Sedation in the ICU-drugs, regimens of administration and monitoring

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PGIMER

22 September 2006.

Sedation in the ICU-why bother?

1.To relieve Dyspnea and intractable coughing

2.For amnesia during critical illness.

3.To manage agitated (delirious) patient from harming self and care-providers

4.To facilitate invasive management like ventilation and improve synchrony

5.To decrease VO_2 and VCO_2 (especially with cardiopulmonary compromise)

6. Unpleasant memories & ?PTSS

The yin of sedation.

Sedatives are commonly over-used.

Substituted as pharmacological restraints.

In a survey, <5% were agitated when assessed objectively. Likely to represent over-sedation.

Ely et al. JAMA 2003; 289(22):2983-91

Associated with

- prolonged ventilation duration
- long ICU stays
- cognitive impairment
- complications of critical care
  - critical care neuropathy
  - critical care myopathy (NM agents with steroids)
- increased cost of care
- complications may be missed
- ? Pain induced immuno-suppression

The yang of sedation.

Agitation is common in the ICU.

Pharmacological & physical measures commonly needed.

Agitation is associated with

- Serious self harm
- Injury to health care providers
- Asynchrony during ventilation
  - Barotrauma
  - Increased WOB
  - Hypoxia and decompensation

Some definitions…

AGITATION: Agitation is characterized by extreme arousal, irritability, excess motor activity driven by internal sense of discomfort such as disease, pain, anxiety and delirium.

Anxiety: A sustained state of apprehension with accompanying autonomic arousal in response to a real or perceived threat.

DELIRIUM: An acute, potentially reversible impairment of consciousness and cognitive function that fluctuates in severity.

PAIN: is an unpleasant sensory & emotional experience associated with actual or potential tissue damage

Delirium in the ICU.

Feature 1: acute onset of mental status changes or a fluctuating course.

