

Delirium: A Case of Hearing Voices

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Key Questions

- What is the definition of delirium?
- What diagnostic tests are indicated in a patient with delirium?
- What is the recommended pharmacologic intervention to manage the agitated patient with delirium?

All of the following are part of the diagnosis of delirium except:

- a) Disturbance in consciousness with reduced ability to focus, sustain or shift attention
- b) Develops over a short period of time (hours to days); tends to fluctuate during the day
- c) The disturbance is caused by the direct physiological consequences of a general medical condition
- d) Disturbance is similar to that seen in dementia

Acute agitation in delirium in the elderly is best treated with which of the following?

- a) Lorazepam
- b) Droperidol
- c) Halperidol
- d) Risperidol
- e) Midazolam

Case Study

- CC: 31 year old woman presented with hearing voices telling her to hurt herself
- Meds: Azithromycin, ciprofloxacin, Tylenol #3
- PMH: None
- PSH: S/P appendectomy 9 days prior
- Nursing Assessment: "Unable to sleep since she came out of hospital...talking to herself, jittery, anxious...apprehensive", "schizophrenia"
- Triaged to the psych ED

Case Study

- According to roommate, patient has been intermittently confused, anxious, and paranoid since leaving the hospital 4 days prior
- No past psychiatric history
- No family history of psychiatric disorders
- History of cocaine, marijuana, and heroin (IV) more than ten years prior
- Social history: college teacher on leave to prepare her PhD

Physical Exam / Mental Status Exam

- VS: T--98.8; P--120; BP--168/74; R--20, SaO₂=98%
- HEENT: Normal
- Neck: Normal thyroid
- Heart: RRR without murmurs
- Lungs: Clear
- Abdomen: Soft, nontender; incision well healed
- Skin: No rashes
- Neurologic exam: CN intact; motor / sensory intact; DTRs symmetrical; Gait normal

Psychiatric Mental Status Exam

- Appearance: Disheveled; poor eye contact; guarded; suspicious
- Speech: Pressured
- Thought process: flight of ideas
- Thought content: paranoid; no suicidal ideation
- Mood: Elated
- Affect: Labile, inappropriate
- Insight /Judgement: Poor
- Cognition: Impaired; could not complete MMSE

Delirium (DSM-IV)

- Disturbance in consciousness with reduced ability to focus, sustain or shift attention
- Change in cognition (i.e memory deficit, disorientation, language disturbance) / development of perceptual disturbance not accounted for by dementia
- Develops over a short period of time (hours to days); tends to fluctuate during the day
- Evidence that disturbance is caused by the direct physiological consequences of a general medical condition

Delirium: Epidemiology

- Prevalence in hospitalized patients 10-30%
 - Up to 40% in the elderly, cancer, HIV, surgical
- 10% of elderly ED patients have delirium
 - 38% go unrecognized and are discharged
- Duration depends on underlying cause
- May progress to stupor / coma / death
 - Mortality in the elderly 20-70%
 - 25% die within 6 months of the hospitalization

Lewis. Unrecognized delirium in ED geriatric patients. Am J Emerg Med 1995; 13:142

Hustey. ED Prevalence and Documentation of Impaired Mental Status in Elderly. *Ann Emerg Med* 2002; 39

- 26% (78/297) of patients had altered ms
- 10% (30/297) had delirium
- 17/30 (57%) had documentation of abnormal mental status by ED provider
- 70% discharged home with cognitive impairment had no evidence available that the mental status abnormality was chronic

Delirium: Differential Diagnosis

- Structural CNS lesion
- Toxic: Overdose vs side effect
 - Anticholinergics
- Withdrawal syndrome
- Metabolic / endocrine
- Infection: Central vs systemic
- Seizure
- Post operative state

Delirium: Examples of Reversible Causes

- Hypoglycemia
- Hypoxia
- Hyperthermia
- Hypertension
- Drug withdrawal
- Wernicke's
- Drug toxicity
 - anticholinergic

Delirium: History and Physical

- History: time course, recent events
 - New medications, drugs, trauma
- Abnormal vital signs, pulse ox, blood sugar
- Toxidromes:
 - Cholinergic, anticholinergic, adrenergic, opioid, hallucinogen, sedative
- Evidence of systemic disease:
 - Dehydration, hypoxia, liver / renal failure, CHF, COPD
- Focal neurologic findings

