

Approach to agitated patient in ICU

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Agitation

- Psychomotor disturbance characterized by a marked increase in both motor and psychological activities, often accompanied by a loss of control of action and disorganization of thought
- Driven by internal sense of discomfort such as disease, pain, anxiety and delirium

Incidence

- Agitation - 16 % of mechanically ventilated medical ICU patients
- 50 % of medical – surgical ICU patients receiving and not receiving mechanical ventilation

Jeffery C Woods et al, Intensive Care Med (2004); 30:1066–1072

Samir Jaber et al, Chest (2005); 128:2749–2757

Causes

Life threatening

- Gas exchange ($\downarrow pO_2 \uparrow pCO_2$)
- Metabolic (hypoglycemia, acidosis)
- Infection
- Drug/alcohol
- Ischemia
- Hypotension

Non life threatening

- Ventilator asynchrony
- Fear/anxiety/pain
- Inability to communicate
- Full bladder
- Need to defecate
- Bed position
- Delirium and drug side effects (paradoxical BZDs & anticholinergics)

Independent risk factors

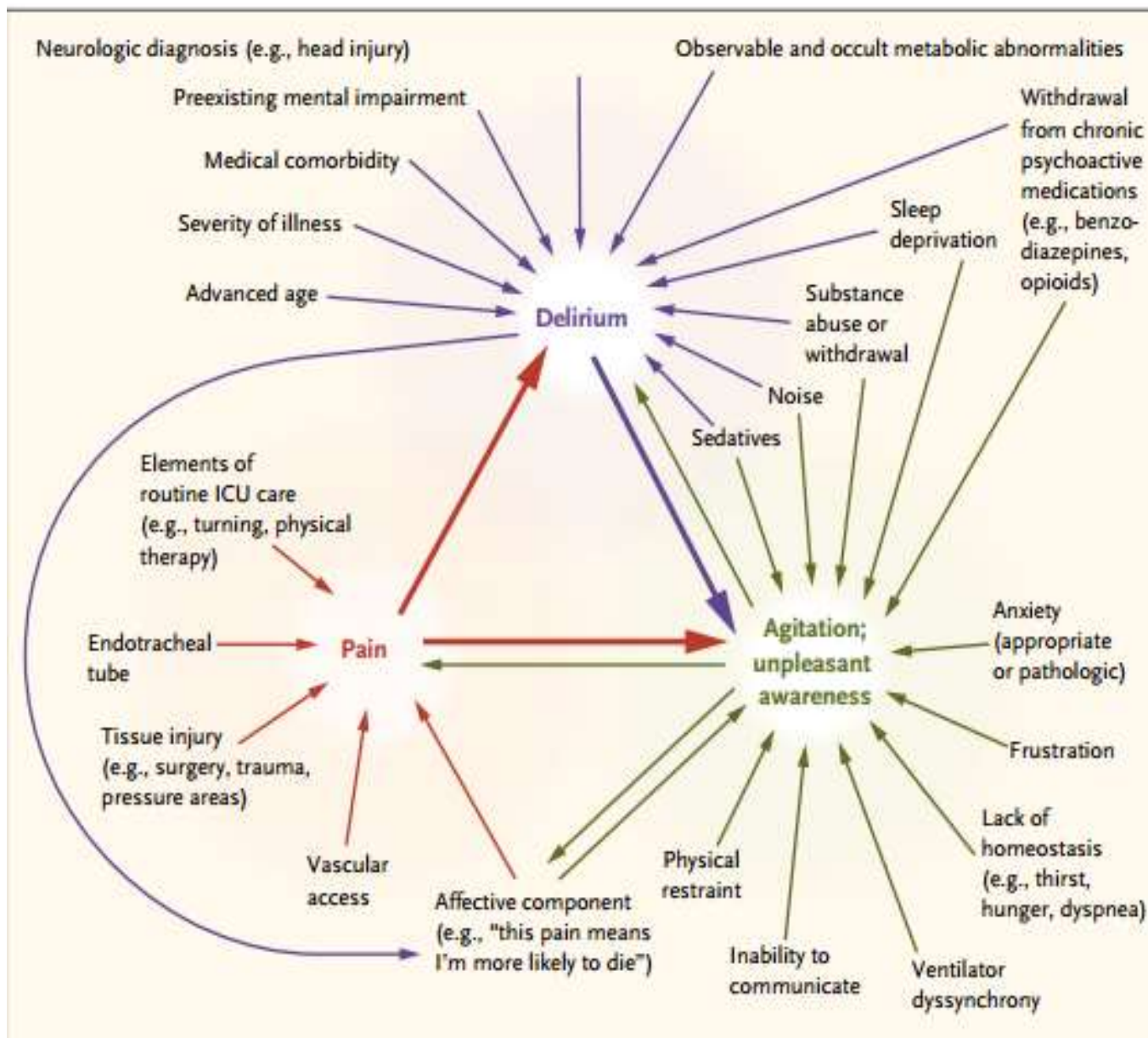
	Odds ratio	CI
Sepsis	2.61	1.03–6.58
Alcohol abuse	3.32	1.12–10.00
Body temperature $\geq 38^{\circ}$ C	4.52	1.80–11.49
Sodium level ≤ 134 mmol/L	4.87	1.58–14.99
Sodium level ≥ 143 mmol/L	4.95	1.95–12.54
Psychoactive drug user	5.63	1.32–23.70
Use of sedatives in 48 h before onset of agitation	4.03	1.62–10.40