and

Feature 2: inattention

and

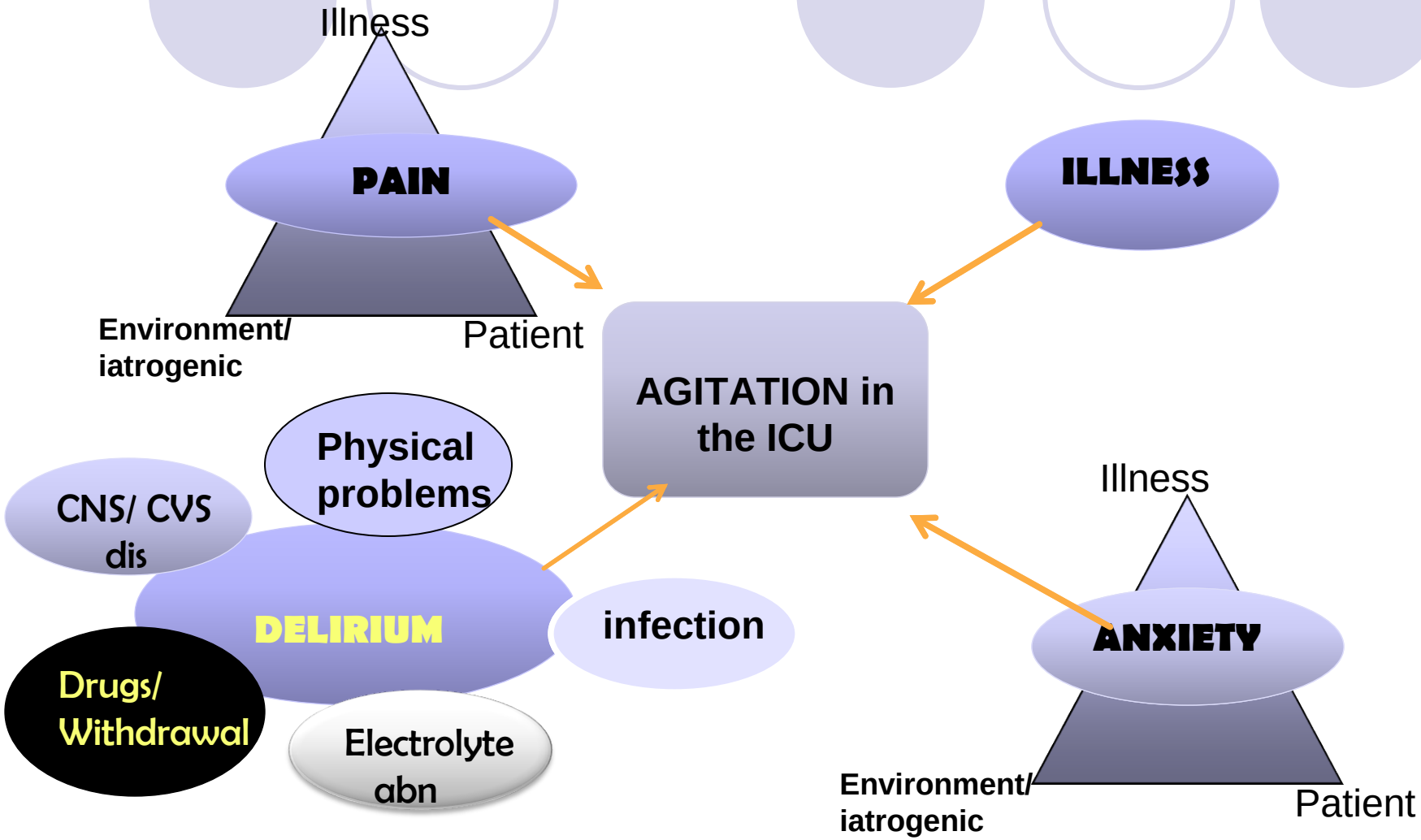
Feature 3: disorganized thinking

or

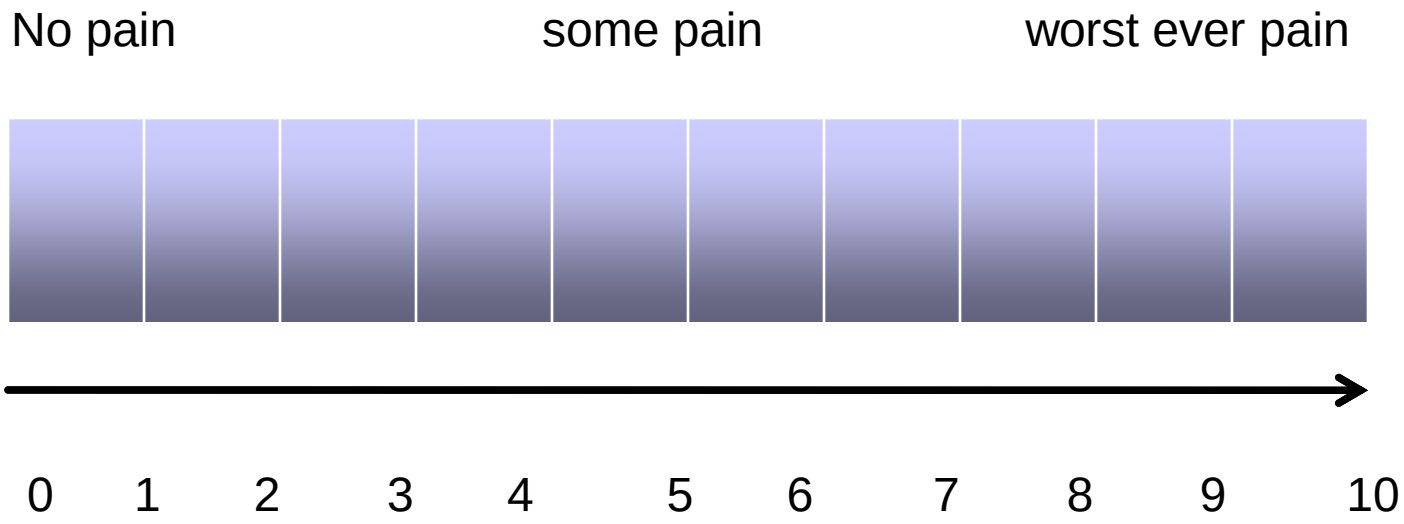
Feature 4: altered level of consciousness

= Delirium

Why agitation occurs in the ICU?



1.Unidimensional pain rating scales
Visual analog scale (for Pain)



Other methods of quantification:

1.Verbal rating scale (VRS)
2.Numeric rating scale (NRS)
3.FACES scale (non verbal, non-oriented)

Multidimensional pain rating scales

Mc Gill pain questionnaire

Wisconsin brief pain questionnaire

Less useful in the ICU

Behavioral pain rating scales

Pain-related behaviors (movement, facial expression, and posturing) and physiological indicators (heart rate, blood pressure, and respiratory rate) and the change in these parameters following analgesic therapy can be used.(Grade of recommendation B)

SCCM, ACCM. Crit Care Med 2002;30:123

Delirium in the ICU.

Extraordinarily common in intensive care. In patients on mechanical ventilation, >80% may be delirious.

Commonly under-diagnosed by care-providers. Agitation & hallucinations NOT required for diagnosis.

Hypoactive or mixed forms more common then hyper-active forms (which is easily recognized)

Age and pre-existing impairment are the most powerful risk factors.

Incidence is hence likely to increase

Confusion assessment method id an useful tool for recognition.

Psychoactive drugs including analgesics & sedatives are major risk factors

Delirium derived from Latin deliria (to be out of your furrow)

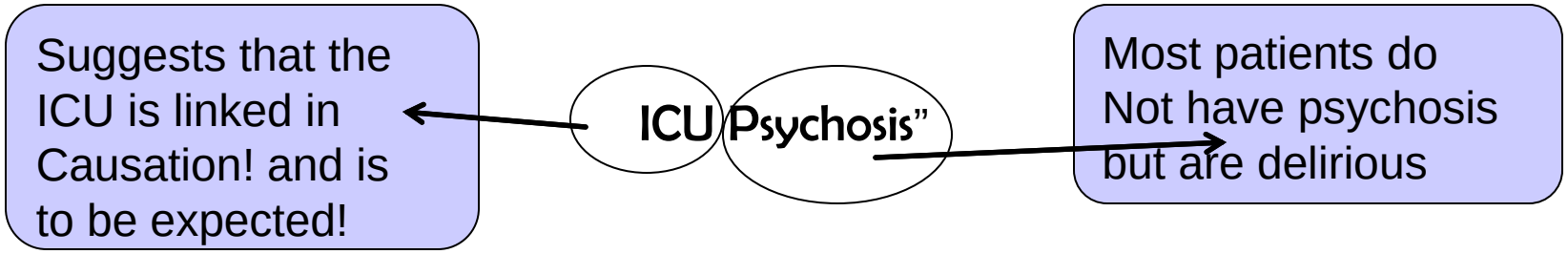
Traditionally, then lethargus (Greek for hypoactive) or hypoactive form has been under-recognized.

Missed in 66-84% of patients

Francis J. J Gen Intern Med 1990;5:65

Is an independent risk factor for increased morbidity, ICU stay and mortality.

ICU literature refers to delirium as "ICU Psychosis"

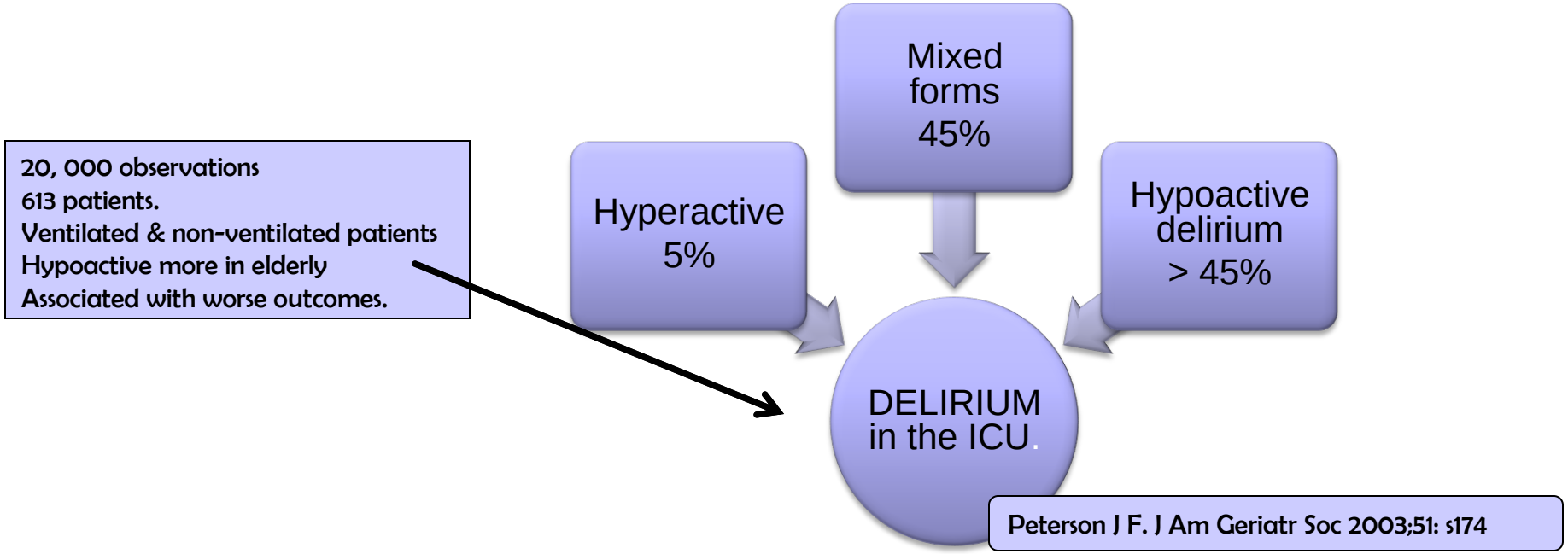


This term should thus be abandoned.

