Chemical Restraint

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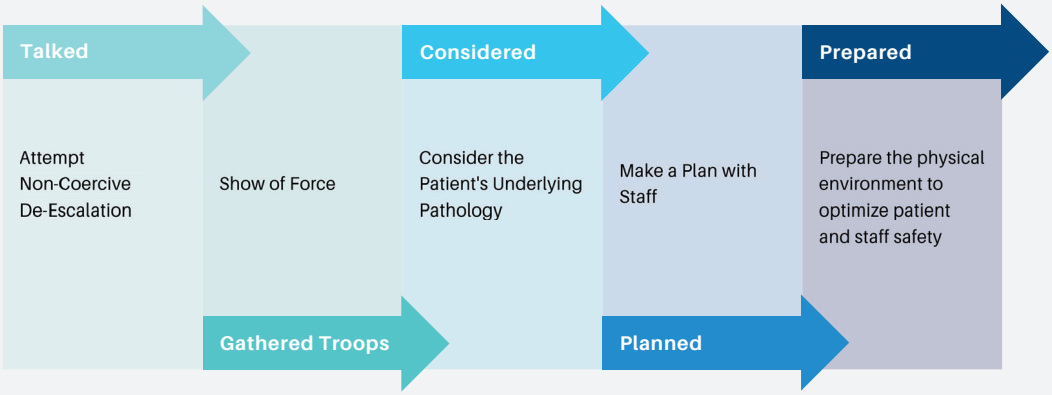
Lecture Objectives

1 **PREPARATION**	Describe the basic elements of non-coercive de-escalation
2 **PHARMACOLOGIC OPTIONS**	List IM medications commonly used in chemical restraint
3 **LITERATURE**	Synthesize the available literature on chemical restraint agents
4 **SPECIAL POPULATIONS**	Describe special considerations in special populations
5 **OTHER CONSIDERATIONS**	Discuss the legal, ethical, and psychological effects of restraint

BEFORE YOU GET TO CHEMICAL RESTRAINT, WE ASSUME YOU HAVE.....



Pharmacologic Options

IM Route

TYPICAL ANTIPSYCHOTICS	ATYPICAL ANTIPSYCHOTICS	BENZODIAZEPINES	NEW AGENTS	ADJUNCTS
Haloperidol	Ziprasidone	Lorazepam	Ketamine	Diphenhydramine
Droperidol	Olanzapine	Midazolam	*Dexmetatomidine* (SL)*	

Typical Antipsychotics

Dopamine D2 Receptor Antagonist

Haloperidol		Droperidol
PO, IM, IV	Routes of Admin	IM, IV
2.5 - 10 mg	Typical Doses	1.25 - 5 mg
5-10 minutes	Onset	3-5 minutes
QT Prolongations, EPS	Special Considerations	QT Prolongations, EPS

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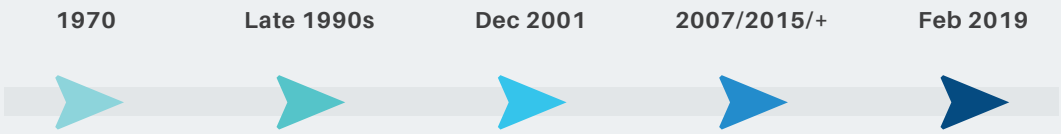
QT Prolongations, EPS	Special Considerations	Black Box Warning

WHAT WAS THE DEAL WITH DROPERIDOL?

An Approximate Timeline



1970	Late 1990s	Dec 2001	2007/2015/+	Feb 2019
Droperidol receives FDA approval: -Antiemetic -Tranquilizing Agent	Reports of Bad Outcomes: -QT Prolongation -Ventricular Arrhythmias -Torsades de Pointes	FDA Black Box Warning -Only for failure of other agents -Required cardiac monitoring	Evidence-Based Medicine Wins? -Multiple studies published touting safety and efficacy similar to other meds	Droperidol Makes a Comeback -Pharm manufacturer reintroduces Droperidol to the US market

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QT Prolongations, EPS	Special Considerations	Black Box Warning

Atypical Antipsychotics

Antagonizes Dopamine + [Norepinephrine, Histamine, Serotonin]