Independent risk factors

	Odds ratio	CI
Younger age	1.51	1.18-1.93
Admitted from outside hospital	2.66	1.17-6.04
Marijuana use	7.94	1.82-34.73
Lower pH	1.62	1.18-2.22
PaO ₂ /FiO ₂ ratio < 200mm Hg	1.81	1.16-2.84

Consequences

- Patient-ventilator dysynchrony
- Increased oxygen consumption
- Inadvertent device and catheter removal
- Compromise care
- Increase length of ICU stay, costs
- Unpleasant memories to posttraumatic stress disorder on long term



Agitation

- Pain, anxiety, and delirium are the most common causes of agitation that require medication
- It is critical to distinguish among them because each requires specific treatment

Agitation

Treatment of agitation that does not address the underlying cause can incite or prolong delirium, whereas successful treatment or responsiveness to the underlying cause can reduce sedation use and can improve clinical outcomes

e.g., benzodiazepine given for agitation due to pain

Pain

- “Unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”
- Pain is a significant problem. Upto 82% of ICU discharged patients remembered pain due to ET tube
- Upto 72% of patients classified their overall pain in the ICU as moderate to severe

Pain



Neuropathic

Acute

Chronic

Underlying illness

Surgical procedures

Multiple arterial or venous blood draws

Dressing changes

Phlebitis

Chest drain related

Invasive devices like central lines, NG tube

Foleys catheters & mechanical ventilation

Pain

- Increased circulating catecholamines
- Arteriolar vasoconstriction, impair tissue perfusion, and reduce tissue-oxygen partial pressure
- Catabolic hyper metabolism
- Impair wound healing
- Suppresses NK cell activity
- Reduction in neutrophil phagocytic activity

Anxiety

- Autonomic excitability, fearful withdrawal, nervousness, and increased motor activity
- Multiple contributing factors
 - effect of illness
 - fear
 - inability to communicate
 - psychiatric disorders
 - personality traits

Anxiety

- Uncontrolled anxiety can also lead to deleterious physiological responses
 - Increased myocardial oxygen demand
 - sympathetic nervous system stimulation
 - increased work of breathing

Delirium

- Acute change in mental status, or a fluctuation of mood, associated with impaired attention, disorganized thinking, confusion and an altered level of consciousness
- Four domains of delirium
 - disturbance of consciousness
 - change in cognition
 - development over a short period
 - fluctuation

Risk factors

Predisposing factors

- Baseline cognitive impairment
- Baseline hypertension
- Alcohol/narcotic/BZD dependence
- Advanced age

Illness related

- High severity of illness
- Hypoxia, hypotension
- Sepsis, metabolic disturbance
- Medication induced coma
- Pain
- Immobilisation
- Isolation

Delirium

- Mainly clinical diagnosis
- No diagnostic blood, electrophysiological, or imaging test

- Types:
 - hypoactive (more common)
 - agitated (or hyperactive)
 - mixed delirium

- Under estimated because it is frequently hypoactive rather than hyperactive

Drug withdrawal

Withdrawal symptoms may result from abrupt discontinuation of:

- 1) Illicit or prescription drugs that patients were taking chronically
- 2) Sedatives or opioids of routine ICU care
- 3) Chronic ethanol use

Asynchrony

- Ultra structural injury to respiratory muscles
- Worsens lung mechanics (Intrinsic PEEP)
- Alters gas exchange (auto-triggering - \downarrow PaCO₂)
- Confounds lung-protective strategy (breath-stacking leads to increased tidal volume)
- Sleep fragmentation
- Patient discomfort and dyspnea (\uparrow sedation)
- Confuse the clinician (weaning decision making)

How Often Does Patient-Ventilator Asynchrony Occur and
What Are the Consequences? Respir Care 2011;56(1)

MONITORING OF AGITATION

Sedation scales

- **Sedation Agitation Scale (SAS)**
- **Richmond Agitation-Sedation Scale (RASS)**
- Observer's assessment of alertness/sedation scale (OAA/S)
- Ramsay sedation scale
- New Sheffield sedation scale
- Sedation Intensive Care Score (SEDIC)
- Motor Activity Assessment Score (MAAS)
- Adaption to Intensive care environment (ATICE)
- Minnesota Sedation Assessment Tool (MSAT)
- Vancouver Interaction and Calmness Scale (VICS)

RASS

Score	Term	Description
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive
+2	Agitated	Frequent nonpurposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive or vigorous

RASS has high reliability and validity in medical and surgical, ventilated and non-ventilated, and sedated and non sedated adult ICU patients

-3	Moderate sedation	Movement or eye opening to <i>voice</i> (but no eye contact)
-4	Deep sedation	No response to voice, but movement or eye opening to <i>physical stimulation</i>
-5	Unarousable	No response to voice or <i>physical stimulation</i>

Rikers sedation agitation scale

Score	Term	Descriptor
7	Dangerous Agitation	Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side-to-side
6	Very Agitated	Requiring restraint and frequent verbal reminding of limits, biting ETT
5	Agitated	Anxious or physically agitated, calms to verbal instructions
4	Calm and Cooperative	Calm, easily arousable, follows commands
3	Sedated	Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
2	Very Sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

Objective measures of monitoring sedation

- Auditory Evoked Potentials (AEP)
- Bispectral Index (BIS)
- Narcotrend Index (NI)
- State entropy (SE)

