


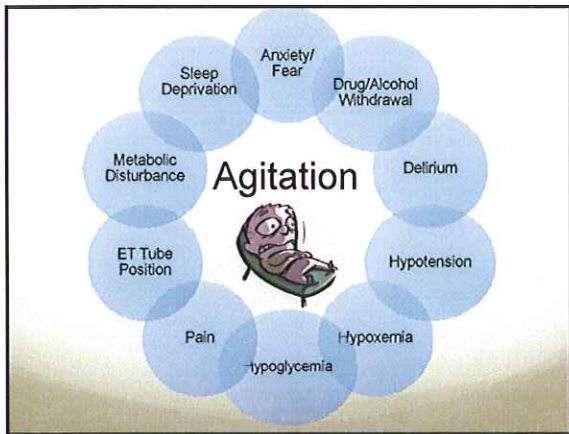
Sedation Strategies: Current Best Evidence

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Objectives


- List the proposed benefits of light sedation versus deep sedation based on current literature
- Describe the rationale for using non-benzodiazepine based sedation regimens




Detriments of Agitation

- Increase oxygen consumption
- Tachycardia
- Hypertension
- Anxiety
- Sleep disturbances
- Ventilator dyssynchrony
- Self inflicted harm
- Post traumatic stress disorder

Sedation in the ICU



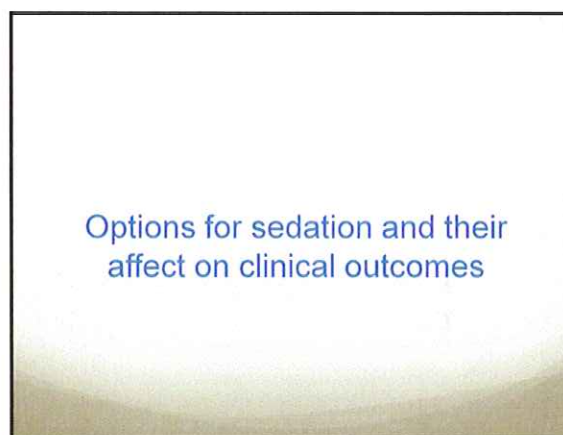
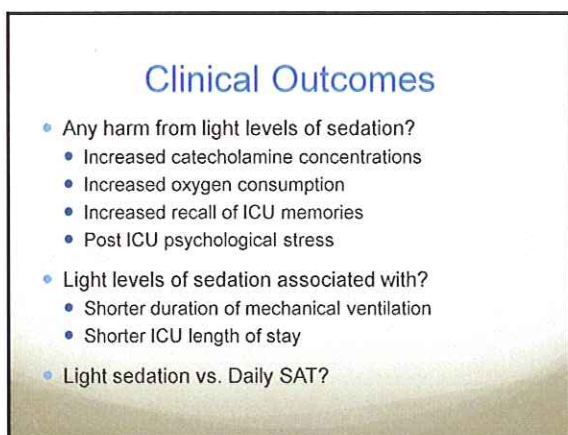
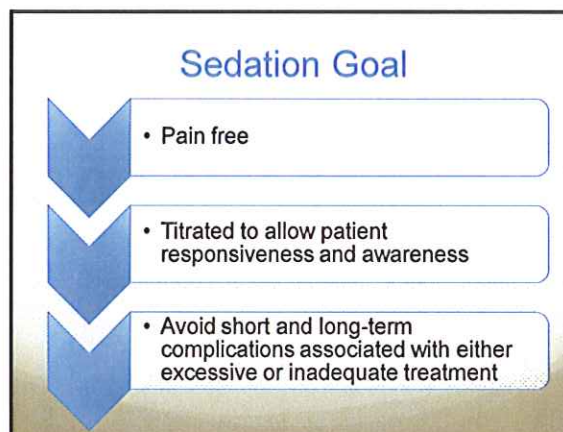
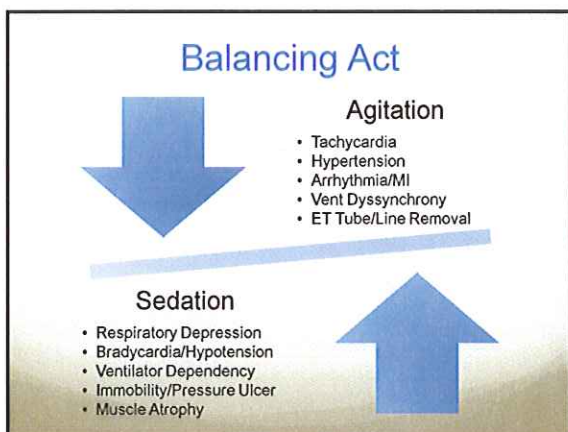
https://blog44.uniconic.co.uk/2015/05/04/psychophd-talk-the-unbearable-brightness-of-light/



