USE OF ANTIPSYCHOTICS FOR THE MANAGEMENT OF DELIRIUM

Sriram Yennu MD, MS, FAAHPM

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Delirium

- Confusion (time, space, recent memory)
- Hallucinations – tactile!
- Delusions
- Agitation
- Disinhibition: symptoms or emotions!!

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2 MAJOR DISORDERS OF COGNITION
DELIRIUM AND DEMENTIA

DELIRIUM:

- Usually acute in onset
- Relatively brief in duration
- Fluctuating level of consciousness
- Can be reversible

DEMENTIA:

- Intellectual deterioration of protracted & usually irreversible nature

- Delirium reported to be most common OMS in Cancer PTS

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Differential diagnosis

- Dementia (easy from history)
- Sedation (opioids)
- Obstructive sleep apnea (Reddy 2008)
- Depression (60% delirium referrals)
- Anxiety/ manic episode
- Akathisia

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Delirium

- 85% cancer pts before death
- Multicausal
- 80% of brain is GABA
- Disinhibition: expression of symptoms and emotions

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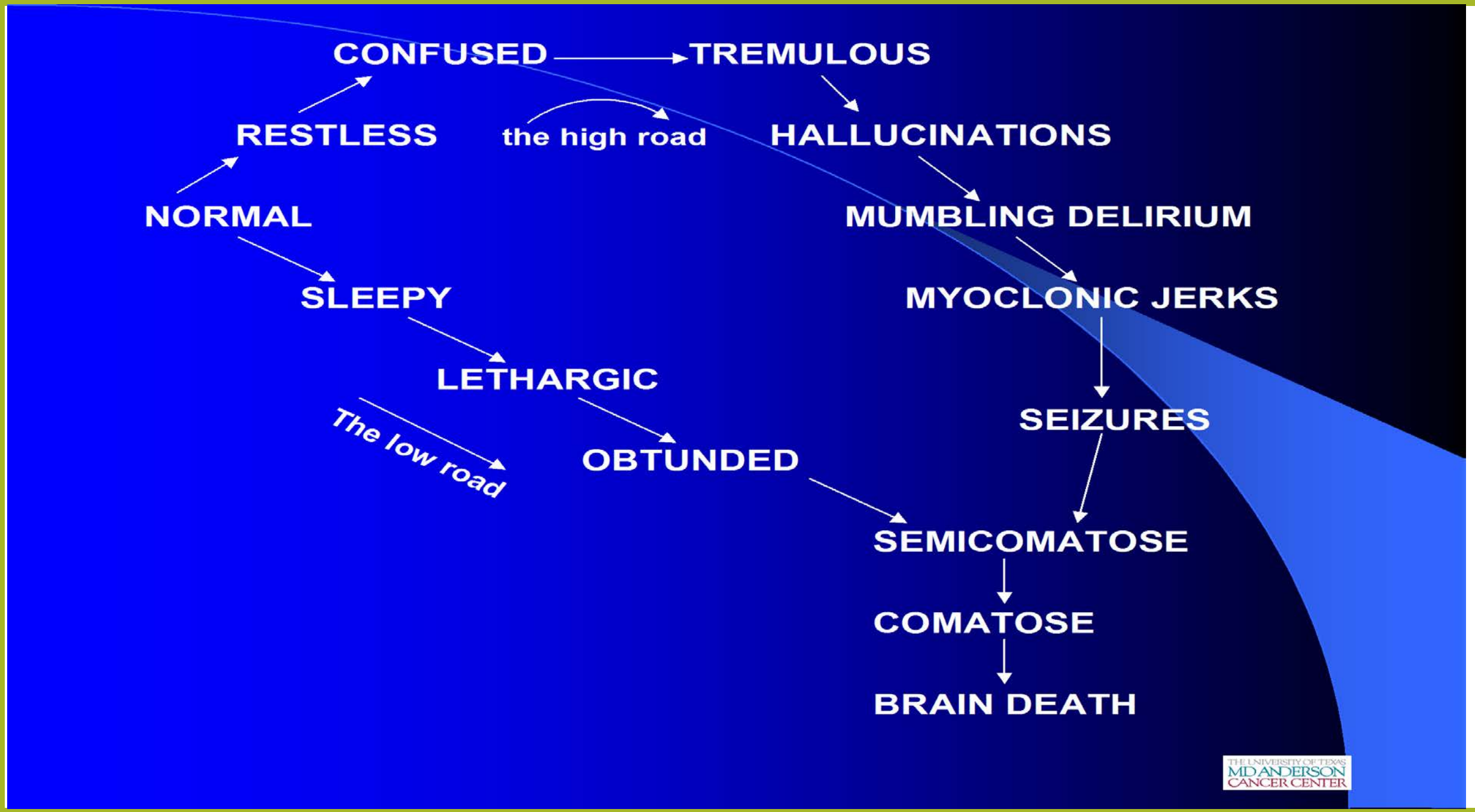
CONFUSED
TREMULOUS
RESTLESS
the high road
HALLUCINATIONS
NORMAL
MUMBLING DELIRIUM
SLEEPY
MYOCLONIC JERKS
LETHARGIC
SEIZURES
The low road
OBTUNDED
SEMICOMATOSE
COMATOSE
BRAIN DEATH
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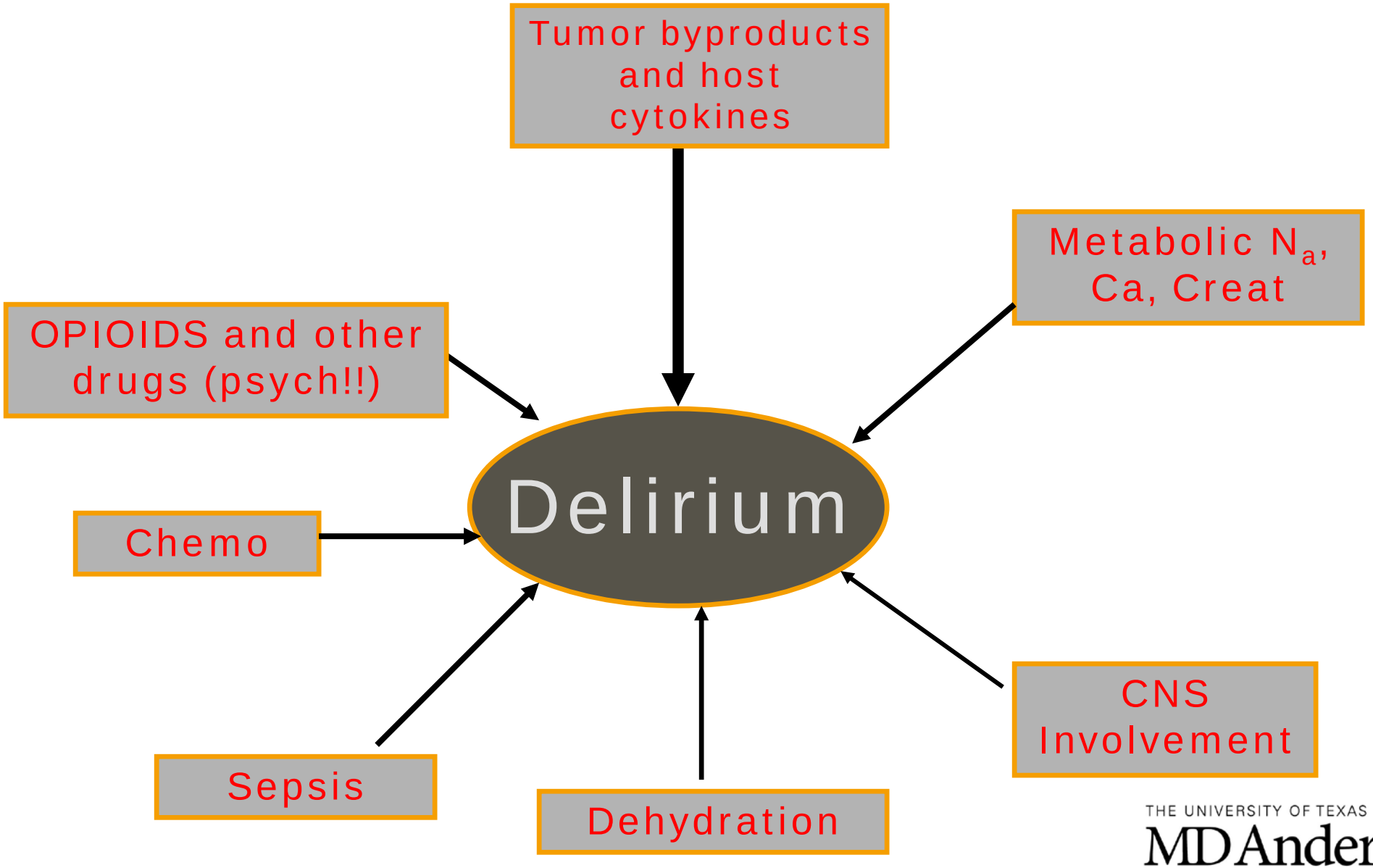