Adjunct to subjective sedation assessments in ICU patients on neuro-muscular blocking agents

EEG monitoring

- Nonconvulsive seizure activity in ICU patients either with known seizure activity or who are at risk for seizures
- Titrating electro suppressive medications to achieve burst suppression in critically ill patients with increased intracranial pressure

- Regardless of which sedation scale is used in the ICU, sedation goals should be individualized for each patient, bearing in mind that most patients can tolerate light or no sedation

Pain assessment & monitoring

- Vital signs do not always correlate with pain, may be used only as a clue to begin further assessment of pain
- Patient's self-report of pain - “gold standard”
quantified by
 - Visual analogue scale
 - Numeric scale
- Unable to communicate - patient's behavioural reactions as surrogate measures of pain as long as their motor function is intact

Critical Care Pain Observational Tool

Indicator	Description	Score
Facial expression	No muscular tension observed	Relaxed, neutral: 0
	Presence of frowning, brow lowering, orbit tightening, and levator contraction	Tense: 1
	All of the above facial movements plus eyelid tightly closed	Grimacing: 2
Body movements	Does not move at all (does not necessarily mean absence of pain)	Absence of movements: 0
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection: 1
	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed	Restlessness: 2
Muscle tension	No resistance to passive movements	Relaxed: 0
	Resistance to passive movements	Tense, rigid: 1
	Strong resistance to passive movements, inability to complete them	Very tense or rigid: 2
Compliance with the ventilator	Alarms not activated, easy ventilation	Tolerating ventilator or movement: 0
	Alarms stop spontaneously	Coughing but tolerating : 1
	Asynchrony: blocking ventilation, alarms frequently activated	Fighting ventilator: 2
OR		
Vocalization (extubated patients)	Talking in normal tone or no sound	Talking in normal tone or no sound: 0
	Sighing, moaning	Sighing, moaning: 1
	Crying out, sobbing	Crying out, sobbing: 2

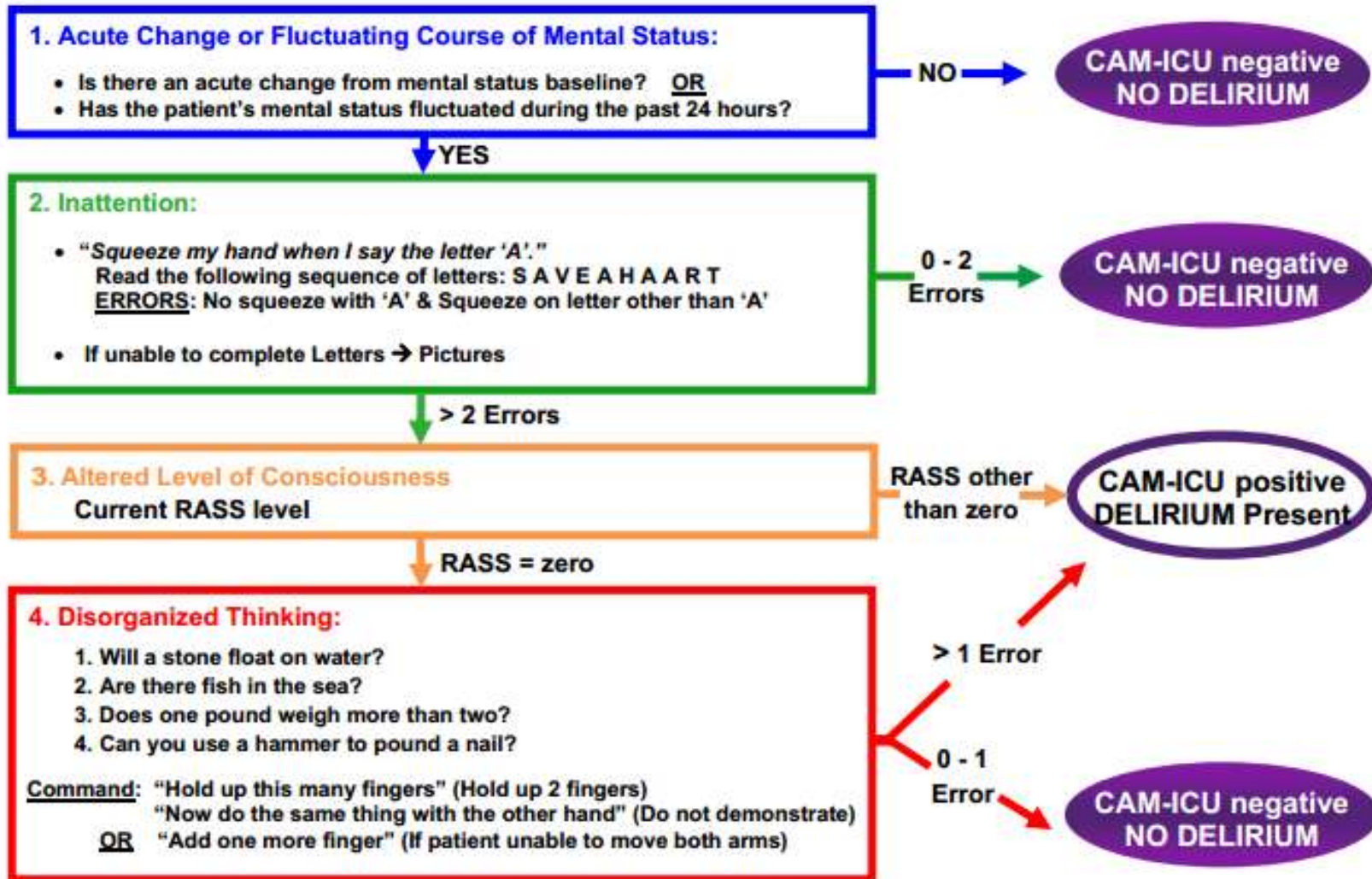
Scores for each of the four domains are summed, with a total score of 0 to 8 [34].

