

1  **Analgesia, Sedation, and Neuromuscular Blockade in the Critically Ill**

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2  **Objectives**

- 1. Identify factors to consider when choosing an analgesic for critically ill patients.
- 2. Describe appropriate medications to use to manage anxiety, agitation, and delirium.
- 3. Compare/contrast neuromuscular blocking agents and identify nursing care priorities for the pt. receiving these medications.

3  **Challenges of Sedation/Neuromuscular Blockade in 2010**

- Drug Shortages
 - Propofol
 - Cisatracurium
 - Vecuronium
 - Dexmedetomidine

4  **Pain Management**

- Trauma
- Surgery
- Diagnostic/therapeutic procedures
- Tubes in every orifice
- Stress/lack of control
- Sleeplessness
- Immobilization
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5  **Pain Assessment**

- Intubated and/or unconscious persons
 - Self-report
 - Nods/gestures
 - Potential causes of pain/discomfort
 - Assumed pain present
 - Observation of patient behavior
 - Behavioral Pain Scale
 - Critical-Care Pain Observation Tool
 - Surrogate reporting of pain
 - Analgesic trial
 - (Recommendations from American Society of Pain Management Nursing, 2005)

6  **Behavioral Pain Scale**

7  **Critical-Care Pain Observation Tool**


8  **Critical-Care Pain Observation Tool**

9  **Pain Assessment Tools for Sedated Adults**

- BPS
 - Evidence to support validity and reliability
 - Has been tested in a variety of ICU settings
 - Concern regarding close relationship between sedation and BPS scores
- CPOT
 - Demonstrated good reliability and validity in all aspects tested
 - Needs further analysis to confirm internal consistency

- Requires validation among broader critical care populations
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(Cade, 2008)

10  **Analgesics - Factors to consider**

11  **Morphine**

- Onset: < 5 minutes
- Peak: 20 minutes
- Duration: 3 – 7 hours
- Pharmacologic effects
 - Analgesia
 - Resp. depression
 - GI effects
 - Sedation/altered mentation

12  **Morphine**

- Adverse effects
 - Release of histamine – venodilation-induced cardiovascular instability
 - Respiratory depression
 - GI hypoactivity
 - Sedation
- Decreased clearance with renal and hepatic insufficiency

13  **Hydromorphone (*Dilaudid*)**

- Onset: 15 – 30 minutes
- Peak: 30 – 60 minutes
- Duration: 4 – 5 hours
- Roughly 3 – 4 times more potent than morphine
- Potential metabolite accumulation in renal failure
- Acceptable alternative to morphine

14  **Fentanyl**

- Onset: Immediate
- Duration: 1 – 2 hours
- 50 to 100 times more potent than morphine
- Has no active metabolite and does not cause venodilation
- Given as bolus or continuous infusion
- Drug of choice with hemodynamic instability

15  **Meperidine**








- Not recommended in critically ill
- Primarily metabolized through the liver
- Active metabolite – normeperidine can produce neurotoxicity
- Use only if allergic or intolerant to morphine or dilaudid
- Or for short duration such as during procedures
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16  **Indications for Sedation**

- To relieve agitation and anxiety
- To improve ventilation by promoting synchrony with mechanical ventilation
- To prevent self-injury or injury to others
- 92% of patients receive one or more analgesic, anxiolytic, or paralytic drug during their ICU stay

17  **Definition**

- Anxiety
 - Prolonged state of apprehension in response to a real or perceived fear