Olanzapine		Ziprasidone
PO, IM, IV	Routes of Admin	PO, IM, IV
5 - 10 mg	Typical Doses	10 – 20 mg
10 - 30 minutes	Onset	15 - 30 minutes
Fewer cardiac/EPS concerns Black Box: dementia; Antimuscarinic	Special Considerations	Reconstitution, Cost

Benzodiazepines

Gamma-amino butyric acid (GABA) receptor agonist

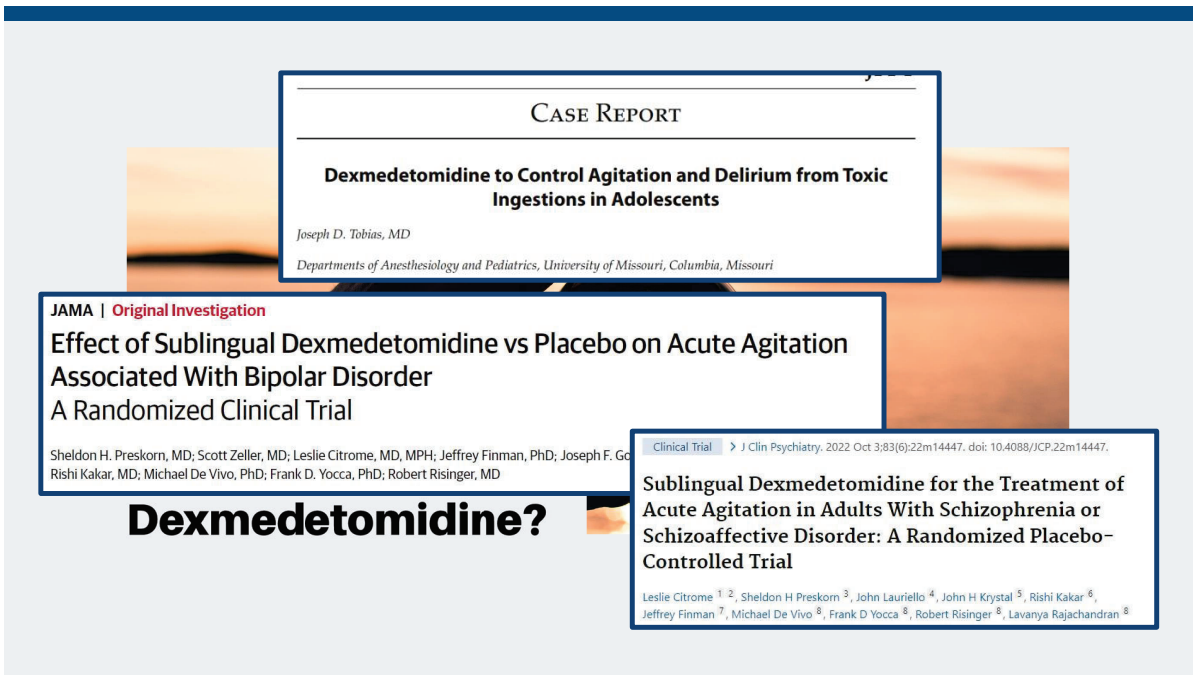
Lorazepam		Midazolam
PO, IM, IV	Routes of Admin	PO, IM, IV
2 - 10 mg	Typical Doses	2.5 – 5 mg
15 minutes	Onset	2 – 5 minutes
Shortages, Caution in Elderly	Special Considerations	Shortages, Caution in Elderly

New Agents

All The Rage

Ketamine NMDA receptor antagonist		Dexmedetomidine α_2-adrenergic receptor agonist
IM, IV	Routes of Admin	SL (IV)
4-5 mg/kg IM; 1 mg/kg IV	Typical Doses	120-180 ug
5-10 minutes	Onset	20 minutes
Procedural Sedation?	Special Considerations	Hypotension, dizziness, dry mouth

Dexmedetomidine?


