Dexmedetomidine for Sedation in the ICU

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The speaker has no conflict to disclose.

How familiar are you with dexmedetomidine?

a) What is that? Is that a medication?

b) I have seen it but don't know much about it

c) I know the basics– but don't know much about the data

d) Very familiar – ask me anything about it

How often are you using dexmedetomidine for sedation in ICU patients?

a) > 1 time per week

b) < 1 time per week but > 1 time per month

c) < 1 time per month

Have you seen an increase in dexmedetomidine use for ICU sedation …?

a) In the past year

b) In the past 6 months

c) Since the propofol shortage

d) Have not had an increase in usage

Do you have dexmedetomidine on your ICU sedation protocol at your institution?

a) Yes

b) No

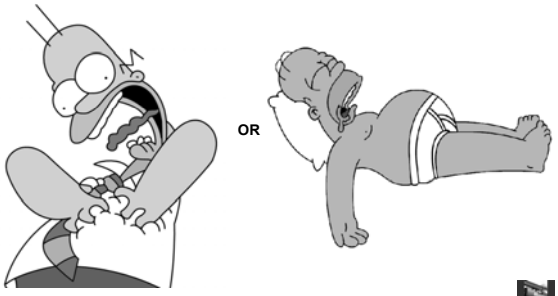
c) In the process of adding it

d) Don't have an ICU sedation protocol

Objectives

- Describe the role of dexmedetomidine for intensive care unit (ICU) sedation
- Review the recent literature relating to the use of dexmedetomidine for ICU sedation

Issues with ICU Sedation



Optimal Agent

- Short half life = rapid on + rapid off
- Does not accumulate
- Both analgesia + anxiolysis
- Sedation but easy to arouse and awaken
- Neutral on hemodynamics
- No respiratory depression
- Does not cause delirium

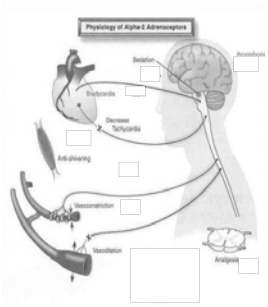
Characteristics of current sedation agents

	Opiates	Midazolam	Lorazepam	Propofol	Dexmed.
Quick onset	X	X		X	X
Quick offset	Depends	Depends	Depends	X	
Cumulative effects	X	X	X		
Hypotension	X	X	X	X	X
Bradycardia	X				X
Respiratory depression	X	X	X	X	
Disorientation	X	X	X	X	

Dexmedetomidine

- **Selective α2-agonist**

- Sites of action
  - CNS - Locus coeruleus
  - Spinal cord
  - Autonomic nerves



Dexmedetomidine, cont.

- **FDA approval**
  - Sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting administered by continuous infusion *not to exceed 24 hours*
  - Sedation of non-intubated patients prior to and/or during surgical and other procedures

- **Dosing based on approval**
  - ICU : 1 mcg/kg bolus, followed by 0.2-0.7 mcg/kg/hr
  - Procedure: 1 mcg/kg bolus, followed by 0.2-1 mcg/kg/hr

Package Insert

Pros and Cons of Dexmedetomidine

PROS	CONS
• Arousable/"cooperative" sedation • Anxiolysis • No respiratory depression • Analgesic properties • Decrease myocardial oxygen demand • Anti-shivering properties	• Bradycardia • Hypotension • FDA indication limited to 24 hours for ICU sedation • Cost?

Optimal indication and dosage for the medical ICU

MENDS Trial

- Lorazepam infusion vs. dexmedetomidine
- 106 patients – mechanically ventilated > 24 hrs
- 70% medical ICU patients
- **Primary outcome:**
  - Delirium-free and coma-free days
  - Efficacy in achieving target sedation

Pandharipande PP, et al. JAMA 2007;298(22):2644-2653.

MENDS Trial – Doses and durations

- Study allowances
  - Max lorazepam dose = 10 mg/hr
  - Max dexmedetomidine = 1.5 mcg/kg/hr
  - Max duration = 120 hrs

	lorazepam	dexmedetomidine
Median dose	3 mg/hr (2.2-6)	0.74 mcg/kg/hr (0.39-1.04)
Median duration (days)	4 (2-6)	5 (2-6)
Median fentanyl ** (mcg/d)	150 (0-922)	575 (140-2206)

Pandharipande PP, et al. JAMA 2007;298(22):2644-2653.