Currently, validated techniques for delirium recognition have changed the Perspective in the ICU.

These tools are as good as diagnosis by a geriatric psychiatric (in the hands of non-psychiatrists, including nurses, pharmacists)

The Society For Critical Care Medicine(SCCM), American College Of Critical Care Medicine(ACCM) recommends daily delirium monitoring in patients on Mechanical ventilation.



IATROGENIC/ENVIRONMENTAL

Sedative/ analgesic use
Immobilization (restraint, catheters)
TPN
Sleep deprivation
Malnutrition
Anemia (phlebotomy)

Delirium in the ICU

HOST FACTORS

Underlying co-morbidities(liver, renal , diabetes, hypertension)
Elderly
Pre-existing cognitive impairment/ dementia
Hearing/ vision impairment
Neurologic disease (stroke, seizure)
Alcoholism, smoking

ACUTE ILLNESS.

Severe sepsis
ARDS
MODS
Drug overdose/ illicit drugs
Nosocomial infection
Metabolic disturbance

Data on delirium & outcomes.

In non-ICU patients:

Mortality (in hospital) of 25-33% (independent)
Hazard ratio of 2.11
Prolonged hospital stay
3 times increased likelihood of discharge to a nursing home

Cusker et al. Arch Int Med 2002;162:457.
Francis & kapoor. Gen Intern Med 1990;5:65

In ICU patients:

Predictor of 6 month mortality
3 fold increase in death (multi-variate analysis)
Increased risk of dementia over 2-3 years.

Rockwood K. Age ageing 1999; 28:551
Rakhonen T. J Neurol Neurosurg Psychiatry 2000; 69:519

Delirium & survival

275 patients in a ICU (81.7% of whom had delirium)

Patients who developed delirium had higher 6-month mortality rates (34% vs 15%, P=.03)

Spent 10 days longer in the hospital than those who never developed delirium

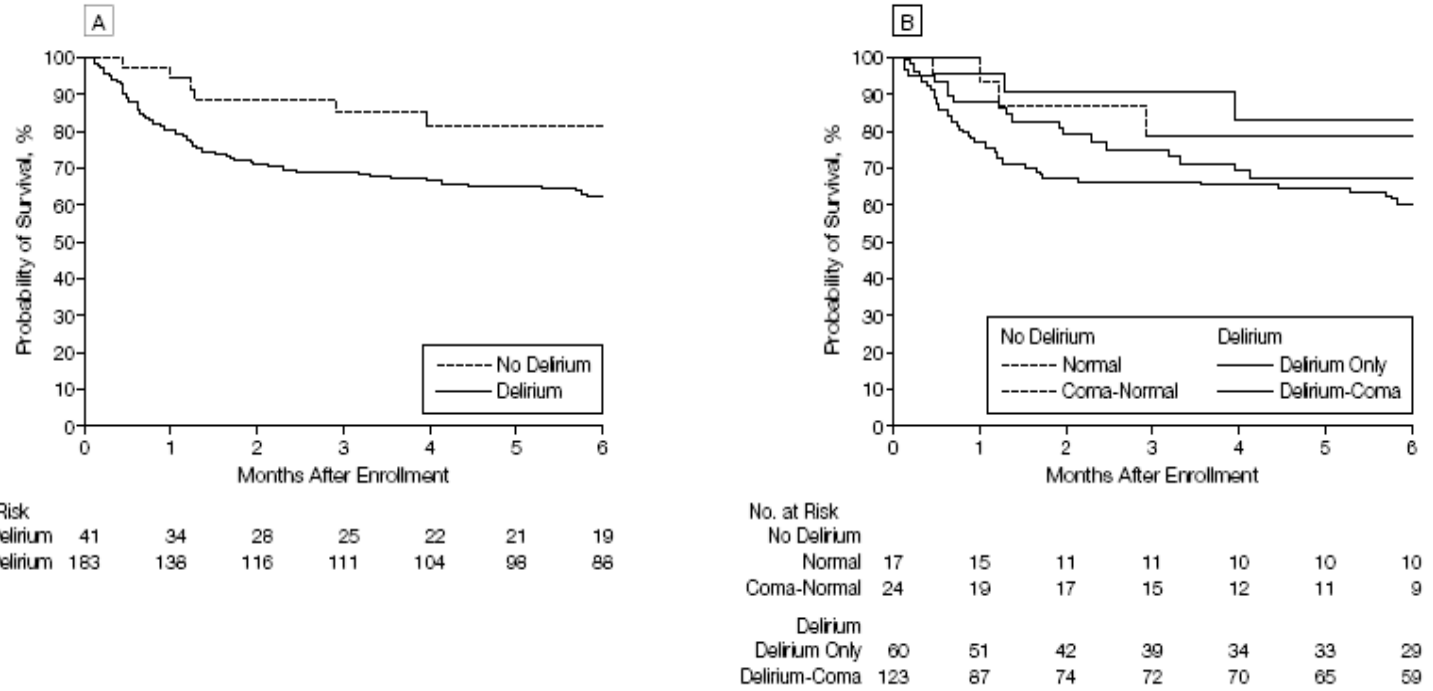
Independently associated with

1.higher 6-month (3.2; 95%CI1.4-7.7; P=.008) mortality
2.longer hospital stay (adjusted HR, 2.0; 95% CI, 1.4-3.0; P.001)
3.longer post-ICU stay (HR, 1.6; 95% CI, 1.2-2.3; P=.009)
4.fewer median days alive and without mechanical ventilation
5.higher incidence of cognitive impairment at hospital discharge (adjusted HR, 9.1; 95% CI, 2.3-35.3; P=.002).

