Clinical Guidelines

3. Burnett AM, Peterson BK, Stellpflug SJ, et al. The association between ketamine given for prehospital chemical restraint with intubation and hospital admission. *Am J Emerg Med.* 2015;33(1):76-79. doi:10.1016/j.ajem.2014.10.016
4. Korczak V, Kirby A, Gunja N. Chemical agents for the sedation of agitated patients in the ED: a systematic review. *Am J Emerg Med.* 2016;34(12):2426-2431. doi:10.1016/j.ajem.2016.09.025
5. Barbic D, Andolfatto G, Grunau B, et al. Rapid agitation control with ketamine in the emergency department (RACKED): A randomized controlled trial protocol. *Trials.* 2018;19(1):1-13. doi:10.1186/s13063-018-2992-x
6. Lin J, Figuerado Y, Montgomery A, et al. Efficacy of ketamine for initial control of acute agitation in the emergency department: A randomized study. *Am J Emerg Med.* 2020;(xxxx). doi:10.1016/j.ajem.2020.04.013
8. Richmond JS, Berlin JS, Fishkind AB, et al. Verbal de-escalation of the agitated patient: Consensus statement of the American Association for emergency psychiatry project BETA De-escalation workgroup. *West J Emerg Med.* 2012;13(1):17-25. doi:10.5811/westjem.2011.9.6864
9. Miner JR, Klein LR, Cole JB, Driver BE, Moore JC, Ho JD. The Characteristics and Prevalence of Agitation in an Urban County Emergency Department. *Ann Emerg Med.* 2018;72(4):361-370. doi:10.1016/j.annemergmed.2018.06.001
10. Sullivan N, Chen C, Siegel R, et al. Ketamine for emergency sedation of agitated patients: A systematic review and meta-analysis. *Am J Emerg Med.* 2020;38(3):655-661. doi:10.1016/j.ajem.2019.11.007
11. Schneider A, Mullinax S, Hall N, Acheson A, Oliveto AH, Wilson MP. Intramuscular medication for treatment of agitation in the emergency department: A systematic review of controlled trials. *Am J Emerg Med.* 2020. doi:10.1016/j.ajem.2020.07.013
12. 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
13. Riddell J, Tran A, Bengiamin R, Hendey GW, Armenian P. Ketamine as a first-line treatment for severely agitated emergency department patients. *Am J Emerg Med.* 2017;35(7):1000-1004. doi:10.1016/j.ajem.2017.02.026
14. Klein LR, Driver BE, Miner JR, et al. Intramuscular Midazolam, Olanzapine, Ziprasidone, or Haloperidol for Treating Acute Agitation in the Emergency Department. *Ann Emerg Med.* 2018;72(4):374-385. doi:10.1016/j.annemergmed.2018.04.027