Chemical Restraint for Agitated Delirium

IHS ECHO
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Objectives

01

Understand that this group of patients is at extremely high risk for morbidity / mortality

02

Review approach to the severely agitated patient

03

Review Drugs of choice for agitated delirium and tailoring the medication to the presentation if possible. Discourage the use of a single cocktail for every situation

04

Review 2021 LLSA article recommendations for rapid sedation

Disclosures

NO
CONFLICTS
OF INTEREST
TO DISCLOSE

What's wrong with this picture?

What is "Samsoniting"?

- "That patient's gonna end up like George Floyd"
- What are the top priorities?
- What tools can you use?

This is how people die in restraints: 36 - 86% mortality in police custody

General approach to severe agitation

- For True ExDS (the severely agitated pt) - Mortality = 8.3 - 16.5%
- Treat this like the medical emergency that it is. Patients should not be placed in a room far far away from monitors and nurses stations. High risk of resp arrest / aspiration / dysrhythmias
- Careful monitoring - think of this as a procedural sedation (which it is.... The procedure is control of agitation)
- Be ready to intubate - uncommon but possible

Degrees of Agitation:

Importance of De-escalation

Use a tiered approach, but gain control of the situation quickly

Agitated but cooperative: have someone sit and talk with pt. If still requiring more intervention, try an oral dose of lorazepam or antipsychotic if appropriate.

Disruptive without danger

agitated intoxicated pt. that can be briefly engaged but can't be redirected. Chemical restraint is indicated.

Be very careful not to over-sedate - patients need monitoring as with procedural sedation

Ativan should be avoided

Severely Agitated: includes ExDS (excited delirium)

Physical restraints

- Topic worthy of a whole presentation
- ACEP 2020: “Patient restraint should be considered when a careful assessment establishes that the patient is a danger to self or others by virtue of a medical or psychiatric condition and when verbal de-escalation is not successful.”
- Make it a team sport: One person per limb
- Protect the patient and protect staff: Ensure no dangerous restraint holds (think George Floyd…)
- Cross tie the limbs and tie down to a fixed location on the gurney
- If someone needs to be tied down, they need sedation

Broad DDX

Broad DDX	Maintain a broad DDX, don't jump to conclusions or make assumptions - there are lots of medical causes for agitation
Toxidromes	Look for toxidromes - sympathomimetic, anticholinergic, serotonin syndrome,
Be thorough	Perform a thorough evaluation - undress completely
Rhabdo	Remember rhabdomyolysis

DDX

Dysregulated central dopamine transporter function, overstimulation of NMDA / Glutamate, catecholamine surge

Remember to maintain a broad DDX

Toxic, metabolic, endocrine, infectious, psychiatric, often multiple

Source: UptoDate

TABLE 1. Potential Underlying Etiologies of Excited Delirium

SYSTEM	ETIOLOGY
Metabolic/ Endocrine	• Electrolyte abnormalities • Hepatic encephalopathy • Hypercarbia • Hyperglycemia • Hypoglycemia • Hypoxia • Thyrotoxicosis • Uremia
Neurologic	• Dementia • Head injury • Paraneoplastic anti-NMDAR encephalitis • Post-ictal state • Seizure
Psychiatric	• Acute psychosis • Mania • Medication stoppage • Personality disorder • Schizophrenia
Infectious/ Inflammatory	• Autoimmune encephalitis • Herpes encephalitis • Meningitis • Sepsis
Toxicologic	• Alcohol • Amphetamines • Cocaine • Neuroleptic Malignant Syndrome • Phencyclidine (PCP) • Polypharmacy • Serotonin Syndrome • Synthetic cannabinoids • Synthetic cathinones

Severe Agitation

Agitated or “excited” delirium = the most severe end of the spectrum

May be uncontrollably violent and are more likely to have a dangerous condition.

Wildly delirious and difficult to assess: combative and uncooperative.

Often struggle with extraordinary strength despite futility without tiring.

Tacycardia, hyperthermia and diaphoresis

High risk of sudden death. respiratory depression, acidosis, hyperthermia, catecholamine induced dysrhythmias

Need immediate control

Higher risk patients: male, black, overweight, young

Think about toxidromes - sympathomimetic - cocaine, meth, mdma, pcp, synthetic cannabinoids

DOC: midazolam and ketamine

Avoid haldol, benadryl

Tailor the therapy

- Don’t give meds that could make the situation worse
  - Ask: What am I treating?
  - Avoid “cocktails” especially the B-52
  - Avoid polypharmacy
  - Avoid benadryl
  - Avoid dirty drugs
- Tailor the treatment to the condition if you have a suspicion as to the underlying cause - pick the right drug for the right receptor

Why not just “5+2” for everyone? Or a B-52?