Ely et al. JAMA 2004; 291:1753

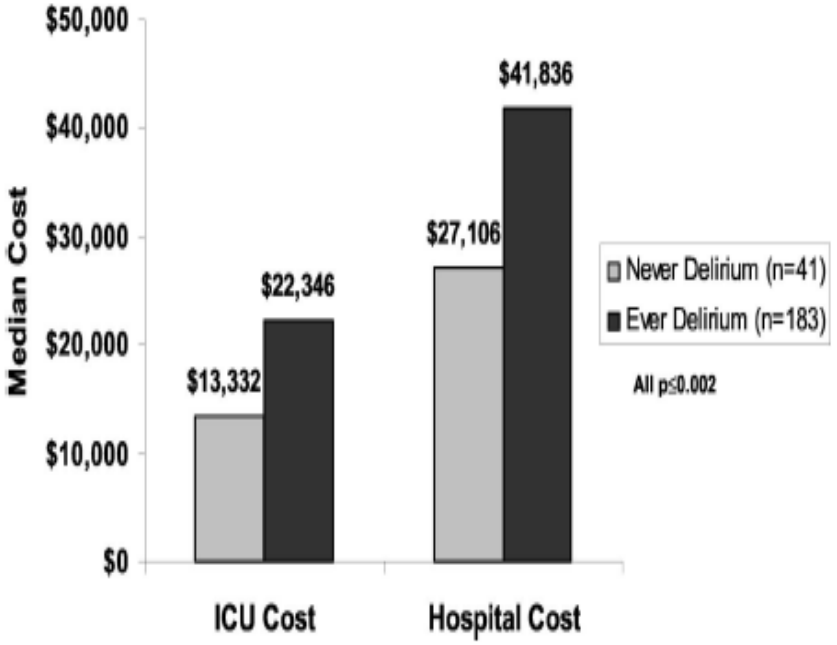
Delirium & survival

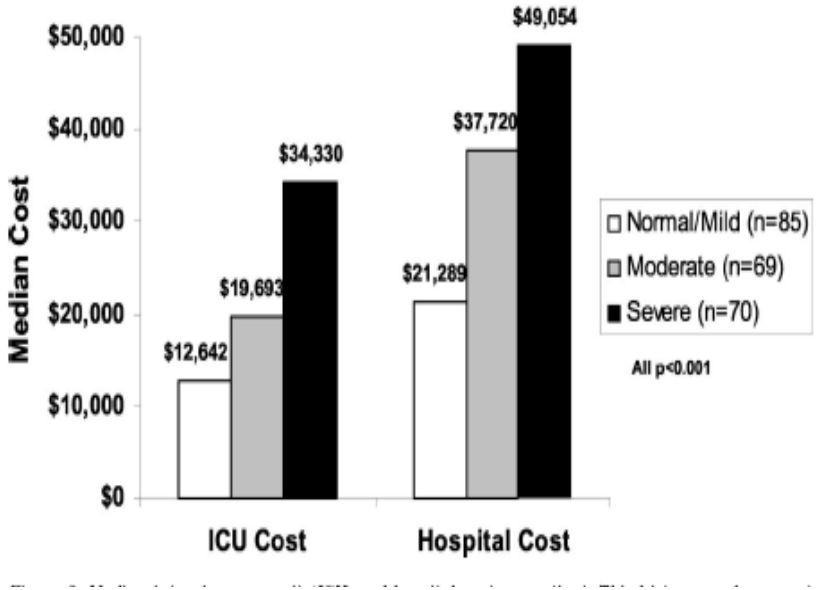
Figure 3. Kaplan-Meier Analysis of Delirium in the Intensive Care Unit and 6-Month Survival



Ely et al. JAMA 2004; 291:1753

Delirium & cost accrued





About 39% higher ICU costs & 31% higher hospital costs.

Individual increase in costs about $9000 per patient.

Milbrant E et al. Crit Care Med 2004; 32:955

Causes of agitation that require specific interventions

Potentially life threatening

1.Gas exchange: Hypoxemia/ Hypercarbia
2.Metabolic: Hypoglycemia/ Acidosis
3.Ventilator related: Endotracheal tube malposition/ Tension pneumothorax
4.Infection: Central nervous system infection/ Sepsis
5.Drug and alcohol related : Intoxication/ Withdrawal
6.Ischemia: Myocardial/ Intestinal/ Cerebral

Miscellaneous

7.Patient-ventilator dyssynchrony/ Inadequate flow rates/Excessive tidal volumes
8.Uncomfortable bed position
9.Fear/ Inability to communicate/ Sleep deprivation
10.Full bladder/ Nausea/ Need to defecate
11.Nicotine withdrawal
12.Drug side effects: Anticholinergic/ Paradoxical response to benzodiazepines

Agitation & delirium: an aide memoire for routine use

I WATCH DEATH
Infection
Withdrawal
Acute metabolic
Trauma/ pain
CNS pathology
Hypoxia
Deficiencies (B1, B12)
Endocrinopathies
Acute vascular
Toxins/ drugs
Heavy metals

DELIRIUM
Drugs
Electrolyte abnormalities
Lack of drugs
Infection
Reduced sensory input
Intracranial problem
Urinary retention & fecal impaction
Myocardial infarction

Drugs that can cause Delirium

Anti-arrhythmics

- Lidocaine
- Mexilitine
- Quinidine

Antibiotics: Penicillin

Anti-cholinergics: atropine

- Anti-histaminics

Beta-blockers: propranolol

Narcotics: meperidine

Morphine

Pentazocine

QUANTIFICATION OF AGITATION: END-POINTS FOR TITRATION

The Ramsay Sedation Scale	
1	Anxious and agitated or restless, or both
2	Co-operative, oriented and tranquil
3	Responsive to commands only
4	Brisk response to light glabellar tap or loud auditory stimulus
5	Sluggish response to light glabellar tap or loud auditory stimulus
6	No response to light glabellar tap or loud auditory stimulus

The Sedation Agitation Scale		
7	Dangerously agitated	Pulls at ET, tries to remove catheters, climbs over rail, strikes at staff, thrashes side to side
6	Very agitated	Does not calm despite frequent verbal reminding of limits, requires physical restraints, bites ET
5	Agitated	Anxious or mildly agitated, attempts to sit up, calms down on verbal instructions
4	Calm, co-operative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
2	Very sedated	Arouses to physical stimuli but does not communicate or follow commands or move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

The Richmond Agitation Sedation Scale

+4	Combative-Combative, violent, immediate danger to staff
+3	Very agitated-pulls or removes tubes or catheters; aggressive
+2	Agitated-frequent, non-purposeful movements, fights ventilator
+1	Restless-anxious, apprehensive but movements not aggressive or vigorous
0	Alert and calm
-1	Drowsy- not full alert, but has sustained(> 10 second) awakening (eye contact) to voice.
-2	Light sedation-drowsy, briefly (<10 second) awakens to voice or physical stimulation
-3	Moderate sedation- movement or eye opening (but not eye contact) to voice
-4	Deep sedation-no response to voice, but movement or eye opening to physical stimulation
-5	Unarousable-no response to voice or physical stimulation.

HOW TO SCORE RASS ?

1. Observe patient. Is patient alert and calm (score 0)?
Does patient have behavior that is consistent with restlessness or agitation (score 1 to 4 using the criteria listed)?

2. If patient is not alert, in a loud speaking voice state patient's name and direct patient to open eyes and look at speaker. Repeat once if necessary. Can prompt patient to continue looking at speaker.
Patient has eye opening and eye contact, which is sustained for more than 10 seconds (score 1).
Patient has eye opening and eye contact, but this is not sustained for 10 seconds (score 2).
Patient has any movement in response to voice, excluding eye contact (score 3).

3. If patient does not respond to voice, physically stimulate patient by shaking shoulder and then rubbing sternum if there is no response to shaking shoulder.
Patient has any movement to physical stimulation (score 4).
Patient has no response to voice or physical stimulation (score 5).