- Agitation
 - Excessive, non-purposeful motor activity associated with increased muscle tone and catecholamine levels
 - Anxiety, depression, delusions, hallucinations, flight of ideas
- 18  **Benzodiazepines**
 - Sedative – anxiolytics
 - No direct analgesic activity
 - Binds to specific receptors adjacent to neuronal cell membrane within CNS and reduces neuronal activity
 - Lowers level of circulating catecholamines
- 19  **Factors to consider**
- 20  **Lorazepam (*Ativan*)**
 - Dose: 1 – 4 mg. every 2 – 4 hrs.
 - 1 to 4 mg/hr by infusion
 - Onset: 5 – 10 minutes
 - Duration: 2 – 6 hours
 - Comments
 - No active metabolite
 - Preferred agent for sedation longer than 24 hrs.
 - Preferred agent for alcohol withdrawal.
- 21  **Midazolam (*Versed*)**
 - Dose: 0.5 – 3 mg. every 1 – 2 hours
 - Infusion: 1 – 15 mg/hr.
 - Onset: 1 – 5 minutes
 - Duration: 1 to 6 hours
 - Comments
 - Accumulation may occur with prolonged continuous infusions due to its high lipophilicity
 - May have prolonged sedation with hepatic or renal impairment
 - Useful when frequent neuro checks needed
- 22  **Side Effects**
 - Hypotension
 - Respiratory depression
 - May have paradoxical effect in pts. with delirium
 - Prolonged clinical effects
 - Marginal or poor liver function
 - Deposition of large amounts of drug in fatty tissues
 - Altered protein binding
- 23  **Complications**
 - Propylene glycol toxicity
 - Metabolic acidosis
 - Hyperosmolar state
 - Elevated osmolar gap
 - May be seen with long term infusions
 - Need to consider withdrawal symptoms
 - High dose infusions
 - Long-term infusions (more than 7 days)
- 24  **Reversal agent - Flumazenil**
 - Binds to benzodiazepine receptors in CNS
 - Dose: 0.2 mg initially, repeat 0.3 mg in 1 minute if needed

- Cumulative dose 1.0 mg in 20 minute period or 3.0 mg in any 1 hour
- 25  **Propofol (*Diprivan*)**
 - Uses
 - To reduce anxiety during short, uncomfortable procedures
 - To reduce restlessness in early post-op period
 - Decrease agitation in pts. with neurologic disorders or injury
 - To promote synchrony during mechanical ventilation
- 26  **Propofol**
 - Non-benzodiazepine sedative-hypnotic
 - Does not have marked analgesic properties
 - Does have amnesic properties at doses of 5 mcg./kg. and above
 - Acts on different receptors than benzodiazepines
- 27  **Propofol**
 - Usual dose: 5 to 50 mcg/kg/min.
 - Onset: 0.5 to 1 minute
 - Half-life: 0.5 to 1 hour
 - Duration: 3 to 8 minutes
 - Metabolism mainly in liver with formation and urinary excretion of inactive conjugates and quinols
 - Should only be given as infusion in critical care
- 28  **Physiological Effects**
 - Hypotension
 - Bradycardia
 - Relaxation of bronchiolar smooth muscle
 - Decreases cerebral blood flow; increases cerebral vascular resistance; decreases cerebral metabolic oxygen requirements
 - Can lead to increased caloric intake and triglyceride levels
- 29  **Nursing considerations**
 - Recommended for short term use
 - Pts. may require analgesics, benzodiazepines, or neuromuscular blocking agents
 - Should be weaned slowly in previously alert pts.
 - Monitor lipid and triglyceride levels with long term use
 - Discard unused drug within 12 hrs. after opening bottle (6 hrs. if bolusing)
 - Replace IV tubing every 12 hrs.
- 30  **Propofol Infusion Syndrome**
 - Reported in adults with use of higher doses for more than 48 hrs.
 - >4mg/kg per hour
 - >67 mcg/kg/min.
 - Priming factor
 - Critical illness
 - Triggering factors
 - High-dose propofol
 - Catecholamines
 - Glucocorticoids
- 31  **Clinical Manifestations of PRIS**
 - Unexplained metabolic acidosis
 - Hypertriglyceridemia
 - Hypotension
 - Lactic acidosis

- Arrhythmia: sudden onset of marked bradycardia resistant to treatment
- Rhabdomyolysis
- Acute renal failure
- Hepatomegaly

■(Zaccheo & Bucher, 2008)

32  **Pathophysiology and Management**

- Impaired utilization of fatty acid in the mitochondria
 - Imbalance between energy supply and demand leads to cardiac and peripheral muscle necrosis
 - Etiology undetermined
- Management
 - Early recognition
 - Discontinue immediately and use alternative sedative
 - Supportive therapy
 - Fluids
 - Vasopressors
 - Cardiac pacing
 - CRRT