	muscle tension		
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Assessment for delirium

- The Confusion Assessment Method for the ICU (CAM-ICU)
- Intensive Care Delirium Screening Checklist (ICDSC)

Confusion Assessment Method for the ICU (CAM-ICU) Flowsheet



Intensive Care Delirium Screening Checklist (ICDSC)

- Patient must show at least a response to mild or moderate stimulation. Then score 1 point for each of the following features :
 - Anything other than “normal wakefulness”
 - Inattention
 - Disorientation
 - Hallucination
 - Psychomotor agitation
 - Inappropriate speech or mood
 - Disturbance in sleep or wake cycle
 - Fluctuation in symptoms

A score of ≥ 4 is positive for delirium (with scores of 1 to 3 termed “subsyndromal delirium”)

GOALS OF AGITATION

Goal of pain management

- Adequate pain control without over sedation and pre-emptive treatment of pain prior to all painful procedures

Target sedation

Under sedation

- Anxiety
- Agitation
- Hypoxemia
- Unplanned extubations
- Increased stress response
- Myocardial ischemia

Over sedation

- Depress the respiratory drive
- Cognitive impairment
- Increase the risk of health care–associated infections
- Drug accumulation

Both of them prolong ICU, hospital stay and increase costs

Depth of sedation

- Medications be titrated to maintain a light rather than deep level of sedation
- Light sedation improves clinical outcomes
 - shorter duration of mechanical ventilation
 - shorter ICU stay
- Increases the physiologic stress response, but is not associated with an increased incidence of myocardial ischemia
- No difference in post ICU psychological outcome based on the depth of sedation

Early deep sedation

- Lighter sedation was associated with
 - Less mortality
 - Fewer tracheostomy placements
 - Less duration of mechanical ventilation
- Early deep sedation constitutes an independent predictor of hospital mortality in mechanically ventilated patients

Early sedation and clinical outcomes of mechanically ventilated patients: a prospective multicenter cohort study; Tanaka et al. Critical Care 2014

Sedate or not to sedate?

	No sedation (n =55)	Sedation (n =58)	p value
Mechanical ventilation free days (from intubation to day 28)	13·8	9·6	0·0191
Length of stay (days)			
ICU	13·1	22·8	0·0316
Hospital	34	58	0·0039
Mortality			
Intensive care unit	12 (22%)	22 (38%)	0·06
Hospital	20 (36%)	27 (47%)	0·27
Tracheostomy	16 (29%)	17 (29%)	0·98
Ventilator-associated pneumonia	6 (11%)	7 (12%)	0·85

Sedate or not to sedate?

- Limitations of Danish trial
- Single centred unblinded study
- A multicentre trial is needed to show the reproducibility of benefits of no sedation strategy
- ICU nurse-to-patient ratio in this institution was 1:1 and a staff person for verbal reassurance was assigned which is not possible in many ICUs
- Morphine boluses were given in both groups which has a sedative effect