Case Report
Dexmedetomidine to Control Agitation and Delirium from Toxic Ingestions in Adolescents
Joseph D. Tobias, MD
Departments of Anesthesiology and Pediatrics, University of Missouri, Columbia, Missouri
JAMA | Original Investigation
Effect of Sublingual Dexmedetomidine vs Placebo on Acute Agitation Associated With Bipolar Disorder
A Randomized Clinical Trial
Sheldon H. Preskorn, MD; Scott Zeller, MD; Leslie Citrome, MD, MPH; Jeffrey Finman, PhD; Joseph F. Go
Rishi Kakar, MD; Michael De Vivo, PhD; Frank D. Yocca, PhD; Robert Risinger, MD
Dexmedetomidine?
Clinical Trial > J Clin Psychiatry. 2022 Oct 3;83(6):22m14447. doi: 10.4088/JCP.22m14447.
Sublingual Dexmedetomidine for the Treatment of Acute Agitation in Adults With Schizophrenia or Schizoaffective Disorder: A Randomized Placebo-Controlled Trial
Leslie Citrome 1 2, Sheldon H Preskorn 3, John Lauriello 4, John H Krystal 5, Rishi Kakar 6, Jeffrey Finman 7, Michael De Vivo 8, Frank D Yocca 8, Robert Risinger 8, Lavanya Rajachandran 8


So, All We Need is a Study To See Which One is Best
Easy.....Right?


Variable Populations
Variable Routes
Variable Drugs
Variable Outcomes

Comparisons of Single Agents: Antipsychotics

The Best of the Best for IM Administration in the ED

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Thomas et al. 1992	Prospective Randomized	Droperidol 5mg IM/IV Haloperidol 5mg IM/IV	IM Droperidol : more rapid control	Small; N = 68 No Difference with IV Comparison

Comparisons of Single Agents: Antipsychotics

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			?	THE FINE PRINT
	Randomized	Haloperidol 5mg IM/IV	more rapid control	Small; N = 68 No Difference with IV Comparison

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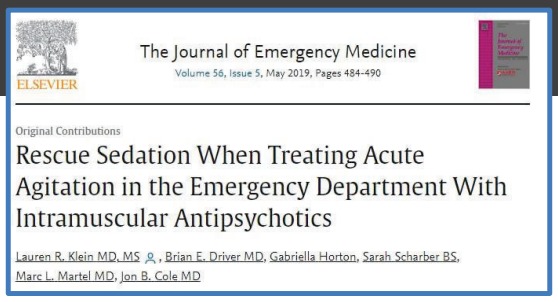
STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Calver et al. 2015	RCT	Droperidol 10mg IM Haloperidol 10mg IM	**Droperidol**: Less need for additional sedation	Droperidol: more adverse effects

Comparisons of Single Agents: Antipsychotics

The Best of the Best for IM Administration in the ED



STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Klein et al. 2019	Retrospective	Droperidol 5-10mg IM Haloperidol 5-10mg IM Olanzapine 10 mg IM	**Droperidol** and **Olanzapine**: Less Need for Rescue Meds	Retrospective N = > 15K

Comparisons of Single Agents: Antipsychotics

The Best of the Best for IM Administration in the ED

PAIN MANAGEMENT AND SEDATION/ORIGINAL RESEARCH

A Prospective Study of Intramuscular Droperidol or Olanzapine for Acute Agitation in the Emergency Department: A Natural Experiment Owing to Drug Shortages

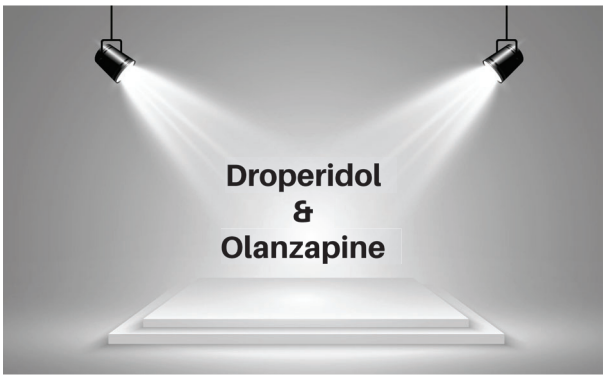
Jon B. Cole, MD*; Jamie L. Stang, BS; Paige A. DeVries, BS; Marc L. Martel, MD; James R. Miner, MD; Brian E. Driver, MD

*Corresponding Author. E-mail: jon.cole@hcmed.org, Twitter: @jonbcole2.