33  **Dexmedetomidine (*Precedex*)**

- Alpha₂ – adrenoceptor agonist
 - Eight times more selective than clonidine
- Has sedative and analgesic properties
- Used for short-term sedation
- Continuous infusion not to exceed 24 hrs.
- Dose
 - Loading: 1 mcg/kg as infusion over 10 min.
 - Onset on action about 15 minutes
 - Maintenance: 0.2 to 0.7 mcg/kg/min. May be used before, during, and after extubation

34  **Dosing Guidelines - *Precedex***

- Pts. who are already on sedatives, hypnotics, or other opioid analgesics
 - Consider lower doses of Precedex
 - Loading dose may not be necessary
 - If giving a loading dose:
 - Initiate therapy at lower than usual loading dose
 - Infuse loading dose for greater than 10 minutes
 - Amount of the other drugs may be reduced

35  **Prolonged infusions of DEX**

- Doses ranged from 0.3 – 1.4 mcg/kg/hr.
- Used for 3.5 – 5 days
- Safety did not seem to be compromised by prolonged use
- Rebound or withdrawal effects upon drug discontinuation were not noted
- Increased rates of cardiovascular effects (bradycardia and hypotension) seen at higher doses
- Deeper sedation goals may not be attainable with DEX alone

36  ***Precedex***

Advantages and Disadvantages

- Advantages
 - Ability to have sedated pts. awakened when stimulated
 - Decreased doses other sedatives

- Decreased doses of analgesics
- Prevention of ICU delirium
- Disadvantages
 - Adverse effects are cardiac
 - Bradycardia
 - Hypertension
 - Hypotension
 - Questions regarding safety of longer infusions
 - Has not been shown to amnesic properties
 - Cost
 - Average wholesale cost for 2 ml. vial of 100 mcg/ml concentrations = \$68.64 (2007)

37  **Delirium**

- Clinical expression of overall brain dysfunction
- Reversible organic mental disorder characterized by abrupt onset and altered LOC
 - Altered perceptions
 - Memory deficits
 - Dramatic changes in severity between extremes within minutes
 - Delusions and/or hallucinations
- Cognitive and behavioral changes due to stress response and associated surges of dopamine in CNS

38  **Risk Factors for Delirium**

- Preexisting cognitive impairment – primary
- Higher age
- Presence of acute systemic illnesses or medical comorbid diseases
- Use of certain medications

39  **Types of Delirium**

- Hypoactive
 - Lethargic; decreased LOC
- Hyperactive
 - Agitation; restlessness; fidgeting; pulling out tubes and lines; combativeness
- Mixed
 - Fluctuate between the two types

40  **Incidence/Adverse Effects**

- Estimated to occur in 50% of non-ventilated pts. and 80 - 87% of ventilated pts.
- Adverse effects
 - Increased risk of death in 6 months
 - Increased LOS in hospital
 - Higher ICU and hospital costs
 - Predisposes to prolonged neuropsychological deficits
 - (Pun, 2007)

41  **Causes of Delirium**

42  **Delirium Assessment**

www.icudelirium.org

- Confusion Assessment Method
 - CAM-ICU
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Intensive Care Delirium Screening Checklist

- Altered LOC
- Inattention

- Disorientation
- Hallucinations, delusions, or psychosis
- Psychomotor agitation or retardation
- Inappropriate speech or mood
- Sleep/wake cycle disturbances
- Symptom fluctuation


44  **Barriers to Delirium Assessment**

(Devlin et al. 2008)

- Difficulty in evaluating delirium in pts. who are intubated
- Inability to complete a delirium assessment in sedated pts.
- Use of delirium assessment tools that are too complex

45  **Treating Delirium**


- Identify the etiology
- Modify risk factors
- Haldol 2 – 10 mg IVP q 20 – 30 minutes
 - Give 25% of loading dose q 6 hrs.
- Atypical antipsychotics
 - Olanzapine (*Zyprexa*)
 - Ziprasidone (*Geodon*)
 - Quetiapine (*Seroquel*)
 - *Need more research
 - (Pun, 2007)

46  **Haloperidol lactate (*Haldol*)**

- Neuroleptic agent
 - Inhibits catecholamine receptors resulting in generalized CNS depression
- Dose individualized to pt. response
- Initial dose: 2 to 5 mg. (5 mg/min.)
- Range: 0.5 to 10 mg.
- Acute psychosis: 2 to 50 mg.
- Critically ill: 3 to 25 mg/hr as continuous infusion
- Not labeled for IV use

47  **Haldol Protocol**

- If initial dose is ineffective in 20 to 30 minutes, double the first dose.
- Continue doubling every 20 – 30 minutes until pt. begins to calm.
- Repeat this dose every hour if needed. Titrate to beginning signs of agitation.
- For maintenance, total required daily dose is divided and given at specific intervals or by continuous infusion.
- Use until source of agitation subsides or is removed.