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Opioid induced neurotoxicity (OIN)

- severe sedation
- cognitive failure
- hallucinosis/delirium
- myoclonus/grand mal seizures
- hyperalgesia/allodynia

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Risk Factors for OIN

- High opioid dose
- Prolonged opioid exposure
- Pre-existing borderline cognition/delirium
- Dehydration
- Renal failure
- Other psychoactive drugs
- Opioids with mixed agonist/antagonist activity

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Delirium management

1. Screening/ early (or late) diagnosis
2. Look for reversible causes
3. Pharmacological treatment
4. Environmental control
5. Bedside nurse/ referring MD education
6. Family education/ counseling

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MDAS

Memorial Delirium Assessment Scale

ITEM 1 – REDUCED LEVEL OF CONSICIOUSNESS (AWARENESS):

- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 2 – DISORIENTATION:

- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 3 – SHORT-TERM MEMORY IMPAIRMENT:

- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 4 – IMPAIRED DIGIT SPAN:

- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 5 – REDUCED ABILITY TO MAINTAIN AND SHIFT ATTENTION

- 0: none
- 1: mild
- 2: moderate
- 3: severe

MDAS

Memorial Delirium Assessment Scale

ITEM 6 – DISORGANIZED THINKING

- ❑ 0: none
- ❑ 1: mild
- ❑ 2: moderate
- ❑ 3: severe

ITEM 7 – PERCEPTUAL DISTURBANCE:

- ❑ 0: none
- ❑ 1: mild
- ❑ 2: moderate
- ❑ 3: severe

ITEM 8 – DELUSIONS:

- ❑ 0: none
- ❑ 1: mild
- ❑ 2: moderate
- ❑ 3: severe

ITEM 9 – DECREASED OR INCREASED PSYCHOMOTOR ACTIVITY:

- ❑ 0: none
- ❑ 1: mild
- ❑ 2: moderate
- ❑ 3: severe

ITEM 10 – SLEEP-WAKE CYCLE DISTURBANCE (DISORDER OR AROUSAL):

- ❑ 0: none
- ❑ 1: mild
- ❑ 2: moderate
- ❑ 3: severe

TOTAL _____

Other tools

- CAM
- DRS
- DSM TN criteria interview
- MMSE

THE MANAGEMENT OF DELIRIUM

1. Assessment
   - Hypoactive
   - Hyperactive
   - Mixed (80 % !!!!)
2. Pharmacological Interventions
   - Haloperidol
   - Other neuroleptics
   - Lorazepam-midazolam
3. Counseling
   - Patient
   - Family
   - Staff
4. Prevention of Delirium
   - Screening- MDAS
   - Opioid rotation
   - Hydration

COUNSELING

1. Patient
   - Brief conversations
   - Avoid Confrontation – Avoid stimulation (hyperactivity)
   - Reassurance: familiar objects, people and sounds

2. Family
   - Monitor behavior regularly
   - Explain the mechanism of delirium
   - Reassure regarding physical suffering
   - Major cause of conflict!!

3. Staff
   - Difference between pain and agitated delirium
   - Aggressive behavior by patient
   - Family distress and dissatisfaction
   - Importance of — consistent behavior!
     team approach!

Environment control

1. Excessive or NO light
2. Loud noises (TV, sitter on cell phone)
3. Stimulation (visitors, consultants, family)
4. Large clock/ calendar
5. Familiar objects, sounds smells
6. Do not ask for consent/ debate

Family

- Global brain dysfunction (blood products, poor quality fuel)
- Very common and poor prognosis
- Disinhibition of symptoms and emotions
- Environmental control
- Expressive/ supportive counseling!!! High distress

Pharmacological Management

- Haloperidol IV/ SC/ PO. Dose: ???.
- “loading (up to 5 mg/ dose q1h) and maintenance”
- “regular (2mg q 6h, etc) and breakthrough (q1-2h)”

Haloperidol

- Onset: 30- 60 min; dose 0.5- 5 mg, half life 18 hs, metabolized and into urine.
- Time to peak: oral 2-6hs; IM 20 min
- DPM blocker
- Extrapyramidal (less in autonomic neuropathy?), tardive diskynesia, NMS
- Q-T prolongation, more IV

Should every delirium be on regular haloperidol?