The Richmond Agitation–Sedation Scale

Validity and Reliability in Adult Intensive Care Unit Patients

Curtis N. Sessler, Mark S. Gosnell, Mary Jo Grap, Gretchen M. Brophy, Pam V. O'Neal, Kimberly A. Keane, Eljim P. Tesoro, and R. K. Elswick

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine; School of Nursing and Nursing Service; Department of Pharmacy; and Department of Biostatistics, Virginia Commonwealth University Health System, Richmond, Virginia

Curtis et al. Am J Respir Crit Care Med 2002 ;166:1338–1344.

Excellent inter-rater reliability(0.956, lower 90% CI 0.948; K=0.73, 95% CI 0.71-0.75) with five investigators & 192 observations (phase 1)

Robust (r =0.922–0.983) (K=0.64–0.82) was demonstrated for patients with and without mechanical ventilation, and with and without sedative medications

Good co-relation with Ramsay & Riker's scales. In phase 2, good reliability with investigator & 27 trainees in 101 observations.

Good predictor of changes with time & co-related with other scales (BSE)

Ely et al. JAMA 2003;289:2983

The CAM-ICU

Until recently, the recognition of delirium in the ICU was limited by the non-verbal state of most patients.

The CAM-ICU is a delirium measurement tool the has recently been developed

Administered by a nurse

Takes < 1-2 minutes

Is 98% as accurate for detecting delirium (compared to DSM-4)

Ely E W, Inouye S K. JAMA 2001;286:2703.

Confusion assessment method for the intensive care unit.

1 Acute onset or fluctuating course absent present

a.Is there an evidence of an acute change in mental status from baseline?

or

b. Did the abnormal behavior fluctuate over the last 24 hours, ie, increase and decrease in severity as evidenced by the sedation scale (RASS, GCS , previous delirium assessment)

2. Inattention absent present

Did the patient have difficulty focusing attention, as evidenced by a score <8 on auditory or visual component of the attention screening examination

3. Disorganized thinking absent present

Is there an evidence of disorganized or incoherent thinking, as evidenced by incorrect answers to >2/4 questions or inability to follow the below?

Set A	**Set B**
Will a stone float on water?	Will a leaf float on water?
Are there fish in the sea?	Are there elephants in the sea?
Can 1 pound weigh more than 2 pounds?	Do 2 pounds weigh more than 1 pound?
Can you use a hammer to pound a nail?	Can you use a hammer to cut wood?

Other

Are you having any unclear thinking?

Hold up this many fingers (hold up 2 fingers in front of the patient)

Now do the same thing with the other hand (do not repeat the number of fingers)

4. Altered level of consciousness. Absent present

Is the patient level of consciousness anything other alert, such as vigilant, lethargic or stuporous (RASS <0)

ALERT: spontaneously fully aware of environment and interacts appropriately

VIGILANT: hyperalert

LETHARGIC: drowsy but easily aroused; unaware of some elements in the environment or spontaneously not interacting with the interviewer; becomes fully aware and appropriately interactive when prodded minimally

STUPOROUS: becomes incompletely aware when prodded ; can be aroused only by strong and repeated stimuli; and as soon as the stimuli ceases, lapses back into unresponsive state

Overall assessment: presence of features 1 & 2 and either feature 3 or 4? Yes no

Can these scales be widely implemented?

Large-scale implementation of sedation and delirium monitoring in the intensive care unit: A report from two medical centers*

Brenda Truman Pun, RN, MSN, ACNP; Sharon M. Gordon, PsyD; Josh F. Peterson, MD, MPH;
Ayumi K. Shintani, PhD, MPH; James C. Jackson, PsyD; Julie Foss, RN, MSN;
Sharon D. Harding, RN, MSN, CCRN; Gordon R. Bernard, MD; Robert S. Dittus, MD, MPH; E. Wesley Ely, MD, MPH

711 admitted to the medical ICUs for >24 hrs and followed over 4,163 days during a 21-month study period.

With minimal training, the compliance of bedside nurses using sedation and delirium instruments was excellent. Agreement of data from bedside nurses and a reference-standard rater was very high for both the sedation scale and the delirium assessment over the duration of this process-improvement project.

The two most-often-cited barriers to implementation were physician buy-in and time.

Crit Care Med 2005; 33:1199 –1205

Limitations of behavior observation scales

1.Require clinical judgment (and hence extensive training)

2.Require institutional validation

3.Little value in those with cognitive dysfunction disorders

4.Not useful in those on neuromuscular blockers

5.Cannot measure depth of sedation in those who are unarousable

What is new in sedation quantification?

Bispectral index monitors, using EEG signals, have been shown to accurately correlate with depth of sedation with non-dissociative general anesthesia in the operating room setting among adults and children

Theoretically appealing but is of unproven role

Does not have discriminating power to quantify sedation in intubated patients.

Gill M. Am J Emerg Med 2004;22:76-82.

Co-relates with but is no better than conventional sedation scaling

Agrawal D. Annals of Emerg med 2004;43:247

The role of BERA is experimental.

SOME GENERAL MEASURES FOR AGITATION:

Reassurance (for fear, anxiety)

Writing board if unable to communicate

Re-positioning the patient

Repositioning ET > 2 cms from carina

Treatment of withdrawal state

Optimization of ventilator settings

Correcting metabolic derangements

Catheterization

Music therapy

Hypnosis

Does primary prevention with general methods prevent delirium?

Data available for non-ICU patients only.

The available evidence is contradictory.

40% reduced risk in 852 general medical patients> 70 years (15% vs 9.9%)

Inouye et al. N Engl J Med 1999; 340: 669.

Only in those without dementia.

Marcantanio et al J Am Geriatr Soc 2001; 49:516.

No benefit at all

Cole M G et al. Can Med Assoc J 2002; 167:753

Costs nothing
Widely applicable
Intitutive
Can be used widely

HOW IS THE USE OF SEDATIVES & ANALGESICS DIFFERENT IN THE ICU?

1.Advanced age

2.Malnutrition

3.Obesity

4.Altered renal & liver function

5.Effects of underlying disease

6.Polypharmacy

7.Slowed metabolism

8.High body water/ increased volume of distribution

9.Decreased protein binding

Opiates in the ICU.

Pharmacologic therapies include opioids, NSAIDs and acetaminophen.

The selection of an agent depends on its pharmacology and potential for adverse effects.

Desirable attributes include
1.rapid onset,
2.ease of titration,
3.lack of accumulation of the parent drug or its metabolites, and
4.low cost

Side-effects are pharmacodynamic. Include
1.Respiratory depression
2.Hypotension
- Sympatholysis (Volume depleted)
- Vagally-mediated bradycardia
- Histamine release (morphine)

3.Ileus
4.Depression of sensorium

Currently Fentanyl infusion is preferred over Morphine (if continuous infusion is to be used)

Use of remifentanil is associated with better hours of optimal sedation, fewer infusion changes, shorter mechanical ventilation time & extubation time

Dahaba, **Anesthesiology, 101:640–646, 2004**

Prevention of pain more effective than treating it.