48  **Complications**

- Extrapyramidal effects – rare
 - Administer anticholinergics as needed
- Prolonged QT interval and torsades de pointes
 - Measure QT interval at start of therapy and at least every 8 hrs.
 - Consider interactions with other drug especially proarrhythmic agents
- Neuroleptic malignant syndrome

49  **Strategies to Decrease Delirium Outside the ICU**

- ¹ ■ Repeatedly reorienting
- Providing cognitively stimulating activities
- Non-pharmacologic sleep protocols
- ROM exercises

- Removal of catheters and restraints
- 2 ■ Use of eyeglasses and magnifying glasses
- Use of hearing aids
- Correcting dehydration
- Scheduled pain protocols
- Minimizing unnecessary noise and stimuli
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■(Pun, 2007)

50  **Factors Affecting Delivery of Sedation Therapy**

- Family influences
- Nurses' knowledge, beliefs and attitudes about sedation and critical illness
- Nurses' interpretation and response to pt. motor activity and LOC
- Cost and system influences
- Nurse-physician communication about sedation
- (Weinert, Chlan, & Gross, 2001)

51  **Monitoring Level of Sedation**

- Know goal of therapy
- Use clinical assessment tools
- Use bispectral index monitoring if available
- Consider combinations of drugs to achieve sedation goal

52  **Ramsey Scale**

53  **Sedation-Agitation Scale**

54  **Richmond Agitation Sedation Scale**

55  **RASS continued**

56  **Limitations of Current Scales**

- Lack of validity and reliability testing in critically ill pts.
- Primary focus on agitation and consciousness
- Fail to address other reasons for sedation
- Lack of discrimination between different levels of sedation
- Poorly developed levels that include more than one aspect of sedation
- (Sedation Expert Panel, 2004)

57  **Recommendations for an "Ideal" Scale**

- Domains should represent each goal for sedation assessment
- Should evaluate only a single goal and avoid combining 2 different concepts into same domain
- Have both subjective and objective measures for each domain
- Should direct clinician to evaluate pain and delirium before assessing sedation
- Should be easy to use at the bedside
- (Sedation Expert Panel, 2004)

58  **Daily Sedation Interruption or "Sedation Vacations"**

1 ADVANTAGES

- 2 ■ Reduces
 - Ventilation time
 - Length of stay in ICU
 - Complications of critical illness
 - Incidence of PTSD
- Used by 15 – 62% of ICU clinicians in Australia, Europe,USA, and Canada
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(O'Conner, Bucknall, Manias, 2008)

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3 LIMITATIONS

- 4 ■ Limitations in research methodology and reporting to date
 - Uncertainty of transferability to other ICU populations other than medical ICU
 - Lack of information of how pt. comfort is affected
 - Variability in implementation
 - Lack of research to support recommendations internationally
 - More evidence for physiological rather than psychological benefits

59 **Bispectral Index Monitoring**

- Objective measure of sedation
- Noninvasive device that reflects signal-processed EEG
- Examines certain EEG features derived from power spectral and bispectral analysis, noting end points of consciousness
- Also displays EMG activity of facial muscles

60 **Potential Indications for BIS Monitoring**

- Used in neuromuscular blockade
- Used in guiding sedation and analgesia
- To titrate sedation/analgesia in pts. receiving controlled ventilation
- To avoid under and over-sedation
- To titrate medications for medication-induced coma
- Procedure sedation
- To determine dosage of sedation/analgesia during end-of-life care

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BIS


- Score ranges from 0 to 100 and is measure of cerebral electrical activity
- Correlation of scores
 - 80 to 100 with awake state
 - Responds to normal voice
 - Anxiolysis
 - 60 to 80 with moderate sedation
 - Responds to loud commands or mild prodding/shaking
 - 40 to 60 with deep sedation
 - Low probability of explicit recall
 - Unresponsive to verbal stimulus
 - 20 with burst suppression