Uninterrupted sedation

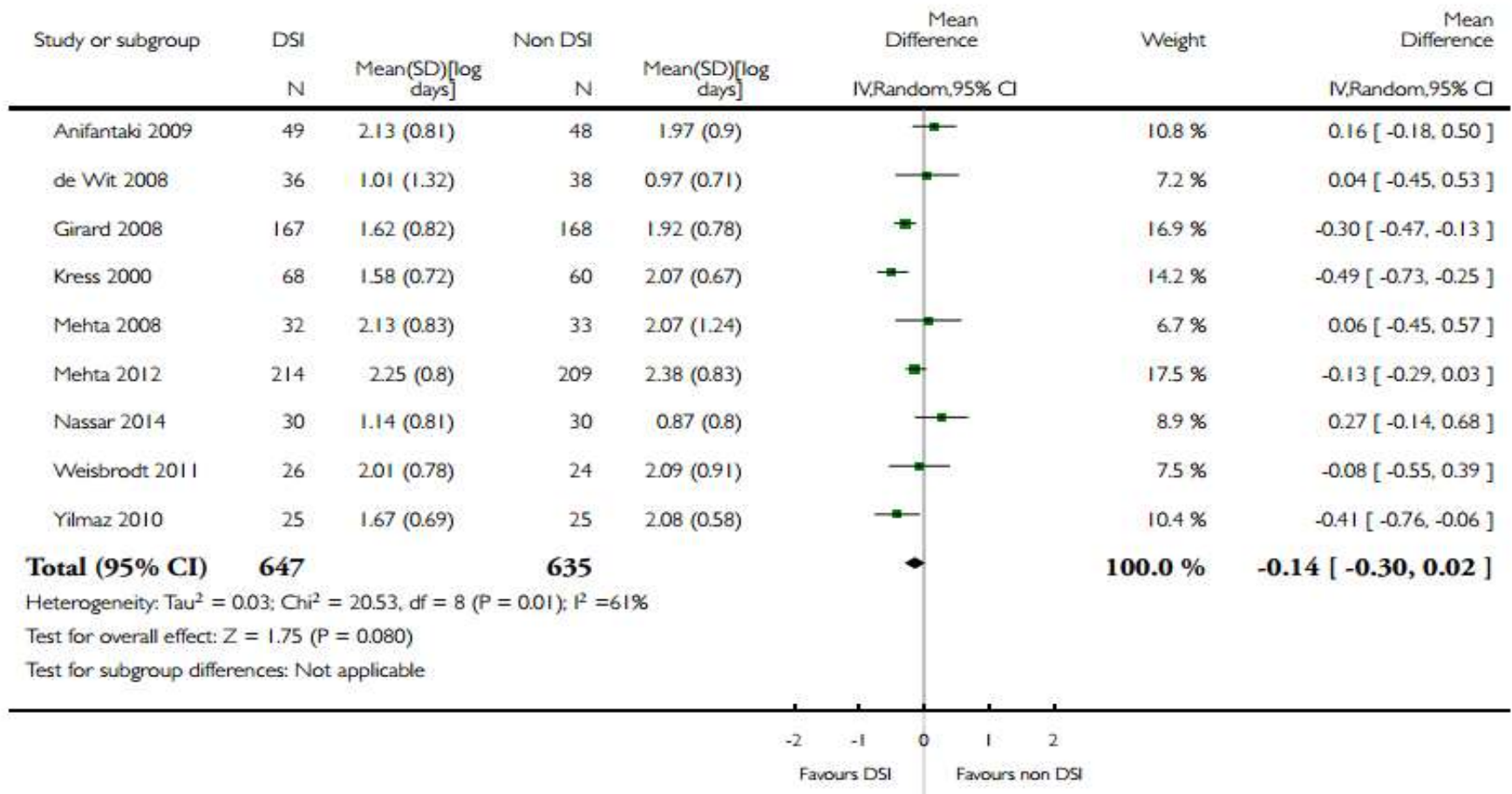
- ARDS, where the extent of hypoxia and/or hypercarbia is such that alternative ventilation strategies or use of a neuromuscular blocking agent is required
- Severe traumatic brain injury-Intracranial hypertension
- Hemodynamic instability - myocardial ischemia
- Intoxications where the agitation of the patient is such that he or she could be a harm to them self or others

Sedation for Critically Ill or Injured Adults in the ICU, a shifting paradigm; Drugs 2012; 72 (14)

Daily sedation interruption

- Short-term suspension or interruption of intravenous sedatives
- Limit drug bioaccumulation
- Promote a more awake state
- Permit assessment of neurological status and readiness for weaning

Daily sedation interruption versus no daily sedation interruption for critically ill adult patients requiring invasive mechanical ventilation (Review)



Daily sedation interruption (DSI)

Secondary outcome	DSI vs. continuous sedation
ICU and hospital mortality	No difference noted
Length of stay, hospital and ICU	
Accidental ETT removal	
New onset delirium	
Catheter removal	
Quality of life (3/9 trials)	
Tracheostomy was performed less frequently in the DSI group (RR 0.73) reported in six trials	

NON PHARMACOLOGIC APPROACH

- Finding a specific cause may allow directed and effective treatment for agitation
- Life threatening causes for agitation must be ruled out first

Asynchrony

- Agitation due to asynchrony relieved by addressing ventilator settings
 - inspiratory flow rates
 - tidal volumes
 - ventilator modes
- Whether strategies to quickly identify and treat patient–ventilator dyssynchrony can decrease sedation requires further study

Sleep promotion

- Almost half of ICU patients report marked sleep disturbances
- Simple interventions such as
 - providing earplugs
 - reducing alarm volumes
 - adherence to natural lighting cycles and avoidance of bright lights at night
 - back massage and relaxation

Richards KC, Am J Crit care;1998

Kirsten M Eliassen et al, Intensive and critical care nursing Vol 27, 2011

Early mobilisation

- Mobilization can be as complete as full physical or occupational therapy treatments or merely passive range-of motion exercises
- Removal of tubes, catheters, or restraints that may prevent early mobilization

Early mobilisation

- A strategy for whole-body rehabilitation—consisting of interruption of sedation and physical and occupational therapy in the earliest days of critical illness was associated with
 - Less days of delirium
 - More ventilator free days
 - Less length of ICU and hospital stay

Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial, Lancet 2009; 373: 1874–82

Re orientation

- Provide visual and hearing aids
- Encourage communication
- Reorient patient repetitively
- Have familiar objects from patient's home in the room
- Consistency in nursing staff
- Allow television during day with daily news

Music therapy

- Beneficial effect on stress, anxiety in mechanically ventilated patients
- Consistently reduces respiratory rate and systolic blood pressure
- Impact on the consumption of sedatives and analgesics
- Improve patients ICU experiences

Music interventions for mechanically ventilated patients
Cochrane Database Syst Rev. 2014

PHARMACOLOGIC APPROACH

Patient factors...