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Cole et al. 2021	Prospective Observational	Droperidol 5 mg IM Olanzapine 10 mg IM	Time to Sedation: It's a Tie	Olanzapine: add'l meds Droperidol: EPS

Comparisons of Single Agents: Antipsychotics

The Best of the Best for IM Administration in the ED



Comparisons of Single Agents: Benzos and Antipsychotics

The Best of the Best for IM Administration in the ED

Clinical Trial > Acad Emerg Med. 2004 Jul;11(7):744-9. doi: 10.1197/j.aem.2003.06.015.

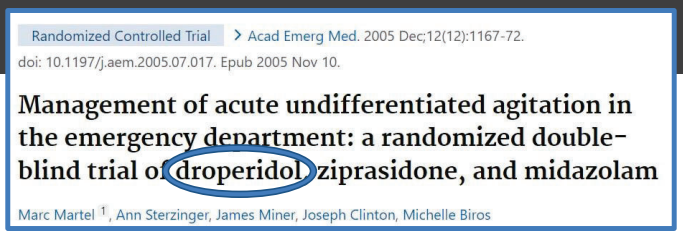
A prospective, double-blind, randomized trial of midazolam versus haloperidol versus lorazepam in the chemical restraint of violent and severely agitated patients

Flavia Nobay [1], Barry C Simon, M Andrew Levitt, Graham M Dresden

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Nobay et al. 2004	Randomized Prospective Double-Blind	Haloperidol 5 mg IM vs Lorazepam 2 mg IM vs Midazolam 5 mg IM	Midazolam Fastest on / Fastest off	No Diff in Adverse Events

Comparisons of Single Agents: Benzos and Antipsychotics

The Best of the Best for IM Administration in the ED



Randomized Controlled Trial > Acad Emerg Med. 2005 Dec;12(12):1167-72.
doi: 10.1197/j.aem.2005.07.017. Epub 2005 Nov 10.

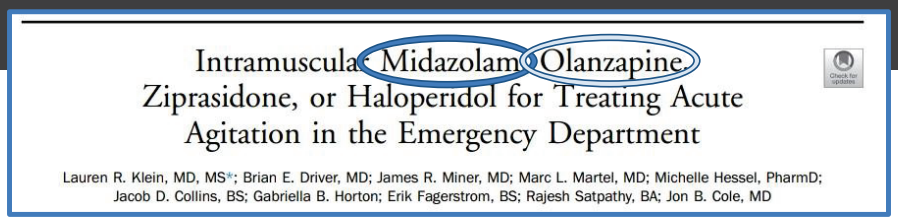
Management of acute undifferentiated agitation in the emergency department: a randomized double-blind trial of droperidol, ziprasidone, and midazolam

Marc Martel [1], Ann Sterzinger, James Miner, Joseph Clinton, Michelle Biros

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Martel et al. 2005	Randomized Prospective Double-Blind	Droperidol 5 mg IM vs Ziprasidone 20 mg IM vs Midazolam 5 mg IM	**Droperidol** = **Goldilocks** Ziprasidone too slow on Midazolam too fast off	No Diff in Adverse Events

Comparisons of Single Agents: Benzos and Antipsychotics

The Best of the Best for IM Administration in the ED



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

Lauren R. Klein, MD, MS*; Brian E. Driver, MD; James R. Miner, MD; Marc L. Martel, MD; Michelle Hessel, PharmD; Jacob D. Collins, BS; Gabriella B. Horton; Erik Fagerstrom, BS; Rajesh Satpathy, BA; Jon B. Cole, MD

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Klein et al. 2018	Prospective Observational	Haloperidol 5 mg IM Haloperidol 10 mg IM Ziprasidone 20 mg IM Olanzapine 10 mg IM Midazolam 5 mg IM	**Midazolam:** Fastest Antipsychotic Race: **Olanzapine** wins	No Diff in Adverse Events

Comparisons of Single Agents: Benzos and Antipsychotics

The Best of the Best for IM Administration in the ED

Randomized Controlled Trial > Acad Emerg Med. 2021 Apr;28(4):421-434.
doi: 10.1111/acem.14124. Epub 2020 Oct 5.