Both Haldol and Ativan have slower onset than other drugs in same class

Prolonged duration - prolonged sedation

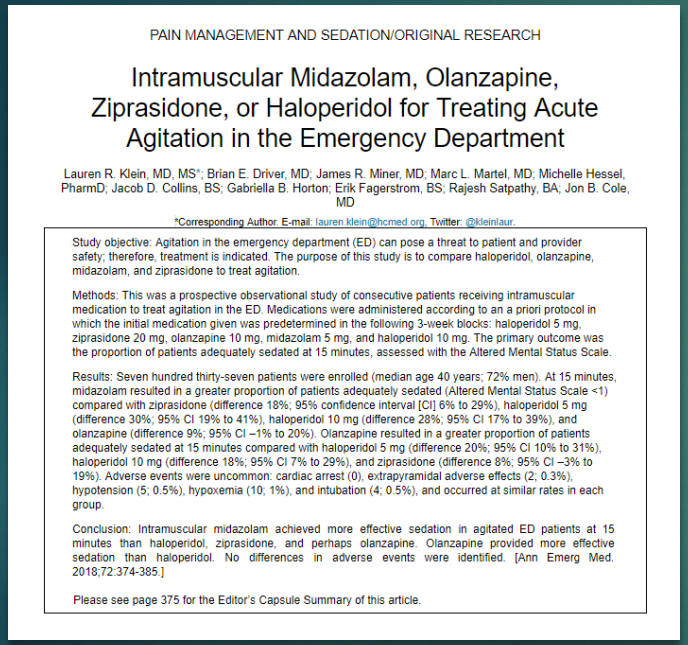
Variable effects - some people take a little, some people take a lot - narrow therapeutic window

Additive Qt prolongation

Oversedation - additive CNS depression - higher risk for complications

Ativan is a high risk medication when given with alcohol

Midazolam IM: when you need something fast and consistent



PAIN MANAGEMENT AND SEDATION/ORIGINAL RESEARCH

Intramuscular Midazolam, Olanzapine, Ziprasidone, or Haloperidol for Treating Acute Agitation in the Emergency Department

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Study objective: Agitation in the emergency department (ED) can pose a threat to patient and provider safety; therefore, treatment is indicated. The purpose of this study is to compare haloperidol, olanzapine, midazolam, and ziprasidone to treat agitation.

Methods: This was a prospective observational study of consecutive patients receiving intramuscular medication to treat agitation in the ED. Medications were administered according to an a priori protocol in which the initial medication given was predetermined in the following 3-week blocks: haloperidol 5 mg, ziprasidone 20 mg, olanzapine 10 mg, midazolam 5 mg, and haloperidol 10 mg. The primary outcome was the proportion of patients adequately sedated at 15 minutes, assessed with the Altered Mental Status Scale.

Results: Seven hundred thirty-seven patients were enrolled (median age 40 years; 72% men). At 15 minutes, midazolam resulted in a greater proportion of patients adequately sedated (Altered Mental Status Scale <1) compared with ziprasidone (difference 18%; 95% confidence interval [CI] 6% to 29%), haloperidol 5 mg (difference 30%; 95% CI 19% to 41%), haloperidol 10 mg (difference 28%; 95% CI 17% to 39%), and olanzapine (difference 9%; 95% CI –1% to 20%). Olanzapine resulted in a greater proportion of patients adequately sedated at 15 minutes compared with haloperidol 5 mg (difference 20%; 95% CI 10% to 31%), haloperidol 10 mg (difference 18%; 95% CI 7% to 29%), and ziprasidone (difference 8%; 95% CI –3% to 19%). Adverse events were uncommon: cardiac arrest (0), extrapyramidal adverse effects (2; 0.3%), hypotension (5; 0.5%), hypoxemia (10; 1%), and intubation (4; 0.5%), and occurred at similar rates in each group.

Conclusion: Intramuscular midazolam achieved more effective sedation in agitated ED patients at 15 minutes than haloperidol, ziprasidone, and perhaps olanzapine. Olanzapine provided more effective sedation than haloperidol. No differences in adverse events were identified. [Ann Emerg Med. 2018;72:374-385.]

Please see page 375 for the Editor's Capsule Summary of this article.

- 2021 LLSA : 737 patients comparing multiple medications for the rapidity of adequate sedation
- IM midazolam more effective sedation in agitated ED patients at 15 minutes than haloperidol, ziprasidone
- Olanzapine provided more effective sedation than haloperidol
- No differences in adverse events were identified

Midazolam IM

- First-line treatment choice for undifferentiated severe agitation. Preferred over Haldol.
- Rapid onset, short-acting, predictable pharmacokinetic profile IV, IO, IM, IN or PO.
- Duration of action favorable for acute intoxication due to sympathomimetics, because its time of effect is similar to cocaine.
- Dosing in adults is 5 mg IV/intraosseous/IM/intranasal
- Onset 3 min IV/intraosseous, 5 min IM, and 15 min intranasal
- Repeat prn q 5 to 10 min.
- Duration of action 30-120 min, although hepatic dysfunction may vary the duration of action.

