

Unmet Needs of Agitated Delirium in the Emergency Department

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Learning Objectives

Upon completion of this presentation, participants should be able to:

- State the risks to both the patient and the emergency department staff when caring for a patient with uncontrolled agitation
- Discuss the toxicologic and nontoxicologic differential diagnosis of a patient with agitated delirium
- Describe the approach to the initial control of a patient in the emergency department with severe agitation

Disclosure

Type of Affiliation Commercial Entity

No financial relationships to disclose.

Dr. Nelson intends to discuss off-label/unapproved uses of products or devices.

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View of Psychotic Agitation

- Behavioral problems
- Autonomic hyperactivity
 - Hypertension
 - Tachycardia
 - Diaphoresis
 - Mydriasis
 - Hyperthermia

Agitation

- Agitation is common in patients in the ED
- Survey of 127 teaching hospitals
 - 32% have at least 1 verbal threat daily
 - 25% must restrain 1 patient daily
 - 13% injured a patient while controlling them
 - ◊ 1 death from strangulation
 - 15% of the hospitals have lawsuits

Lavoie FW et al. *Ann Emerg Med.* 1988;17:1227-1233.

Agitation: *Diagnosis and Management*

- Agitated patients strain both the staff and function of the ED
- Need a management strategy that is
 - Rapid and orderly
 - Safe and effective
 - Etiology-neutral
 - Legal!

Agitation: *Clinical Concerns*

- Self-injury
 - Trauma
 - Hyperthermia
 - Rhabdomyolysis
- Staff injury
 - Patient unpredictability
- Iatrogenic injury to the patient

Differentiating Causes of Agitation

- Among the greatest difficulties is determining the etiology
- Psychiatric (functional)
- Nonpsychiatric (organic)
 - Medical
 - Toxicologic
- Approximately two thirds have organic etiology

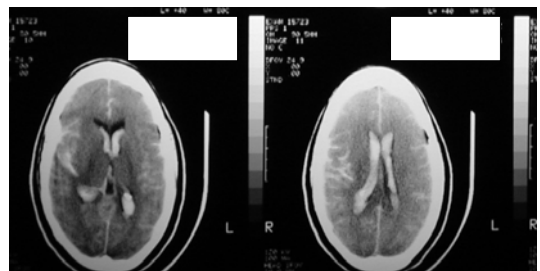
General Guidelines

- Delirium = organic
- Older age = organic
- Younger age = organic
- Known medical disorder = organic

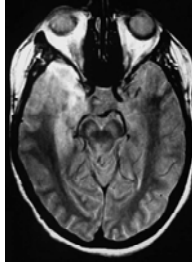
Differential Diagnosis: *Clues to the Etiology*

- Physical examination
 - Odors
 - Pupils
 - Toxicologic syndromes
- Pulse oximetry
 - Hypoxia
- Capillary glucose
 - Hypoglycemia

CT Scan: *Patient with Meningismus/Retinal Hemorrhages*



MRI: *Patient with Meningismus/Fever of Unexplained Origin*



Ethanol Intoxication

- Clinical evaluation of 58 consecutive agitated patients in France
 - 50 of 58 had biochemical ethanol intoxication
 - 39 patients had clinical diagnosis of ethanol intoxication
 - ◊ 1 patient had no serum ethanol
- How good is clinical evaluation?

Moritz F et al. *Intensive Care Med.* 1999;25:852-854.

Presumptive Evidence of Intoxication

- Simple observation
 - Alcohol on breath
 - Clumsiness/fumbling
 - Difficulty with balance/walking
 - Inappropriate behavior
 - Slurred speech

Agitation: *Differential Diagnosis*

- Ethanol intoxication
- Ethanol withdrawal
 - A constellation of symptoms and signs that follow acute abstinence or decreased use of alcohol in patients dependent on ethanol

Caution with Ethanol

- It is very important to differentiate intoxication from withdrawal
 - Therapy very different
 - Many similar features
 - ◊ ability never studied

Agitation: *Differential Diagnosis*

- Ethanol intoxication
- Ethanol withdrawal
- Phencyclidine/hallucinogens

Phencyclidine/Ketamine

- Clinical: dissociative anesthetic
 - High dose
 - ◇ coma
 - ◇ preserved respirations
 - Low dose
 - ◇ dysphoria, disorientation, violence
 - ◇ nystagmus (horizontal, vertical, rotatory)

Illy: *Embalming Fluid-Dipped Marijuana*

- Sold to unsuspecting users as “potent pot”
 - Severe dysphoria
- Not an effect of formaldehyde on THC
- Formalin serves as a solvent for PCP
- AKA: wet, hydro, blunts

Agitation: *Differential Diagnosis*

- Ethanol intoxication
- Ethanol withdrawal
- Phencyclidine/hallucinogens
- Anticholinergics

Anticholinergic Syndrome (Antimuscarinic)

- Clinical diagnosis
 - Toxidrome
 - Classic speech pattern

Hot as a hare,
Dry as a bone,
Blind as a bat,
Red as a pepper,
Full as a flask,
Mad as a hatter.