Continuous or scheduled intermittent bolus better than prn dosing

<u>Other routes of delivery:</u>

1.Patient controlled analgesia
- cognition
- hemodynamic reserve
- previous opioid use.

2. Transdermal patch.

	Morphine	Fentanyl	Meperidine	Methadone
Starting dose	2-5 mg	25-50 μg	20-50 mg	5-10 mg
Onset	10 min	0.5-1 min	3-5 min	10-20 min
Duration	4 h	0.5-1 h	1-4 h	6-24 h
Metabolism	Hepatic			
Elimination	Renal			
Anxiolysis	+	++	++	+
Analgesia	++++			
Hypnosis	No reliable effect	No reliable effect	No reliable effect	No reliable effect
Amnesia	No reliable effect	No reliable effect	No reliable effect	No reliable effect
Sz threshold	No effect	May decrease	No effect	No effect
Dyspnea	++++			
CV effect	Venodilatation			
Respiratory effect	Hypoventilation			
Side effects	N/V, ileus, itching	N/V, ileus, itching, seizures	N/V, ileus, itching seizures	N/V, ileus, itching

Protocol For Haloperidol Use

In the ICU, large doses are required

Starting doses are 2-10 mg (5 mg) bolus over 5-10 minutes. Repeated every 20 minutes till end-point achieved.

25% of the cumulative dose is given q6 hourly.

In the non-ICU setting, the starting dose is 0.5-1 mg oral or parenterally every 20 minutes till en-point.

The basis is to block 60% of the D2 receptor while avoiding side-effects associated with complete D2 blockade.

Once calm, smaller doses can be used.

Available parenteral preparations of Haloperidol.

Depidol 1ml(50 mg/ml)	Torrent Rs. 110.00
Seronorm 5 mg(1 ml)	Sun Pharma Rs.4.85
Serenase 5 mg/ ml(5 1 ml)	RPG Life Sciences Rs. 25.00

Estimated cost with the given regimen & use< 25 mg/day is Rs. 25.00

Typical adverse effects of haloperidol include:

1.Hypotension
2.Acute dystonias
3.Extra-pyramidal side-effects
4.Laryngeal spasm
5.Malignant hyperthermia
6.Glucose & lipid dysregulation
7.Anticholinergic side-effects
8.Torsade de pointes arrhythmia

Adverse effects are rare and these agents are usually well tolerated

ECG monitoring of QT_c when large doses are used (in ICU)

What is the data on the newer anti-psychotics on Delirium in the ICU?

Newer agents include atypical agents like risperidone, quetapine and olanzapine

Rationale is the possible antagonism of other neurotransmitters also.

Adequately powered RCT's not available.

All agents are associated with significant side-effects.

At present, there is no data for routine use of these agents.

	Midazolam	Lorazepam	diazepam
Starting dose	1-2 mg	.5-1 mg	5-10 mg
Onset	.5-2 min	3-5 min	1-3 min
Duration action	2 h	6-10 h	1-6 h
Metabolism	Hepatic	Hepatic(age, liver disease less influence)	Hepatic
Elimination	Renal	Renal	Renal
Anxiolysis	++++	++++	++++
Analgesia	No	No	No
Hypnosis	++++	++++	++++
Amnesia	++++	++++	++++
Seizure threshold	+++	++++	+++
Dyspnea	+	+	+
CV effect	Venodilatation		
Respiratory depression	Hypoventilation		
Side effects	Paradoxical agitation		

Continuous infusion or intermittent bolus?

INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION

DAILY INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION

JOHN P. KRESS, M.D., ANNE S. POHLMAN, R.N., MICHAEL F. O'CONNOR, M.D., AND JESSE B. HALL, M.D.

128 adult patients who were receiving mechanical ventilation and continuous infusions of sedative drugs in a medical ICU.

Median duration of mechanical ventilation was 4.9 vs 7.3 days (P=0.004),

Median length of stay in ICU was 6.4 vs 9.9 days (P=0.02).

Complications (e.g., removal of the endotracheal tube by the patient) occurred in three of the in the intervention group (4 %) and four of the patients in the control group (7%, P=0.88).

Daily interruption of sedative infusions and complications of critical illness in mechanically ventilated patients*

William D. Schweickert, MD; Brian K. Gehlbach, MD; Anne S. Pohlman, RN, MSN; Jesse B. Hall, MD; John P. Kress, MD

Crit Care Med 2004; 32:1272–1276

Available preparations of Midazolam

Midaz 10 ml vial	NPIL Rs.52.95
Sedoz 10 ml vial	Claris life sciences Rs. 53.00
Fulsed 10 ml	Ranbaxy Rs.60.40
Mezolam 10 ml	Neon Labs Rs.54.00
Midapic 10 ml	Rusan HC Rs.50.00

Estimated cost of therapy: 5 mg/hr= 120 mg/day
Rs.600/ day

Available preparations of Lorazepam

Lopez
2 ml amp(1 ml=2 mg)

Calmese

10 2 ml

Intas
Rs.15.00

Themis

Rs 118

Estimate cost of therapy(at 4 mg/ 3hrly=30 mg/ day)
<Rs 100/ day

A case for Lorazepam in the ICU.

NOT metabolized by the CYP450 system- less of drug interactions.

Less subject to toxicity in hepatic dysfunction.

No active metabolites

Less expensive (10 times)

Compared with Midazolam, sedation targets met more often & earlier recovery (data conflicting)

High doses can cause high AG acidosis because of accumulation of propylene glycol.

Propofol

The active ingredient in Propofol is 2,6-diisopropylphenol in 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide.

Disodium EDTA (0.05 mg/ml) or sodium metabisulfite (0.25 mg/ml) is added to inhibit bacterial growth.

Is hepatically modified & renally excreted

Key benefits include:
1.Rapid onset & offset of action.
2.Easy titration
3.Metabolism independent of hepatic & renal function
4.Sedative-hypnotic with anxiolytic & amnestic properties
5.Is also a bronchodialtor, anti-epileptic,muscle relaxant and anti-oxidant.