Drugs of Choice - crank up the GABA

Undifferentiated Initial take down:

- <u>IM meds</u>
  - Midazolam IM 4-5mg, more rapid and predictable absorption
  - Droperidol - 5-10mg IM
  - Ketamine - 4mg/kg IM
  - Haldol (if you don't have droperidol) - 5mg IM (or more)
- Excited Delirium: midazolam, ketamine

Target your approach:

- Psychiatric (bipolar, psychosis, alzheimer's agitation): antipsychotic Olanzapine 10 mg IM/dissolving PO wafer, Haldol for injection
- Sympathomimetic (meth, cocaine, synthetic marijuana, etc): Benzos
- Alcohol: droperidol. Use benzos with caution
- Alcohol withdrawal: phenobarbital. Do not use haldol, droperidol or benadryl

ACEP

LEVEL OF AGITATION	FIRST-CHOICE DRUG, DOSE, ROUTE	ALTERNATIVE OR ADJUNCT DRUG
Mild	Lorazepam 1–2 mg sublingual	Oral antipsychotic that has previously been effective for that patient
Moderate	Midazolam 2–5 mg IM	Haloperidol 5–10 mg IM
Severe	Ketamine 5 mg/kg IM	Haloperidol 10 mg IM and midazolam 10 mg IM

Recommend substituting droperidol for haldol at sites that have this on formulary

https://www.acepnow.com/article/a-5-step-approach-to-the-agitated-patient/?singlepage=1

Cautions

Use Benzos in the hyperthermic, hypertensive, tachycardic patient. Why? Sympathomimetic toxidromes.

Once patients sedated, they need to be monitored like a procedural sedation patient

Ketamine can cause tachycardia and hypertension.

Benzodiazepines are pharmacologically pure and preferred by toxicologists.

Droperidol: sedates more rapidly and more cleanly than haldol or lorazepam either separately or in combination

Lorazepam - need redosing 5x more than w/ droperidol, dose stacking due to slow CNS penetration - sedation then 6-8 - 24 hours at higher doses

Avoid Polypharmacy: Haldol alone not a great sedative, thus frequent addition of lorazepam

Can you give Haldol IV? Yes.

MYTH: Haldol can only be given IM

Facts: Haldol has been safely IV used for decades in emergency medicine

- Product insert states that the only indications for haloperidol use are treatment of schizophrenia and of Tourette's Disorder.
- The product insert recommends an initial IM dosage from 2 to 5 mg for controlling acutely agitated schizophrenic patients.
- No mention of using it for acute agitation for other conditions - so you are already using it "off-label"
- **IM is not preferred - slower and more unpredictable absorption**

MYTH: you can't give Haldol IV because it's "off label"

Facts: You use off-label medications every day.

- Who has used gabapentin for neuropathy?
- What's it mean to be "labeled"?
- Despite the lack of formal FDA approval, intravenous haloperidol is commonly used "off label"
- Off-label use of medications is a common practice and is medically appropriate. A formal statement from the FDA noted that "unlabeled uses [of medications] may be appropriate and rational in certain circumstances."
- Court decisions have also held that off-label use of medications can be both legal and medically appropriate.

EPM:J Sulllivan https://epmonthly.com/article/final-analysis-off-label-use-of-haldol-meets-the-standard/?utm_source=TrendMD&utm_medium=cpc&utm_campaign=EPMonthly_TrendMD_0


droperidol

Resources / works cited

- EPM:J Sulllivan https://epmonthly.com/article/final-analysis-off-label-use-of-haldol-meets-the-standard/?utm_source=TrendMD&utm_medium=cpc&utm_campaign=EPMonthly_TrendMD_0
- Gonin, Beysard. Yersin. "Excited Delirium: A Systematic Review. Acad Emerg Med Oct 2017, Vol 25, Issue 5
  - https://www.acepnow.com/article/a-5-step-approach-to-the-agitated-patient/?singlepage=1
- ACEP Policy on the Use of Patient Restraints, Feb 2020: use-of-patient-restraints.pdf (acep.org)
- EMRAP October 2018, Vol 18, Issue 10; Annals of Emergency Medicine: Restraining the Agitated Patient Jess Mason MD, Billy Mallon MD and Chris Colwell MD
- Cochrane Database Syst Rev . 2016 Dec 15;12(12):CD002830. doi: 10.1002/14651858.CD002830.pub3.
- Droperidol for psychosis-induced aggression or agitation, Mariam A Khokhar 1, John Rathbone 2
  - 2018 Oct;72(4):374-385. doi: 10.1016/j.annemergmed.2018.04.027. Epub 2018 Jun 7. Intramuscular Midazolam, Olanzapine, Ziprasidone, or Haloperidol for Treating Acute Agitation in the Emergency Department. Lauren R Klein 1,et al.