Randomized Double-blind Trial of Intramuscular Droperidol, Ziprasidone, and Lorazepam for Acute Undifferentiated Agitation in the Emergency Department

Marc L Martel [1], Brian E Driver [1], James R Miner [1 2], Michelle H Biros [2], Jon B Cole [1]

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Martel et al. 2021	Randomized Prospective Double-Blind	Droperidol 5 mg IM vs Ziprasidone 10 mg IM vs Lorazepam 2 mg IM	**Droperidol:** more effective at 15 minutes	No Diff in Adverse Events

Comparisons of Single Agents: Benzos and Antipsychotics

The Best of the Best for IM Administration in the ED

Droperidol (goldilocks)
Midazolam (speed)

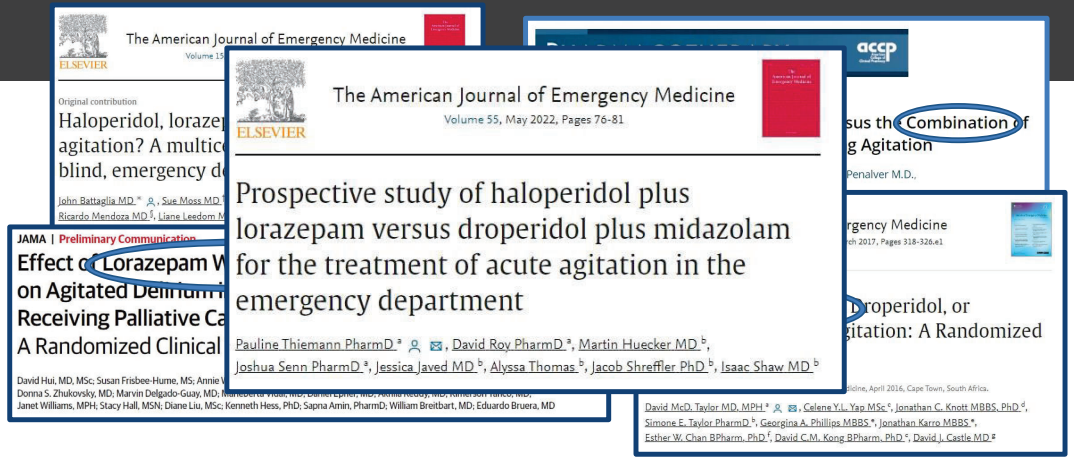
Olanzapine

Comparisons of Combinations: Benzos + Antipsychotics

Is a Combination Optimal?

Comparisons of Combinations: Benzos + Antipsychotics

Combinations Are Optimal



Comparisons of Combinations: Benzos + Antipsychotics

The Best of the Best for IM Administration in the ED

The American Journal of Emergency Medicine
Volume 55, May 2022, Pages 76-81

Prospective study of haloperidol plus lorazepam versus droperidol plus midazolam for the treatment of acute agitation in the emergency department

Pauline Thiemann PharmD [a], David Roy PharmD [a], Martin Huecker MD [b], Joshua Senn PharmD [a], Jessica Javed MD [b], Alyssa Thomas [b], Jacob Shreffler PhD [b], Isaac Shaw MD [b]

STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Thiemann et al. 2022	Prospective Unblinded Observational Single Site	Haloperidol 5 mg IM + Lorazepam 2 mg IM vs Droperidol 5 mg IM + Midazolam 5 mg IM	**Droperidol/Midazolam** Better at 10 min mark	Droperidol/Midazolam needed more supp oxygen

Comparisons of Combinations: Benzos + Antipsychotics

The Best of the Best for IM Administration in the ED

The World of Ketamine

Contents lists available at ScienceDirect
American Journal of Emergency Medicine
journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Ketamine as a first-line treatment for severely agitated emergency department patients☆

Jeff Riddell [a,*], Alexander Tran [b], Rimon Bengiamin [c], Gregory W. Hendey [d], Patil Armenian [c]

Randomized Controlled Trial > Ann Emerg Med. 2021 Dec;78(6):788-795.
doi: 10.1016/j.annemergmed.2021.05.023. Epub 2021 Aug 2.