Available preparations of Propofol

Freseofol	Fresenius Kabi
50 ml(I ml=10 mg)	Rs. 388
Profol 1%	Claris Lifesciences
50 ml	Rs.350.00
100 ml	Rs.600
Cleofol	Themis
20 ml	Rs. 150.00(500 mg=Rs375)
Rofol	Neon labs
50 ml	Rs.351.00

Estimated cost of therapy (at) 1 mg/ kg/hr infusion (after 0.3 mg/kg bolus)
= 2.5 vials (Rs. 875.00)
At maximum doses(3 mg/kg/hr, often required)=Rs.2520.00

Problems with Propofol

1.Hypotension

2.Hypertriglyceridemia

3.Sepsis due to contamination

4.Pancreatitis

5.Metabolic acidosis

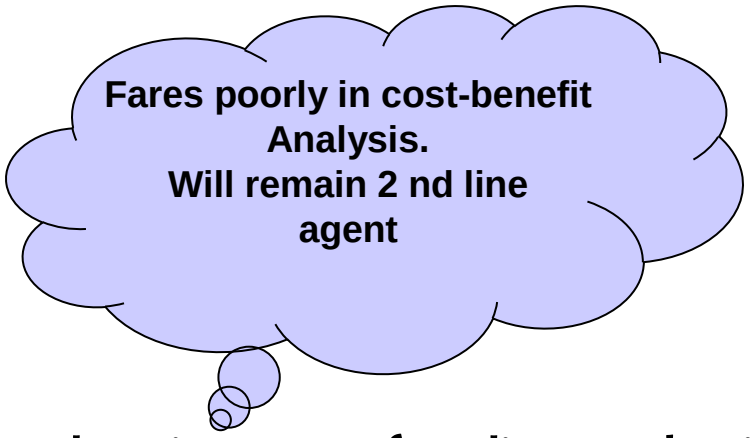
6.Adrenal insufficiency

7.Immune dysfunction

8.PRIS

9.Is very expensive

10.Practically no benefit over Midazolam in terms of earlier extubation and shorter stay.



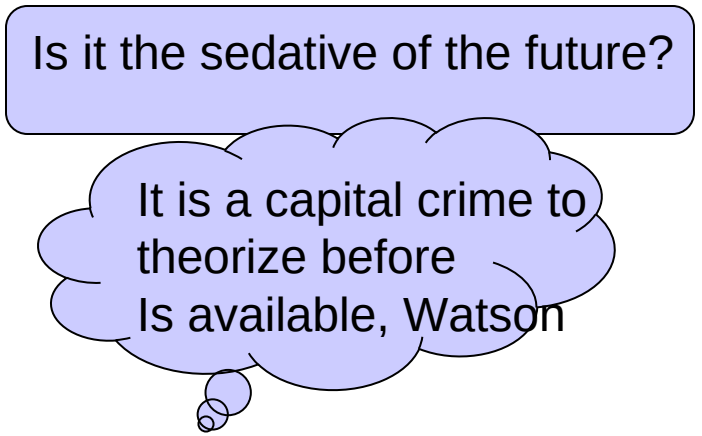
Role of Dexmedetomidine

Is an α2 agonist.

Increasing role, especially in post-operative patients

Advantages include

1. Maintenance of respiratory drive
2. Rapid awakenings
3. Analgesia
4. Amnesia
5. Good hemodynamic tolerance
6. Decreased requirement for other medications



Propofol infusion syndrome (PRIS)

PRIS defined as the occurrence of acute bradycardia resistant to treatment and progressing to asystole associated with Propofol infusion.

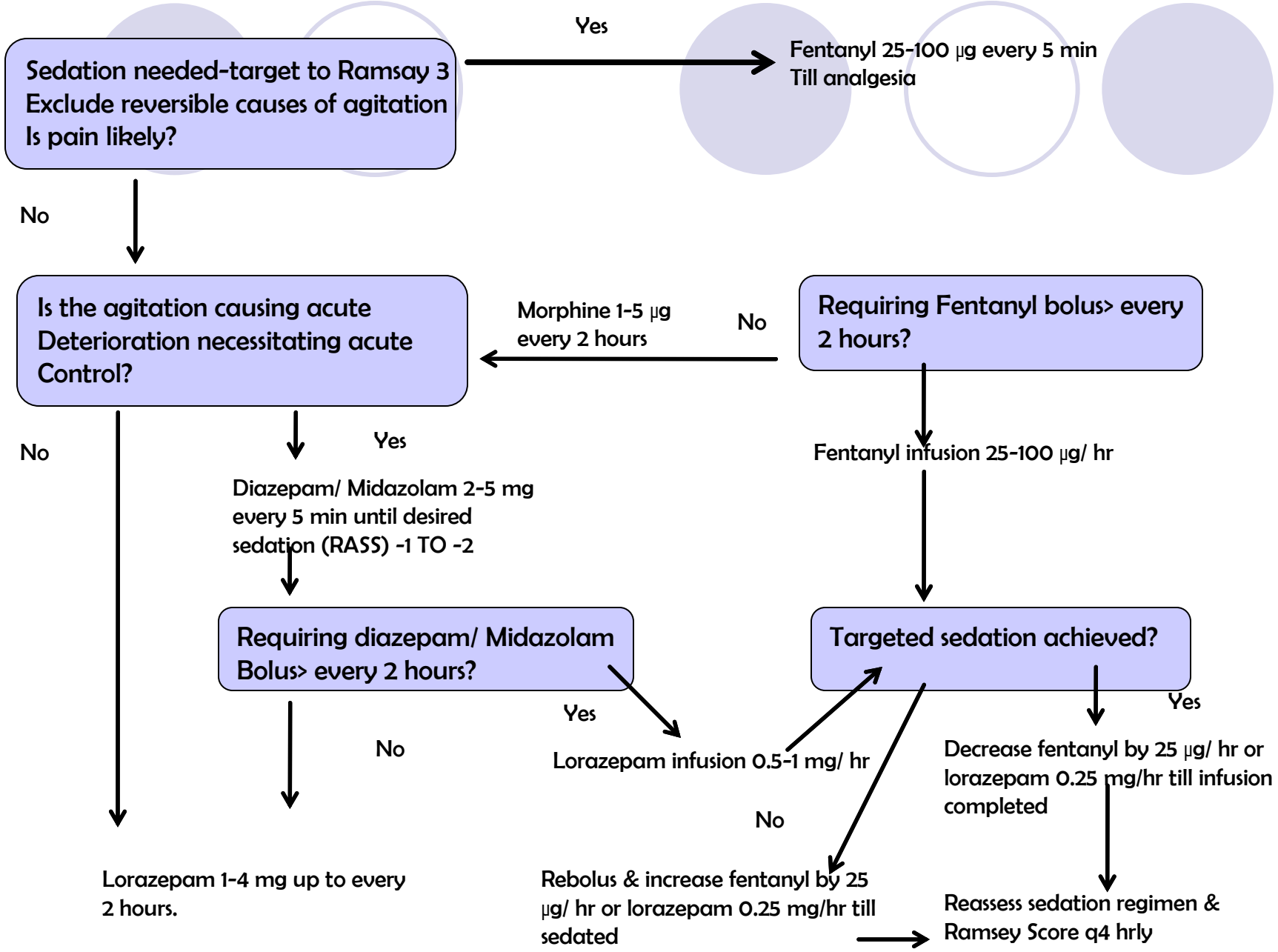
Bradycardia has to be combined with lipaemic plasma, fatty liver enlargement, metabolic acidosis with base excess<10mmol/l, rhabdomyolysis or myoglobinuria