- Advanced age
- Malnutrition / Obesity
- High total body water
- Increased volume of distribution
- Altered liver and renal function
- Underlying illness
- Prior substance abuse
- Polypharmacy

Management of pain

- IV opioids - first-line drug class of choice to treat non-neuropathic pain in critically ill
- Gabapentin or carbamazepine - neuropathic pain
- Non-opioid analgesics
 - decrease the amount of opioids administered
 - decrease opioid-related side effects

	Onset (min)	Duration (hrs)	
Morphine	5-10	3-4	Active glucuronated metabolites Avoided in renal insufficiency Histamine release- rarely clinically relevant
Hydro-morphone	5-10	3-4	Metabolites are not active
Fentanyl	<1	2-4	More lipophilic – rapid onset Less hypotension than other opioids More risks for accumulation Delayed recovery after long administration
Remi-fentanil	1-3	3-4 min	Rapid hydrolysis by plasma, tissue esterases Unaffected by organ function

Opioids - side effects

- Respiratory depression in a dose-dependent manner
- Nausea, vomitings and ileus
- Hypotension
 - Minimal hemodynamic effects in euvolemics
 - Only seen in volume depleted, hemodynamically unstable and who have high sympathetic tone
- Dependence and withdrawal effects in prolonged infusions
- Muscle rigidity (high doses of fentanyl)

- Intravenous route - preferred in critically ill
- Scheduled intermittent dosing - recommended rather than a continuous infusion
- Incorporating daily awakening has been shown to decrease the amount of opioid administered and to shorten both duration of mechanical ventilation and stay in the ICU

Analgo-sedation

- Primary goal is to address pain and discomfort first, and then add a hypnotic agent if necessary
- As effective as sedative-hypnotic approach
- Reduced dose requirements of hypnotic medications
- Majority of trials - remifentanyl as an analgesic
- Disadvantages:
 - recall for unpleasant events before regaining consciousness
 - nightmares
 - hallucinations
 - influence on outcomes such as delirium, self extubation, VAP, mortality, cost of ICU care, and long-term cognitive function not explored

Optimal features of sedative

- Provide adequate sedation and pain control
- Provide prompt relief from distress
- Rapid recovery after discontinuation
- Minimal adverse effects
- Inexpensive

Sedative medications

Agent	Onset After IV Loading Dose	Elimination Half-Life	Active Metabolites	Loading Dose (IV)	Maintenance Dosing (IV)
Midazolam	2–5 min	3–11 hr	Yes ^a	0.01–0.05 mg/kg over several minutes	0.02–0.1 mg/kg/hr
Lorazepam	15–20 min	8–15 hr	None	0.02–0.04 mg/kg (\leq 2 mg)	0.02–0.06 mg/kg q2–6 hr prn or 0.01–0.1 mg/kg/hr (\leq 10 mg/hr)
Diazepam	2–5 min	20–120 hr	Yes ^a	5–10 mg	0.03–0.1 mg/kg q0.5–6 hr prn
Propofol	1–2 min	Short-term use = 3–12 hr Long-term use = 50 ± 18.6 hr	None	5 μ g/kg/min over 5 min ^b	5–50 μ g/kg/min
Dexmedetomidine	5–10 min	1.8–3.1 hr	None	1 μ g/kg over 10 min ^c	0.2–0.7 μ g/kg/hr ^d

Barr J, et al. Critical care medicine. 2013;41(1):263-306.

Benzodiazepines

- GABA- A central nervous system receptors
- Metabolized by the liver, excreted through kidneys
- Reduced clearance in hepatic dysfunction except for Lorazepam
- Long half life in renal failure- prolonged effect
- Elderly patients clear more slowly
- S/E - respiratory depression and hypotension

Lorazepam

- Propylene glycol (1,2-propanediol) is the solvent used to deliver lorazepam and diazepam IV
- Close monitoring of all patients receiving IV lorazepam or diazepam for early evidence of propylene glycol toxicity is warranted
- Life threatening iatrogenic complication that is preventable
 - unexplained anion gap
 - unexplained metabolic acidosis
 - hyperosmolality
 - clinical deterioration

Benzodiazepine and opioid use and the duration of intensive care unit delirium in an older population*

Margaret A. Pisani, MD, MPH; Terrence E. Murphy, PhD; Katy L. B. Araujo, MPH; Patricia Slattum, PharmD, PhD; Peter H. Van Ness, PhD, MPH; Sharon K. Inouye, MD, Mph

Objective: There is a high prevalence of delirium in older medical intensive care unit (ICU) patients and delirium is associated with adverse outcomes. We need to identify modifiable risk factors for delirium, such as medication use, in the ICU. The objective of this study was to examine the impact of benzodiazepine or opioid use on the duration of ICU delirium in an older medical population.

Design: Prospective cohort study.

Setting: Fourteen-bed medical intensive care unit in an urban university teaching hospital.

Patients: 304 consecutive admissions age 60 and older.

Interventions: None.

Main Outcome Measurements: The main outcome measure was duration of ICU delirium, specifically the first episode of ICU delirium. Patients were assessed daily for delirium with the Confusion Assessment Method for the ICU and a validated chart review method. Our main predictor was receiving benzodiazepines or opioids during ICU stay. A multivariable model was developed using Poisson rate regression.

Results: Delirium occurred in 239 of 304 patients (79%). The median duration of ICU delirium was 3 days with a range of 1–33 days. In a multivariable regression model, receipt of a benzodiazepine or opioid (rate ratio [RR] 1.64, 95% confidence interval [CI] 1.27–2.10) was associated with increased delirium duration. Other variables associated with delirium duration in this analysis include preexisting dementia (RR 1.19, 95% CI 1.07–1.33), receipt of haloperidol (RR 1.35, 95% CI 1.21–1.50), and severity of illness (RR 1.01, 95% CI 1.00–1.02).