- Hyperactive and mixed YES!!
- In cancer 80 % are MIXED!!
- In PURE hypo no evidence, prn needed in case of change to mixed

Delirium

Different Settings, Different Patients

[Intervention Review]

Drug therapy for delirium in terminally ill adult patients

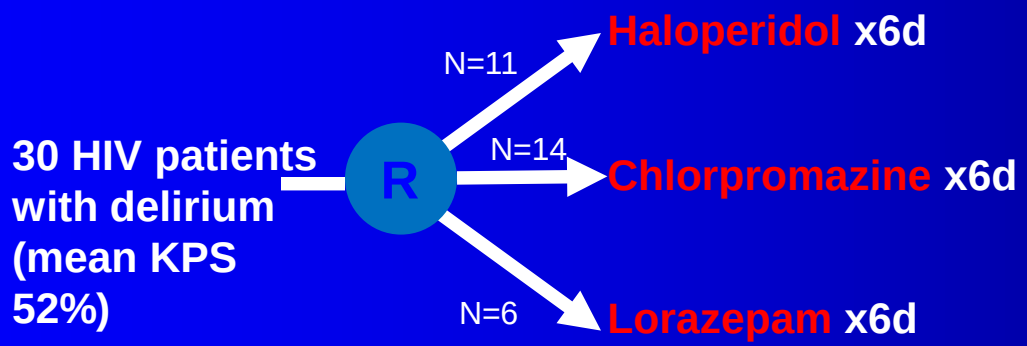
Bridget Candy[1], Kenneth C Jackson[2], Louise Jones[1], Baptiste Leurent[1], Adrian Tookman[1], Michael King[3]

There is limited evidence from clinical trials on the role of drug therapy for the treatment of delirium in terminally ill patients. The key feature of delirium is a decreased level of consciousness (awareness). People may experience impaired memory, thinking and judgement, and become disorientated. They may experience distressing hallucinations or delusions. It occurs frequently in patients with terminal illness, and may be caused by the illness itself or occur as a side effect of drug treatments for symptom management. Our search of the international literature for trials of drug therapies for the treatment of delirium in patients with terminal illness yielded one small study, and therefore it was not possible to assess the effectiveness of drug treatment options. It is hoped that this review will provide an incentive for further research.

Candy et al. *Cochrane Database* 2012

Haloperidol vs. Chlorpromazine vs. Lorazepam: HIV Patients

Double-blind, randomized controlled trial



Outcomes

- Delirium Rating Scale
- Mini-Mental State Examination
- Extrapyramidal Symptom Rating Scale
- Other Side Effects
- Karnofsky Performance Status
- Medical Status Profile

Breitbart et al. *Am J Psychiatry* 1996

Haloperidol vs. Chlorpromazine vs. Lorazepam: HIV Patients

TABLE 1. Drug Dosing Protocol for Treatment of Delirium in Hospitalized AIDS Patients

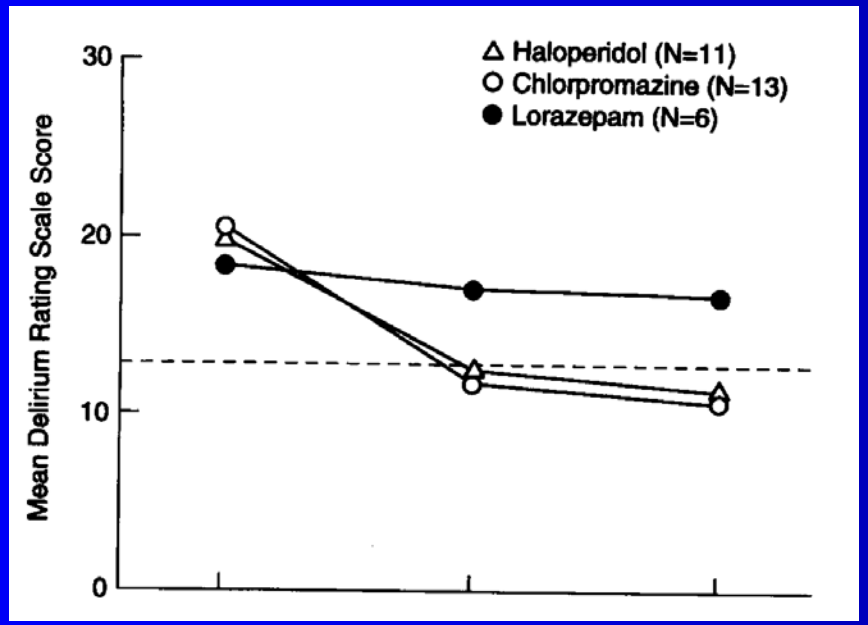
	Dose (mg/hour)					
	Haloperidol		Chlorpromazine		Lorazepam	
Dose Level	Oral	Intramuscular	Oral	Intramuscular	Oral	Intramuscular
1	0.25	0.125	10	5	0.50	0.20
2	0.50	0.50	20	10	1.00	0.50
3	1.00	0.50	40	20	1.50	0.70
4	2.00	1.00	80	40	2.00	1.00
5	2.50	1.50	100	50	2.50	1.25
6	2.50	1.50	100	50	2.50	1.25
7	2.50	1.50	100	50	2.50	1.25
8	5.00	3.00	200	100	4.00	2.00
9	5.00	3.00	200	100	4.00	2.00