http://www.sedation.org/nature/deep-ocean-lance-120h-ride-powerful-eyes/273/

Sedation in the ICU

- Light sedation
 - Patient is arousable and able to purposefully follow simple commands
- Deep sedation
 - Patient is unresponsive to painful stimuli
 - Indications
 - Intracranial hypertension
 - Severe respiratory failure
 - Refractory status epilepticus
 - Use of neuromuscular blocking agents
 - Other



Dexmedetomidine vs. Benzodiazepine

- Ideal agent?
 - Analgesic sparing effects
 - Less respiratory depression
 - Light level of sedation allowing patients to communicate
- Multiple studies comparing outcomes produced variable results
- Compared to lorazepam and midazolam, dexmedetomidine results shorter duration of mechanical ventilation
- Patients spend less time in delirium and have reduced prevalence

SEDCOM Trial

- Prospective, double-blind, randomized, and multi-center
- Patient population
 - Adults, mechanically ventilated for < 96 hours
 - Anticipated duration of at least 3 days
- Randomized to dexmedetomidine or midazolam (n =375)
 - RASS goal -2 to +1
 - Open label fentanyl and midazolam boluses permitted
 - Haloperidol permitted for agitation or delirium

JAMA. 2009;301(5):482-90

SEDCOM Trial

	Dexmedetomidine	Midazolam	p value
% time within target sedation	77.3%	75.1%	0.18
Open label midazolam (1 st day of randomization)	43%	30%	0.02
Open label midazolam (entire treatment period)	63%	49%	0.02

- Delirium
 - 24.9% (95% CI, 16 to 34%; p<0.001) reduction of delirium in patients treated with dexmedetomidine
 - Prevalence: 54% vs. 76.6% (22.6% 95% CI, 14 to 33%; p<0.001)

JAMA. 2009;301(5):482-90

SEDCOM Trial

- Delirium free days
 - 2.5 days. vs. 1.7 days; p = 0.002
- Time to extubation & ICU LOS

- Bradycardia: 42.2% vs. 18.9%; p < 0.001

JAMA. 2009;301(5):482-90

Propofol vs. Benzodiazepines

- Outcomes should be assessed individually for each patient population
 - Medical/surgical
 - Cardiovascular
 - Neurologic
- Overall, shorter duration of mechanical ventilation without a decrease in ICU LOS
- Weak data and evidence to conclude on difference in delirium

Dexmedetomidine vs. Propofol or Midazolam

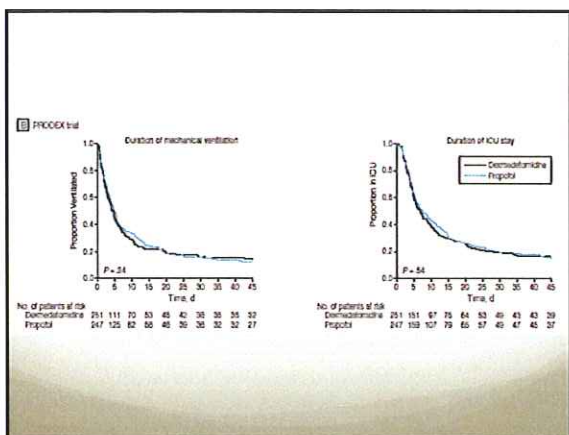
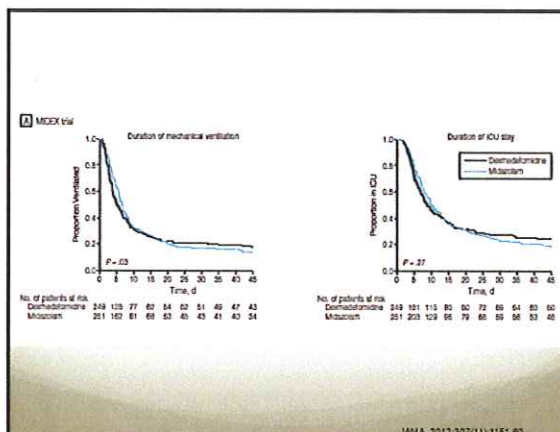
- 2 parallel, multicenter, randomized, double-blinded non-inferiority trials
 - MIDEX (n = 501) and PRODEX (n = 500) trials
- Patient population
 - Adults requiring invasive mechanical ventilation with need for light to moderate sedation
 - Sedation required for at least 24 hours
 - Randomized within 72 hours of ICU admission
- Bedside nurses titrated medications to achieve goal RASS and fentanyl boluses were permitted