Conclusions: The use of benzodiazepines or opioids in the ICU is associated with longer duration of a first episode of delirium. Receipt of these medications may represent modifiable risk factors for delirium. Clinicians caring for ICU patients should carefully evaluate the need for benzodiazepines, opioids, and haloperidol. (Crit Care Med 2009; 37:177–183)

KEY WORDS: delirium; critical care; risk factors; aged; benzodiazepines; opioids; haloperidol

Propofol

- Activates GABA receptors & inhibits NMDA glutamate receptors
- Rapid onset and offset of sedation
- Helpful in patients requiring frequent awakenings for neurologic assessments and it may facilitate daily sedation interruption protocols
- Not dependent on hepatic and renal function

Propofol

- Respiratory depression
- Systemic vasodilatation – hypotension
- Bradycardia
- Hyper triglyceridemia
- Acute pancreatitis
- Propofol infusion syndrome (PRIS)
 - metabolic acidosis
 - hypertriglyceridemia
 - hypotension, arrhythmias
 - AKI, liver dysfunction

Dexmedetomidine

- Alpha 2 adrenergic agonist
- Slower onset of action (10–15 min)
- Analgesic/opioid sparing
- Different quality of sedation – tend to be more awake and interactive
- Minimal respiratory depression

Dexmedetomidine

- Decreases sympathetic nervous system activity and associated with an increase in cardiovascular adverse events
- Most pronounced in patients with *decreased autonomic nervous system response*
 - elderly
 - diabetic patients,
 - patients with chronic hypertension or severe cardiac disease such as valve stenosis or regurgitation, advanced heart block, severe coronary artery disease
 - who are already hypotensive and/or hypovolemic

BZDs Vs non BZDs

Outcome	n (trials) (follow-up)	Benefit with non BDZ
ICU length of stay	1235 (6) (45 d f/u)	-1.64 d
Duration of mechanical ventilation	1101 (4) (45 d f/u)	-1.87 d
Mortality	1101 (4) (45 d f/u)	1.01
Delirium	469 (2) (during ICU stay only)	0.82

Fraser GL, et al. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials. Critical care medicine. 2013;41

BZDs Vs non BZDs

- Thirteen trials analyzed
- No consistent differences in ICU LOS
- ICU length of stay shortened approximately by 0.5 days (non BDZ arm) -six trials ranked as moderate to high quality
- No mortality difference noted
- Overall conclusion: Non BDZ modestly effective in reducing ICU LOS than BDZ sedation

The use of propofol for medium and long-term sedation : a meta-analysis

- Propofol vs alternative sedative
- A total of 16 trials studied in a meta-analysis
 - Mortality reported in 14 trials
 - Length of ICU stay in 9 trials
 - Duration of ventilation in 4 trials
- No difference in mortality
- But significantly lesser duration of ventilation and ICU stay
(In both long term and medium term usage of propofol)

Dexmedetomidine

- Dexmedetomidine vs alternative sedative
- A total of 27 trials studied in a meta-analysis
 - propofol in 11 arms, midazolam in 10 arms, placebo in 5 arms, morphine in 2 arms, haloperidol and lorazepam in one study
- Reduced time of stay in ICU
- It might reduce the time of extubation
- ↑ risk of bradycardia with a trend toward an ↑ risk of hypotension, but no detrimental effects on mortality were detected

Pasin L et al; PLoS one. 2013;8(12):e82913 table showing outcomes for only ICU related studies

Dexmedetomidine

- Dexmedetomidine vs alternative sedative
- A total of 16 RCTs studied in a meta-analysis
 - propofol in 7 arms, midazolam in 5 arms, 2 with either midazolam or propofol, haloperidol and lorazepam in one study
- 48 hour-reduction in ICU LOS, mechanical ventilation duration
- Reduction in delirium incidence
- Bradycardia and hypotension were more frequently reported

Efficacy and safety of sedation with dexmedetomidine in critical care patients: A meta-analysis of randomized controlled trials;
Anaesth Crit Care Pain Med 2015

Choice of sedation

- Midazolam or diazepam - for rapid sedation of acutely agitated patients
- Propofol - when rapid awakening (e.g., for neurologic assessment or extubation) is important
- Midazolam is recommended for short term use only, as it produces unpredictable awakening and time to extubation when infusions continue longer than 48–72 hours
- The titration of the sedative dose to a defined endpoint is recommended with systematic tapering of the dose or daily interruption with re-titration to minimize prolonged sedative effects

Choice of sedation

- Sedation strategies using **non BZD sedatives (either propofol or dexmedetomidine)** may be preferred over sedation with BZD (either midazolam or lorazepam) to improve clinical outcomes in mechanically ventilated adult ICU patients
- Ultimately, therapeutic decisions should always be guided by patient context and by available financial and clinical resources

Haloperidol

- A loading regimen starting with a 2-mg dose, followed by repeated doses (double the previous dose) every 15–20 minutes while agitation persists
- 25% of the cumulative dose q6 hourly for maintenance
- After delirium control, regularly scheduled doses (every four to six hours) may be continued for a few days
- Adverse events
 - Extra pyramidal symptoms
 - Malignant hyperthermia
 - Torsade de pointes