67 **Can of worms – Controversies Associated with Sedation**

68 **Neuromuscular Blocking Agents**

- Indications
 - Prevent patients from moving
 - Facilitate mechanical ventilation
 - Improve chest wall compliance
 - Reduce peak airway pressures

- Prevent pt. from “fighting” the ventilator
- Improve gas exchange in ARDS
- Reduce risk of barotrauma

69  **NMBA - Indications**

- Facilitate endotracheal intubation
- Control increases in ICP
- Reduce muscle tone in certain medical conditions
- Facilitate procedures or diagnostic studies
- Reduce oxygen consumption requirements

70  **Selection of drug**

- Organ dysfunction
- Adverse effects
- Interactions with other medications
- Duration of blockade
- Cost considerations

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72  **Succinylcholine**

- Depolarizing agent
- Used for rapid sequence intubation
- Loading dose: 1 – 1.5 mg/kg (over 30 sec.)
- Onset of action: 30 – 60 seconds
- Duration: 4 – 12 minutes
- Avoid use in pts. at risk for developing hyperkalemia
 - Those with SCI or neuromuscular disease

73  **Rocuronium (*Zemuron*)**

- Nondepolarizing agent
- May be used as alternative to succinylcholine for intubation
- Loading dose: 0.45 – 0.6 mg/kg q 1 hr
- Onset: 30 – 60 seconds
- Duration: 30 minutes

74  **Pancuronium bromide (*Pavulon*)**

- Onset: 2 – 3 minutes
- Duration: 40 – 60 minutes
- Loading dose – bolus injections: 0.1 to 0.2 mg/kg every 1 to 3 hours
- Continuous infusion: Load with 0.03 – 0.1 mg/kg followed by 0.06 – 0.1 mg/kg/hr
- Elimination: Renal – 40 to 60%; biliary – 10%; hepatic – 30 to 40%

75  **Pancuronium**

- Been around the longest
- Least costly agent
- Adverse effects
 - Hypertension and tachycardia
 - Prolonged paralysis has been reported with renal impairment

76  **Vecuronium (*Norcuron*)**

- Onset of action: 1 – 3 minutes
- Duration of action: 30 – 40 minutes
- Loading dose: 0.1 mg/kg.
- Continuous infusion: 0.05 – 0.1 mg/kg/hr (50 – 100 mcg/kg/min)

- Elimination
 - Hepatic: 15 – 20%
 - Biliary: 40%

77 **Cisatracurium besylate (*Nimbex*)**

- Onset: 2 – 3 minutes
- Duration: 35 – 45 minutes
- Loading dose: 0.1 to 0.2 mg/kg
- Continuous infusion: 0.06 – 0.18 mg/kg/hr; begin at 3 mcg/kg/min. (range: 0.5 to 10.2 mcg/kg/min.)
- Elimination: Hoffman degradation
- Decreased laudanosine production
- Less histamine release

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86 **Interpretative problems with PNS**

- Patient-related problems
 - Edema
 - Moist skin
 - Difficulty with accurate electrode placement
- Equipment-related problems
 - Dry electrodes
 - Battery weakness
 - Frayed lead wires

87 **Operator-related Problems**

- Incorrect electrode placement
- Inter and intra-observer reliability
- Variability in interpretation of twitch response
- False negative responses
- False positive interpretations

88 **Reasons PNS not Used**

- Equipment unavailability
- Lack of training
- Insufficient evidence PNS improves care
- Problems associated with using device
 - False negative

89 **Frequency of Monitoring**

- One suggestion
- Q 30 minutes X4 after initiation or manipulation of drip
- Q 4 hours once desired level of blockade achieved
- Q 8 hours if no manipulations required
 - X 24 hours

(Jones, 2003)

90 **Clinical indicators**

- Use clinical assessment in addition to PNS to assess level of blockade
 - Tachycardia

- Hypertension
- Lacrimination
- Diaphoresis
- Spontaneous breathing
- Body movement