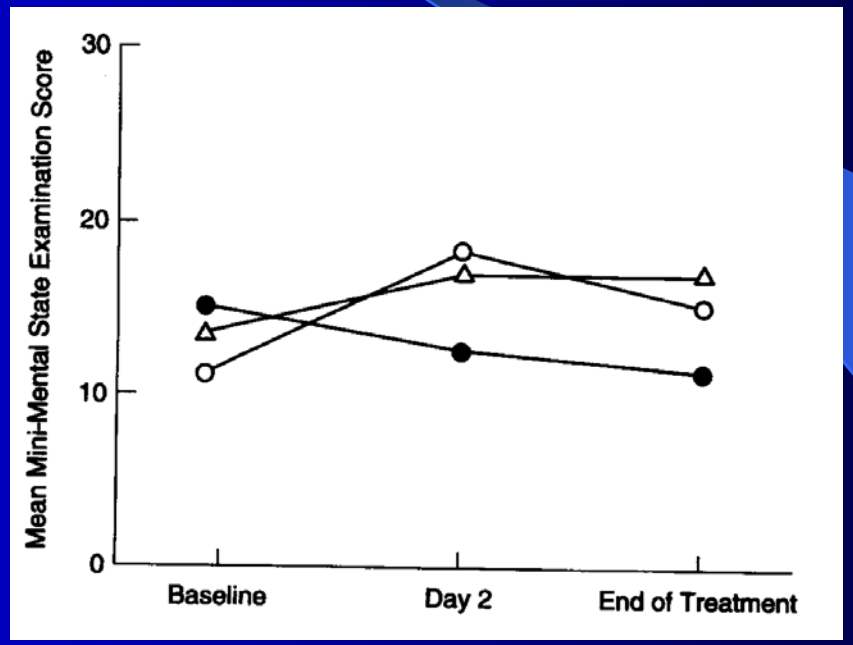
Day 1: Increase dose to next level every hour if DRS >13
Day 2-6: Give total dose from day 1, div BID

- **Mean drug doses in first 24 h**
  - Haloperidol 3.8 (2.4) mg
  - Chlorpromazine 50 (23.1) mg
  - Lorazepam 3 (3.6) mg
- **Mean maintenance drug doses**
  - Haloperidol 1.4 (1.2) mg
  - Chlorpromazine 36 (18.4) mg
  - Lorazepam 4.6 (4.7) mg

Breitbart et al. *Am J Psychiatry* 1996

Haloperidol vs. Chlorpromazine vs. Lorazepam: HIV Patients





- Improvement seen within 24 hours of treatment in haloperidol and chlorpromazine arms
- All 6 patients on lorazepam arm developed treatment limiting side effects (sedation, disinhibition, ataxia, increased confusion)

Breitbart et al. *Am J Psychiatry* 1996

Delirium RCTs

At a Glance

Study	Setting	Design	Findings
Breitbart 1996	HIV	DB-RCT H/C/L; N=30	H~C>L
Hu 2004	Med	OL-RCT H/O/X; N=175	H=O>X
Han 2004	Med	DB-RCT H/R; N=28	H~R
Kim 2010	Med	DB-RCT O/R; N=32	O~R
Tahir 2010	Med/Surg	DB-RCT Q/P; N=42	Q~P (AstraZeneca IIS)
Grover 2011	Med/Surg	SB-RCT H/O/R; N=74	H~O~R
Skrobik 2004	ICU	DB-RCT O/H; N=73	O~H (Eli-Lilly IIS)
Pandharipande 2007	ICU	DB-RCT D/L; N=106	D>L (Hospira IIS)
Riker 2009	ICU	DB-RCT D/M; N=375	D>M (Hospira study)
Reade 2009	ICU	OL-RCT D/H; N=20	D>H (Hospira, drug)
Devlin 2010	ICU	DB-RCT Q/P; N=36	Q>P (AstraZeneca IIS)