Rapid Agitation Control With Ketamine in the Emergency Department: A Blinded, Randomized Controlled Trial

David Barbic [1], Gary Andolfatto [2], Brian Grunau [3], Frank X Scheuermeyer [3], Bill Macewan [4], Hong Qian [5], Hubert Wong [5], Skye P Barbic [6], William G Honer [4]

The American Journal of Emergency Medicine
Volume 44, June 2021, Pages 306-311

Efficacy of ketamine for initial control of acute agitation in the emergency department: A randomized study

Justin Lin Pharm.D. [a], Yelena Figuerado Pharm.D. [a], Adrienne Montgomery Pharm.D. [a], Jonathan Lee M.D. [b], Mark Cannis M.D. [b], Valerie C. Norton M.D. [b], Richard Calvo Ph.D. [c], Harminder Sikand Pharm.D. [a]

The World of Ketamine

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STUDY	STUDY TYPE	COMPARISON	WINNER?	THE FINE PRINT
Barbic et al. 2021	RCT	Ketamine 5 mg/kg IM vs Midazolam 5 mg IM +Haloperidol 5 mg IM	**Ketamine:** Shorter Median Time to Sedation	Ketamine: More adverse events

The World of Ketamine

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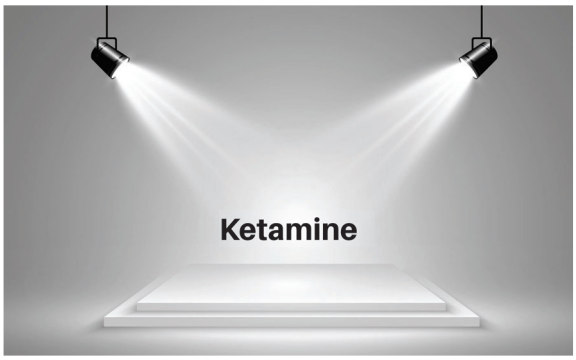
Lin et al. 2021	RCT	Ketamine 4 mg/kg IM or 1 mg/kg IV vs Lorazepam 1-2 mg IM/IV +Haloperidol 5-10 mg IM/IV	**Ketamine:** Shorter Median Time to Sedation	No Diff in Adverse Events

Comparisons with Ketamine

A Wonder Drug?



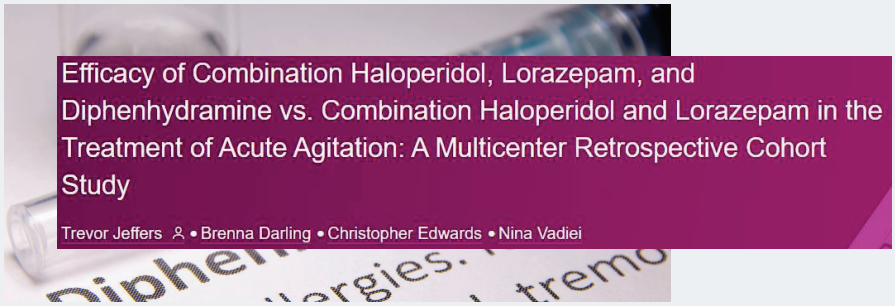
So... What Do You Want Doc?

An Summary of Imperfect Data

Typical Antipsychotic?	Droperidol: more rapid
Atypical Antipsychotic?	Olanzapine: front runner
Benzodiazepine?	Midazolam: faster on, faster off
Should I Do A Combo?	Yes: decreases time to sedation
Ketamine?	Go For It: monitoring needed

What About the B in B52?

Study of the Classic "B52" vs "52"



With Diphenhydramine:

- More oxygen desaturation
- More hypotension
- More physical restraint use
- Longer length of stay

Special Populations

Unique Considerations

West J Emerg Med. 2019 Mar; 20(2): 409–418.
Published online 2019 Feb 19. doi: 10.5811/westjem.2019.1.41344
PMCID: PMC6404720
PMID: 30881565

Best Practices for Evaluation and Treatment of Agitated Children and Adolescents (BETA) in the Emergency Department: Consensus Statement of the American Association for Emergency Psychiatry