91  **Adverse effects/complications**


- Inability to evaluate neurologic changes
- Inability to adjust position
 - Skin breakdown and pressure ulcers
- Inability to constrict leg muscles
 - Deep vein thrombosis
- Inability to cough
 - Ventilator-associated pneumonias
- Inability to blink
 - Corneal abrasions or long-term damage to cornea

92  **Critical Illness Polyneuropathy/
Critical Illness Myopathy**

- Neuropathy of critical illness
- Prolonged paralysis associated with NMBA use
- Small percentage of patients
 - Prolonged weakness associated with build up of the drug or their metabolites
 - No association with delayed excretion or clearance of the drug
 - Use of aminosteroid – based NMBAs in conjunction with corticosteroids

93  **Prevention Strategies**

- Avoidance of corticosteroids and/or neuromuscular blocking agents, where possible
- Tight glycemic control on ventilator pts.
- Early mobilization

94  **NMBAs – Potentiated by:**

- Antibiotics
 - Aminoglycosides – gentamicin, tobramycin
 - Clindamycin
 - Piperillin
- Diuretics (furosemide and thiazides)
- Magnesium sulfate
- Muscle relaxants
- Calcium channel blockers
- Anti-arrhythmic medications – lidocaine, propranolol, quinidine
- Morphine
- Meperidine

95  **NMBAs – Antagonized by:**

- Carbamazepine
- Phenytoin
- Theophylline
- Action is altered by:
 - Hypokalemia
 - Dehydration
 - Body temperature
 - Acid-base balance

96  **Patient perceptions/recall**

- These drugs have no analgesic or sedative properties
- Pain; discomfort; anxiety

- Sleeplessness
- Delusions or hallucinations
- Time distortion
- Lost sense of body position
 - (Parker, Schubert, & Parrillo, 1984)

97  **Patients' Recollection of Therapeutic Paralysis**

- Back and Forth
 - Weird dreams
 - Distressing and disconcerting
- Loss of control
 - Out of control in every facet of existence
 - Fighting or being tied down
 - Being scared
- Almost Dying
- Feeling cared for
 - Presence, touch, voice
 - (Ballard et al., 2006)

98  **Interventions**

- Always administer analgesics and sedatives
 - Preferably by infusion
- Reorient frequently to time
- Explain what you are doing repeatedly
- Talk to the patient
- Patient may misinterpret what they hear
 - Be reassuring

99  **Pain Management Monitoring**

- 1. How would you assess pain in the following pts.?
 - A. Intubated and mildly sedated
 - B. Intubated and deeply sedated
 - C. Intubated, sedated, and receiving neuromuscular blockade

100  **Sedation Monitoring**

- How would you evaluate level of sedation in the following pts.?
 - A. Intubated and mildly to moderately sedated
 - B. Intubated and deeply sedated
 - C. Intubated and receiving neuromuscular blockade

101  **Neuromuscular Blockade Monitoring**

- How would you assess level of blockade in your pt. receiving NMB agents?

102  **Patient Situation**

- 24 y/o trauma pt. post-op from exp. laparotomy and ORIF of femur
- Injuries include: ruptured spleen/liver lac./femur and pelvis fractures/multiple abrasions
- Second hour post-op, pt. is awake and indicating he is in pain
- SBP is 80 and pt. is receiving blood
- How would you manage his pain?

103  **Patient Situation**

- 67 y/o with history of COPD who is Day 2 post-op from CABG surgery
- Pt. was extubated today, has been awake, alert, following commands.
- You enter room and find the pt. trying to get out of bed by himself, removing IVs & electrodes, and is pulling on his chest tubes.
- Pt. is disoriented to place and situation and insists he is going outside.
- What non-pharmacologic and pharmacologic interventions might be used in this situation?
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104  **Patient Situation**

- 35 y/o female has just been admitted to the ICU following an MVA.
- Injuries include facial and scalp lac., rib fractures and pulmonary contusions. Pt. was intubated at the scene for decreased LOC.
- Currently the pt. is arousable to voice and able to follow commands.
- Plastic surgeons arrive to repair scalp and facial lacerations. Pt. is moving while the repair is being attempted. The physician asks you to give the pt. 20 mg. of Nimbex for the procedure.
- What other medications should you request to give the pt.?

105  **Questions????**