Modified Mini-mental Status Exam. (Used to diagnose cognitive impairment)

Time Orientation - date, day, season
Place Orientation - City, State, Building
Attention - serial 7s, months forward / reverse
Registration of 3 objects (immediate recall)
Memory - 3 objects in 3 minutes (delayed memory)
Language / Visual Spatial: repeat "no ifs ands buts, 3 stage command, write sentence, copy design

23 or less = cognitive abnormality

Delirium: Laboratory Work-up

- CBC / Metabolic panel
- LFTs
- Toxicology Screen
- Brain imaging / LP
- Blood cultures if sepsis suspected
- EEG in select patients

Laboratory Testing

- Henneman et al. Prospective evaluation of ED medical clearance. *Ann Emerg Med* 1994; 24: 672
- 100 ED patients with new psychiatric complaints
- H&P, ETOH, urine tox, CBC, SMA 7; CT optional, LP if febrile
- Excluded known patients with psych disorders, psych patients with medical complaints, known drug use or suicide attempt
- 63/100 had medical cause identified: 30/63 tox, 25/63 neurologic, 5/63 infectious (3 CNS)

AAP. Practice guideline for the treatment of patients with delirium.

Am J Psychiatry 1999; 156 (suppl):1-20

- Monotherapy with a typical antipsychotic: haloperidol or droperidol
 - Droperidol has a faster onset and less frequent need for a second dose
 - Need to monitor ECG and serum Mg levels
- Benzodiazepines as a monotherapy is reserved for delirium from drug withdrawal
 - Generally avoided as monotherapy in the elderly
 - Lorazepam possibly preferred in patients with liver disease
- Combined therapy of a antipsychotic plus a benzodiazepine may have faster onset of action with fewer side effects

ACEP Clinical Policy:
What is the most effective pharmacologic treatment for the acutely agitated patient in the Emergency Department?

- Emphasizes the importance of:
 - Assessing for violence
 - Assessing for reversible medical causes:
 - Hypoxia
 - Hypoglycemia
 - Verbal de-escalation techniques and safe setting
- Undifferentiated agitation (medical vs psychiatric) versus exacerbation of a known mental illness

ACEP Clinical Policy:
What is the most effective pharmacologic treatment for the acutely agitated patient in the ED?

- Multiple Class II studies show that benzodiazepines (lorazepam and midazolam) are at least as effective as haloperidol in controlling agitation
 - Nobay et al: IM Midazolam 5 vs lorazepam 2 vs haloperidol 5: Midazolam had faster onset and shorter duration
 - Battaglia et al: Supported the use of combined lorazepam plus haloperidol: Lower doses of each and less EPS than haloperidol alone
- Benzodiazepines promote sedation and do not necessarily address psychosis

Acad Emerg Med 2004; 11:744-749
Am J Emerg Med 1997; 15:335-340

ACEP Clinical Policy:
What is the most effective pharmacologic treatment for the acutely agitated patient in the ED?

- Conventional antipsychotics:
 - Most experience with haloperidol
- Droperidol, a butyrophenone, has rapid onset but became controversial due to ECG concerns
 - Richards et al: Class II study comparing droperidol to lorazepam showed faster onset and less agitation and less sedation

J Emerg Med 1998; 16:567-573

ACEP Clinical Policy:
What is the most effective pharmacologic treatment for the acutely agitated patient in the ED?

- Atypical antipsychotics
 - All studies in known psychiatric populations
 - Olanzapine, ziprasidone, quetiapine, and risperidone all prolong the QTc
- Reported to cause less EPS, less sedation
- Preval et al: reported ziprasidone 20 mg IM decreased agitation scores equally to haloperidol plus lorazepam
- Meehan et al: reported olanzapine, 10 mg, equivalent to lorazepam
 - May cause hypotension

Gen Hosp Psych 2005; 27; 140-144
J Clin Psychopharmacol 2001; 21:389-397

ACEP Clinical Policy:
What is the most effective pharmacologic treatment for the acutely agitated patient in the ED?