MENDS Trial

Clinical Outcomes

- Dexmedetomidine
  - More delirium-free and coma-free days (7 vs 3; p = 0.01)
  - Lower prevalence of coma (63% vs 92%; p < 0.001)
- No difference:
  - mechanical ventilator-free days, ICU LOS, or 28-day mortality
- Safety:
  - dexmedetomidine grp - more bradycardia (17% vs 4 %; p=0.03)

Efficacy of sedation

- Dexmedetomidine
  - More time within 1 point of RASS point target sedation (80% vs 67%; p = 0.04)
- Lorazepam
  - Sedated deeper than goal RASS score (15% vs 33%; p = 0.01)
- No difference
  - Adjunct need for antipsychotics or propofol

Pandharipande PP, et al. JAMA 2007;298(22):2644-2653.

SEDCOM Trial

- Midazolam infusion vs dexmedetomidine
- 375 patients - mechanical ventilation > 24 hrs
- 80% medical ICU patients
- Primary outcome:
  - Percentage of time within the target sedation range (RASS -2 to +1)
- Secondary outcomes:
  - Prevalence and duration of delirium
  - Use of open-label fentanyl and midazolam
  - Nursing shift assessments

Riker RR, et al. JAMA 2009;301(5):489-499

SEDCOM trial – Dosing and durations

- Study allowances:
  - Max midazolam = 0.12 mg/kg/hr
  - Max dexmedetomidine = 1.4 mcg/kg/hr
  - Max duration = 30 days

	midazolam	dexmedetomidine
Median dose	0.056 mg/kg/hr (SD 0.028)	0.83 mcg/kg/hr (SD 0.37)
Median duration ** (days)	4.1 (2.8-6.1)	3.5 (2-5.2)
Median fentanyl use (mcg/kg)	9.6 (2.9-28.6)	6.4 (1.8-26.3)
midazolam use ** (% treated)	63%	49%

Riker RR, et al. JAMA 2009;301(5):489-499

SEDCOM trial

Clinical Outcomes

- Dexmedetomidine
  - shorter median time to extubation (days) (3.7 vs 5.6; p = 0.01)
  - decreased prevalence of delirium (54% vs 76.6%; p<0.01)
  - More delirium-free days (2.5 vs 1.7; p 0.24)
- No difference
  - Time in target sedation range
  - ICU LOS or 30-day mortality

Safety Outcomes

- Dexmedetomidine
  - Bradycardia (42.2% vs 18.9%)*
  - Hyperglycemia (56.6% vs 42.6%)*
- Midazolam
  - Tachycardia (25.4% vs 44.3%)*
  - More hypertension needing intervention (18.9% vs 29.5%)*
  - More infections (10.2% vs 19.7%)*
- No difference
  - Bradycardia needing intervention, tachycardia needing intervention, or hypotension

Riker RR, et al. JAMA 2009;301(5):489-499

Comparison of trials

MENDS (lorazepam)	SEDCOM (midazolam)
• Dexmedetomidine – Dose up to 1.5 mcg/kg/hr for up to 120 hrs – More delirium & coma-free days – More accurate attainment of sedation scores (RASS) – More bradycardia – but not bradycardia needing intervention	• Dexmedetomidine – Dose up to 1.4 mcg/kg/hr for up to 30 days – Decreased time to extubation – Decreased delirium – More bradycardia – but not bradycardia needing intervention
• No difference – Ventilator-free days – ICU LOS – Mortality	• No difference – Time in target sedation range – ICU LOS – Mortality

Dexmedetomidine

FDA Approved Uses

- ICU sedation for up to 24 hours (0.2-0.7 mcg/kg/hr)
- Procedural sedation (0.2-1 mcg/kg/hr)

Future indications?

- ICU sedation for > 24 hours
- Higher doses for ICU sedation
- Delirium
- Alcohol withdrawal
- Anti-shivering

Which of the following would be benefits of dexmedetomidine for ICU sedation?

a) Arousable/ “cooperative” sedation
b) No respiratory depression
c) Anxiolysis and analgesia
d) a and b
e) All of the above

Which of the following would be adverse effects associated with dexmedetomidine?

a) Tachycardia
b) Bradycardia
c) Hypotension
d) a and c
e) b and c

Which of the following were concluded in the MENDS and SEDCOM trials? Dexmedetomidine…

a) Decreases ICU length of stay
b) Decreases total fentanyl use
c) Decreases the prevalence of delirium
d) All of the above
e) None of the above

Questions??

ICHP Spring Meeting 2010
Ronald – Dexmedetomidine for Sedation in the ICU
121-000-10-015-L01-P

Post Test Questions

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