Delirium treatment

- No efficacy or safety of any antipsychotic agent in the management of delirium in ICU patients
- Lack of data on haloperidol in ICU patients as compared to non ICU patients
- Antipsychotics be judiciously used with careful monitoring of ECG changes & EPS

Other antipsychotics

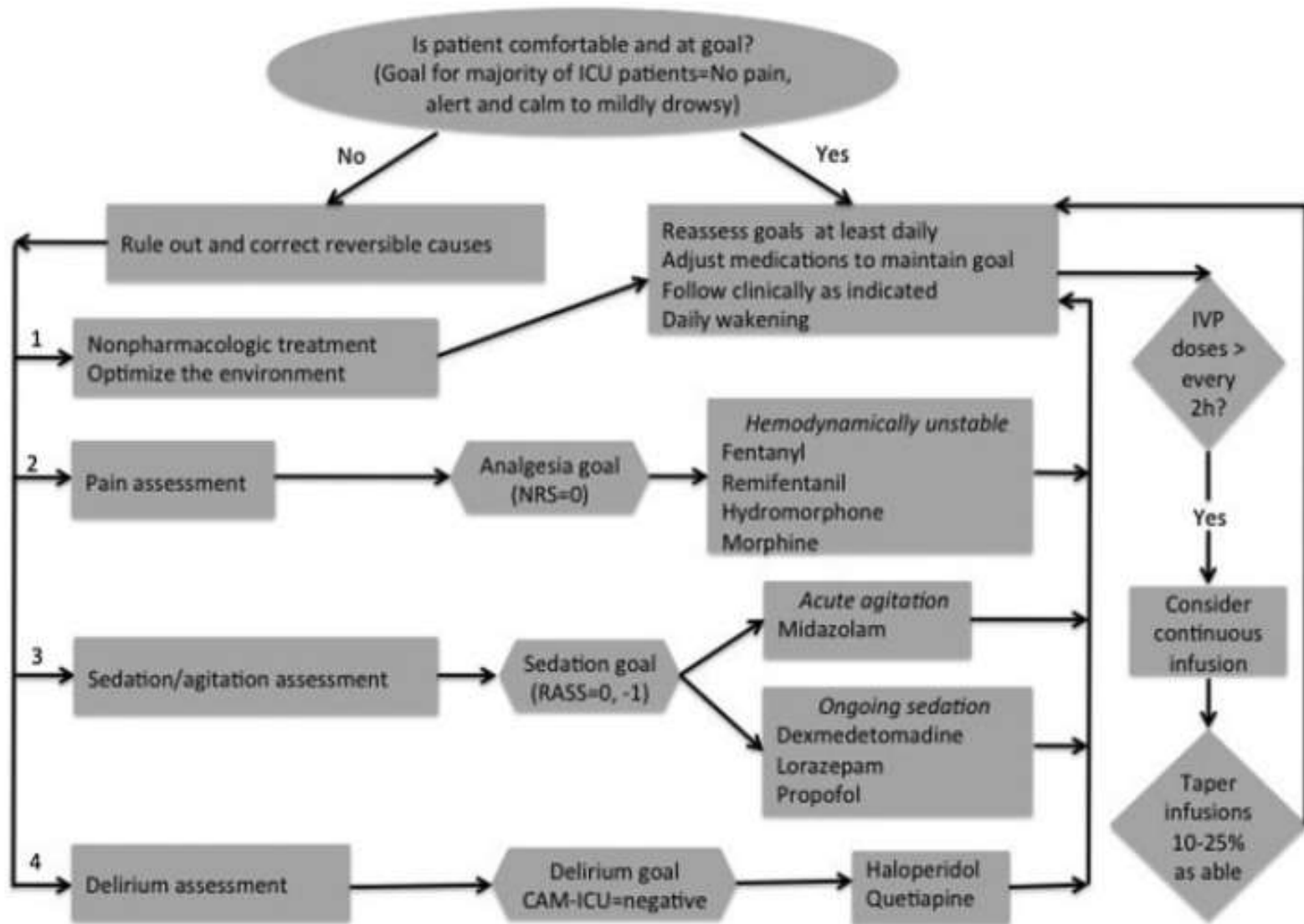
- Olanzapine is a safe alternative to haloperidol, particularly in whom haloperidol is contraindicated
- Quetiapine added to as-needed haloperidol results in faster delirium resolution, less agitation, and a greater rate of transfer to home or rehabilitation

Prevention of delirium

- Significant decrease in the incidence of delirium with haloperidol use within the first 7 days after surgery and a decrease in length of ICU stay
- ICU patients with delirium unrelated to alcohol or BZD withdrawal, continuous IV infusions of dexmedetomidine rather than BZD infusions be administered for sedation in order to reduce the duration of delirium

Wang W et al, Crit Care Med 2012, 40(3):731–739

Barr J, et al. Critical care medicine. 2013;41(1):263-306



Adapted from Jacobi J, Fraser GL, Coursin DB et al. Clinical practice guidelines for sustained use of sedatives and analgesic in critically ill adult. Crit Care Med. 2002; 30:119-141.

NRS=Numeric Rating Scale; RASS=Richmond Agitation Sedation Scale; CAM-ICU=Confusion Assessment Method-ICU; IVP=intravenous push

Summary

- Agitation is a distressing issue in ICU
- “Look around” before reaching for syringe
- Patient focused & target based sedation
- Choice of sedation – patient context and resources
- Reassess on a daily basis for pain & delirium