JAMA. 2012;307(11):1151-60

Dexmedetomidine vs. Propofol or Midazolam

- Time in target sedation goal without rescue bolus
 - MIDEX: midazolam 56.6% vs. dexmedetomidine 60.7%, 1.07 (95% CI, 0.97 – 1.18; p = .15)
 - PRODEX: propofol 64.7% vs. dexmedetomidine 64.6%, 1.00 (95% CI, 0.92 – 1.08; p = 0.97)
- Dexmedetomidine patients had higher actual RASS scores (p < 0.001)
- Drug discontinuation rates
 - MIDEX: 4% vs. 9%; p = 0.02
 - PRODEX: 5% vs. 14%; p = <0.001
 - Discontinuation secondary to lack of efficacy within 24 hours more common in dexmedetomidine group

JAMA. 2012;307(11):1151-60



Dexmedetomidine vs. Propofol or Midazolam

- Hospital LOS
 - No difference
- Delirium
 - Not solely assessed; included in "neurocognitive disorders"
- Adverse Events
 - Hypotension
 - MIDEX: 11.6% vs. 20.6%; p = 0.007
 - PRODEX: NS
 - Bradycardia
 - MIDEX: 5.2% vs. 14.2%; p < 0.001
 - PRODEX: NS

JAMA. 2012;307(11):1151-60

Benzodiazepine vs. Nonbenzodiazepine

- 13 studies including over 1500 patients
 - No consistent difference in ICU LOS
- Meta-analysis performed including 6 trials
 - Sedation with benzodiazepines increased ICU LOS by 0.5 days; p = 0.04
- Duration of mechanical ventilation
 - Limited data suggest prolonged use with benzodiazepines
- No apparent difference in mortality

Benzodiazepine vs. Nonbenzodiazepine

- Meta analysis of 6 trials including over 1200 patients
 - Midazolam vs. dexmedetomidine
 - Lorazepam vs. dexmedetomidine
 - Midazolam vs. propofol
 - Lorazepam vs. propofol
- Eligibility criteria
 - Randomized, controlled, parallel trial
 - Adult medical or surgical ICU patients
 - Predefined outcomes
- Excluded studies evaluating cardiac surgery and critically ill obstetrical patients

Crit Care Med. 2012;41:835-38

Benzodiazepine vs. Nonbenzodiazepine

- Patient characteristics
 - Mean age: 59
 - Medical ICU patients majority
 - APACHE II score: 21
- Clinical Outcomes
 - ICU LOS: mean 1.65 d; $p = 0.0005$
 - Mechanical ventilation duration: mean 1.9 d; $p < 0.00001$
 - Delirium: variation within each study
 - All cause short term mortality: RR 0.98; (95% CI, 0.76 – 1.27; $p = 0.94$)

Crit Care Med. 2013;41:530-38

Summary

- Agitation is a common occurrence in the ICU that requires prompt identification and treatment
- Light sedation is preferred over deep sedation
- Nonbenzodiazepine sedation has positive effects on multiple clinical outcomes
 - Duration of mechanical ventilation
 - ICU LOS
 - Delirium
- There is still a role for benzodiazepine based sedation in the ICU
- How do you extrapolate the data?

Learning Assessment Question

1. Non-benzodiazepine based sedation regimens have been suggested to:
 - A. Decrease the incidence of delirium
 - B. Increase ICU length of stay
 - C. Prolong the length of mechanical ventilation
 - D. Increase use of ICU resources

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<http://treattrends.com/blog/the-power-of-question-based-selling>

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