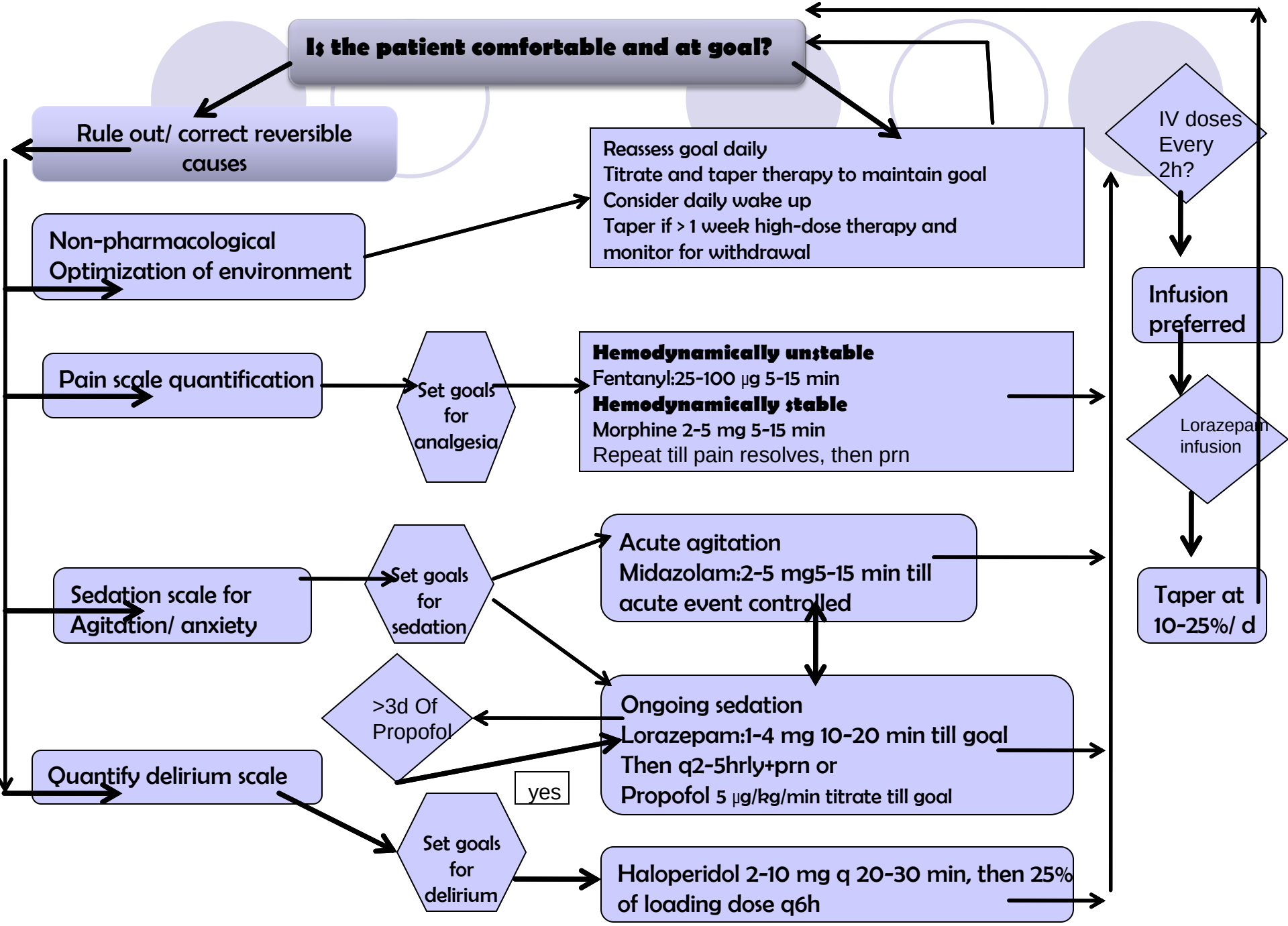
The syndrome usually leads to fatal cardiac and renal failure (24 children & 14 adults).

Identified risk factors are
1.airway infection,
2.Severe head injury,
3.high-dose long-term sedation for more than 48 h at more than 5 mg/kg per hour, increased catecholamine and
4.Increased glucocorticoid serum levels and
5.low energy supply

The infusion rates described in publications reporting on Propofol have used upto 44.2 mg/kg/hr.

Management includes stopping drug, dialysis, carbohydrates & supportive care


Sedation needed-target to Ramsay 3
Exclude reversible causes of agitation
Is pain likely?
Yes
Fentanyl 25-100 µg every 5 min
Till analgesia
No
Is the agitation causing acute
Deterioration necessitating acute
Control?
Morphine 1-5 µg
every 2 hours
No
Requiring Fentanyl bolus> every
2 hours?
No
Yes
Diazepam/ Midazolam 2-5 mg
every 5 min until desired
sedation (RASS) -1 TO -2
Fentanyl infusion 25-100 µg/ hr
Requiring diazepam/ Midazolam
Bolus> every 2 hours?
Targeted sedation achieved?
Yes
No
Yes
Lorazepam infusion 0.5-1 mg/ hr
Decrease fentanyl by 25 µg/ hr or
lorazepam 0.25 mg/hr till infusion
completed
No
Lorazepam 1-4 mg up to every
2 hours.
Rebolus & increase fentanyl by 25
µg/ hr or lorazepam 0.25 mg/hr till
sedated
Reassess sedation regimen &
Ramsey Score q4 hrly


Is the patient comfortable and at goal?
Rule out/ correct reversible causes
Reassess goal daily
Titrate and taper therapy to maintain goal
Consider daily wake up
Taper if > 1 week high-dose therapy and monitor for withdrawal
Non-pharmacological Optimization of environment
IV doses Every 2h?
Infusion preferred
Pain scale quantification
Set goals for analgesia
Hemodynamically unstable
Fentanyl:25-100 µg 5-15 min
Hemodynamically stable
Morphine 2-5 mg 5-15 min
Repeat till pain resolves, then prn
Lorazepam infusion
Sedation scale for Agitation/ anxiety
Set goals for sedation
Acute agitation
Midazolam:2-5 mg5-15 min till acute event controlled
Taper at 10-25%/ d
>3d Of Propofol
Ongoing sedation
Lorazepam:1-4 mg 10-20 min till goal
Then q2-5hrly+prn or
Propofol 5 µg/kg/min titrate till goal
Quantify delirium scale
yes
Set goals for delirium
Haloperidol 2-10 mg q 20-30 min, then 25% of loading dose q6h

CONCLUSIONS

Sedatives are commonly (over)used in the ICU.

Pharmacokinetics varies widely from other arenas.

Structured approach to agitation (like hypoxemia) required.

Adequate sedation begins with adequate analgesia & appropriate general measures.

Evaluation of sedation efficacy by scales (RASS) regularly is useful & simple
Protocol driven sedation improves outcomes.

Delirium (hypoactive) is common and missed. CAM-ICU scale useful adjunct

Downward titration protocols after 48 hours must irrespective of bolus or continuous infusion strategies.

For the latter strategy, daily interruption & re-starting at half the dose useful