- Level B Recommendations:
 - Use a benzodiazepine or a conventional antipsychotic as effective monotherapy for the initial drug treatment of the acutely agitated undifferentiated patient in the ED
 - If rapid sedation is required, consider droperidol instead of haloperidol
- Level C Recommendation: The combination of a parenteral benzodiazepine and haloperidol may produce more rapid sedation than monotherapy in the acutely agitated psychiatric patients in the ED

Addendum: Pharmacotherapy

- Randomized double blind clinical trial comparing IV midazolam and droperidol for sedation of the acutely agitated patient in the ED. Ann Emerg Med 2006; 47:61-67
 - 74 patients midazolam 5 mg / 79 patient droperidol 5 mg
 - 35% drug related / 65% mental illness related
 - No difference in sedation at 10 min
 - 3 patients receiving droperidol had dystonic reaction
 - 3 patients receiving midazolam needed airway support
- Midazolam had a slightly faster onset of action but more need for rescue med within one hour; droperidol lasted longer but risk of dystonic reaction

Addendum: Pharmacotherapy

- Management of acute undifferentiated agitation in the ED: A randomized double blind trial of droperidol 5 mg, ziprasidone 20 mg, and midazolam 5 mg
- Convenience sample of 144 patients (primarily drug / alcohol intoxication, head trauma)
 - Midazolam fastest sedation but more frequent rescue meds
 - Midazolam had more respiratory depression / no intubations
 - Ziprasidone slowest onset but equal to droperidol at 30 min; more reported akathisia; deeper sedation
- Study does not demonstrate a benefit of ziprasidone in any category

Case Continued

- WBC: 11.4K (79% neut)
- H/H: 12.6/37.3
- Electrolytes: 138/4.2/100/24 Cr .9
- Glu: 105
- UA: negative
- Icon: negative
- U tox: (+) BZ
- ECG: QTc 340

Test results...

HVA:	2 (0.0 - 3.0)	Blood Cult. X 2	neg
Metaneph:	1.4 (0.1 - 1.2)	Stool O + P	neg
VMA:	2.5 (0.3 - 3.5)	C. diff	neg
		Urine Cult.	neg
CSF:	glu 56; prot <10	VDRL	non- reactive
	1 WBC, 60 RBC	ESR	55

Thyroid Function Tests

TSH:	< 0.01	(0.2 - 5.0)
Total T4:	12.4	(4.5 - 12.5)
Total T3:	341	(100 - 200)
TBG:	19.2	(14.5 - 32.0)

TSH Receptor Ab: 65% (0 - 12%)

Graves' Disease

- Peak incidence in third and fourth decades
- Female:male as high as 7:1
- Hyperthyroidism with diffuse goiter, ophthalmopathy, dermopathy
- HLA B8 and DRw3 in Caucasian, Bw36 in Japanese, and Bw46 in Chinese
- Clinical and immunologic overlap with Hashimoto's and pernicious anemia

Graves' Disease: Manifestations

- Nervousness, emotional lability, inability to sleep, tremors, frequent bowel movements, excessive sweating, heat intolerance, weight loss
- Proximal muscle weakness
- Lid lag, infrequent blinking, widened palpebral fissures
- Sinus tach / atrial arrhythmias, cardiomegaly, CHF
- Diffuse toxic goiter
- Exophthalmic ophthalmoplegia

Thyroid / Psych

- Psych patients:
 - 0.4% hyperthyroid
 - 0.01% hypothyroid (incr. w/ lithium)
 - 6.5% TSH abnormalities
- Hyperthyroid patients:
 - 3% mania
 - 0.001% depression
 - 0.0001% delirium

Why today?

“The patient was prepped and draped in the usual sterile fashion...”

Environmental Triggers

- Iodine Administration
- Key manifestation of Graves Disease: needs substrate
 - Initial effect : “iodine induced HYPOthyroidism” (Wolff-Chaikoff effect)
 - Final effect : iodine induced HYPERthyroidism”(Jod-Basedow phenomenon)

Jod Basedow

Daily dietary supply - ~500mcg/day
Medications - amiodarone ~75,000 mcg/tab
Disinfectants - tincture of iodine ~200,00 mcg/tsp
Radiologic contrast - >300,000 mcg/ml

Conclusions

- Patients with an acute change in behavior require a careful medical evaluation
- Historical and physical findings provide the baseline necessary to determine diagnostic testing
- Delirium is a medical emergency
- In general, antipsychotics are still the pharmacologic intervention of choice in the acutely agitated patient

Thank you.

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