Pediatrics

- Avoid combinations
- Based on etiology, select:
  - Olanzapine (less cardiac/EPS risk)
  - Benzos (but not w/i 1 hr Olanzapine)
- Beware Paradoxical Disinhibition
  - Delerium - Diphenhydramine/Benzos
- No good data for ketamine

Pregnancy

- Avoid physical restraints
- Benefit > Risk

- There is no antipsychotic or benzodiazepine that is absolutely contraindicated
- Haloperidol + Benzo
- Atypical Antipsychotics also okay

Geriatrics

- American Geriatrics Society Beers Criteria
  - Benzodiazepines
  - Antipsychotics
- FDA Black Box
  - Dementia + Atypical Antipsychotics

- Start with a lower dose
- Benzos: paradoxical reaction
- Avoid diphenhydramine: anticholinergic

Additional considerations

Convey a great number of information in an effective manner

DOCUMENTATION

Use of these medications = Restraint

Face to Face < 1 hr
Renewal q4 hr

LEGAL

Justify reasoning

ETHICAL

Never punitive

Always respecting patient autonomy when possible

PSYCHOLOGICAL

High rates of long term psychological distress after utilization of common interventions

Chemical Restraint

Nicole McCoin, MD
Chair, Department of Emergency Medicine
Ochsner Medical Center

Carmen Wolfe, MD
Program Director, TriStar Emergency Medicine
TriStar Skyline Medical Center

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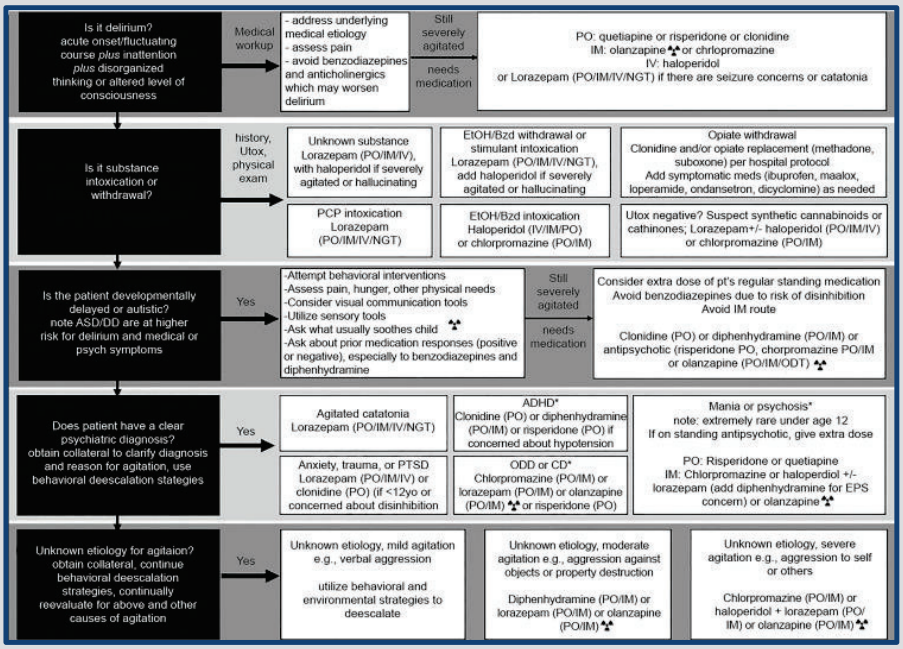
Lin et al. 2021	RCT	Ketamine 4 mg/kg IM or 1 mg/kg IV vs Lorazepam 1-2 mg IM/IV +Haloperidol 5-10 mg IM/IV	**Ketamine:** Shorter Median Time to Sedation	No Diff in Adverse Events

Non-Coercive De-Escalation

Step 1: Verbally Engage the Patient	Step 2: Establish a Collaborative Relationship	Step 3: Verbally De-Escalate the Patient
Respect Personal Space	Be Concise	Set Clear Limits
Do Not Be Provocative	Establish Wants and Feelings	Offer Choices and Optimism
Establish Verbal Contact	Listen Closely	Debrief the Patient
	Agree or Agree to Disagree	

American Association for Emergency Psychiatry:
Project BETA (Best Practices in the Evaluation and Treatment of Agitation)



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