Anticholinergic Syndrome: *Identification of the Source*

- Antihistamines
- Tropane alkaloids
 - Scopolamine
 - Atropine
- Tricyclic antidepressant



Scopolamine Poisoning among Heroin Users — New York City, Newark, Philadelphia, and Baltimore, 1995 and 1996

Heroin is mixed (“cut”) frequently with other substances primarily to increase its weight for retail sale (e.g., mannitol and starch) and to add pharmacologic effects (e.g., dextromethorphan and fentanyl). During 1995 and 1996, health departments and poison-control centers in New York City (NYC), Newark, New Jersey, Philadelphia, and Baltimore reported at least 325 cases of drug overdoses requiring medical treatment in persons who had used “street drugs” sold as heroin that probably also contained scopolamine, an anticholinergic drug. This report summarizes the clinical and epidemiologic features of these cases, which represent a new type of drug overdose.

New York City

On March 16, 1995, eight persons were treated in the emergency department (ED) of a Bronx hospital for acute onset of agitation and hallucinations approximately 1 hour after “snorting” heroin. On physical examination, all three persons had clinical manifestations of anticholinergic toxicity (i.e., tachycardia, mild hypertension, dilated pupils, dry skin and mucous membranes, and diminished or absent bowel sounds); five had urinary retention. All were initially febrile; and became agitated and combative after emergency medical service (EMS) personnel treated them with parenteral naloxone, which is routinely used for suspected heroin overdose to reverse the toxic effects of opioids (e.g., coma and respiratory depression). All patients received diazepam or lorazepam for sedation, and signs and symptoms resolved during the next 12–24 hours.

MMWR Morb Mortal Wkly Rep. 1996;45:457-460.

Agitation: *Differential Diagnosis*

- Ethanol intoxication
- Ethanol withdrawal
- Phencyclidine/hallucinogens
- Anticholinergics
- Cocaine and amphetamines

Cocaine vs Methamphetamine

- | | |
|-----------------------------------------------------------------------------------------------|------------------------------|
| • Cocaine | • Methamphetamine |
| – More prevalent in the East | – More prevalent in the West |
| – Short-lived effects | – Effects may last hours |
| – Seizures | – Seizures uncommon |
| – ECG abnormalities <ul style="list-style-type: none">◊ sodium channel blockade | – ECG abnormalities uncommon |

Young Woman on a Sunday Morning



Initial Management

- Physical restraint
- Chemical restraint
 - “Medicate for agitation”

Pharmacologic Management

- Benzodiazepines
 - Diazepam (only IV)
 - Lorazepam
- Generally very safe
- Work rapidly
- Cross-tolerant with ethanol for withdrawal
- Major problems
 - Sedation rather than tranquilization
 - Potential respiratory depression

Pharmacologic Management

- Antipsychotics
 - Butyrophenones
 - ◊ haloperidol (IM, IV?)
 - ◊ droperidol (IM, IV?)
 - Atypicals
 - ◊ ziprasidone (IM)
 - ◊ risperidone (PO)
- Less sedating than benzodiazepines
- No respiratory depression
- Not cross-tolerant with ethanol

Droperidol (Inapsine®)

WARNING

Cases of QT prolongation and/or torsades de pointes have been reported in patients receiving INAPSINE at doses at or below recommended doses. Some cases have occurred in patients with no known risk factors for QT prolongation and some cases have been fatal.

Due to its potential for serious proarrhythmic effects and death, INAPSINE should be reserved for use in the treatment of patients who fail to show an acceptable response to other adequate treatments, either

Based on these reports, all patients should undergo a 12-lead ECG prior to administration of Inapsine to determine if a prolonged QT interval (ie, QTc greater than 440 ms for males or 450 ms for females) is present. If there is a prolonged QT interval, Inapsine should NOT be administered.

administered. For patients in whom the potential benefit of INAPSINE treatment is felt to outweigh the risks of potentially serious arrhythmias, ECG monitoring should be performed prior to treatment and continued for 2-3 hours after completing treatment to monitor for arrhythmias.

INAPSINE should be administered with extreme caution to patients who may be at risk for development of prolonged QT syndrome (e.g., congestive heart failure, bradycardia, use of a diuretic, cardiac hypertrophy, hypokalemia, hypomagnesemia, or administration of other drugs known to increase the QT interval). Other risk factors may include age over 65 years, alcohol abuse, and use of agents such as benzodiazepines, volatile anesthetics, and IV opiates. Droperidol should be initiated at a low dose and adjusted upward, with caution, as needed to achieve the desired effect.

US Food and Drug Administration. Important drug warning. Available at: <http://www.fda.gov/medwatch/SAFETY/2001/inapsine.htm>. Accessed September 28, 2003.

Initial Management

- Physical restraint
- Chemical restraint
 - “Medicate for agitation”
- Pursue the diagnosis
- Cool
- Volume correct

Unmet Needs in the Agitated Patient

- Rapidly confirming the etiology
 - Differential diagnosis is broad
 - Testing is frequently limited
 - History and clinical evaluation, despite their limitations, remain the most useful tools
- Treatment varies with the etiology, and mistakes may be costly