The Patient ICU Experience

SEDATION AND PAIN CONTROL IN THE ICU

Karalyn Hillebrecht, DO – Surgical Critical Care Fellow

Disclosures

- I have no financial or professional conflicts of interest to disclose

Objectives

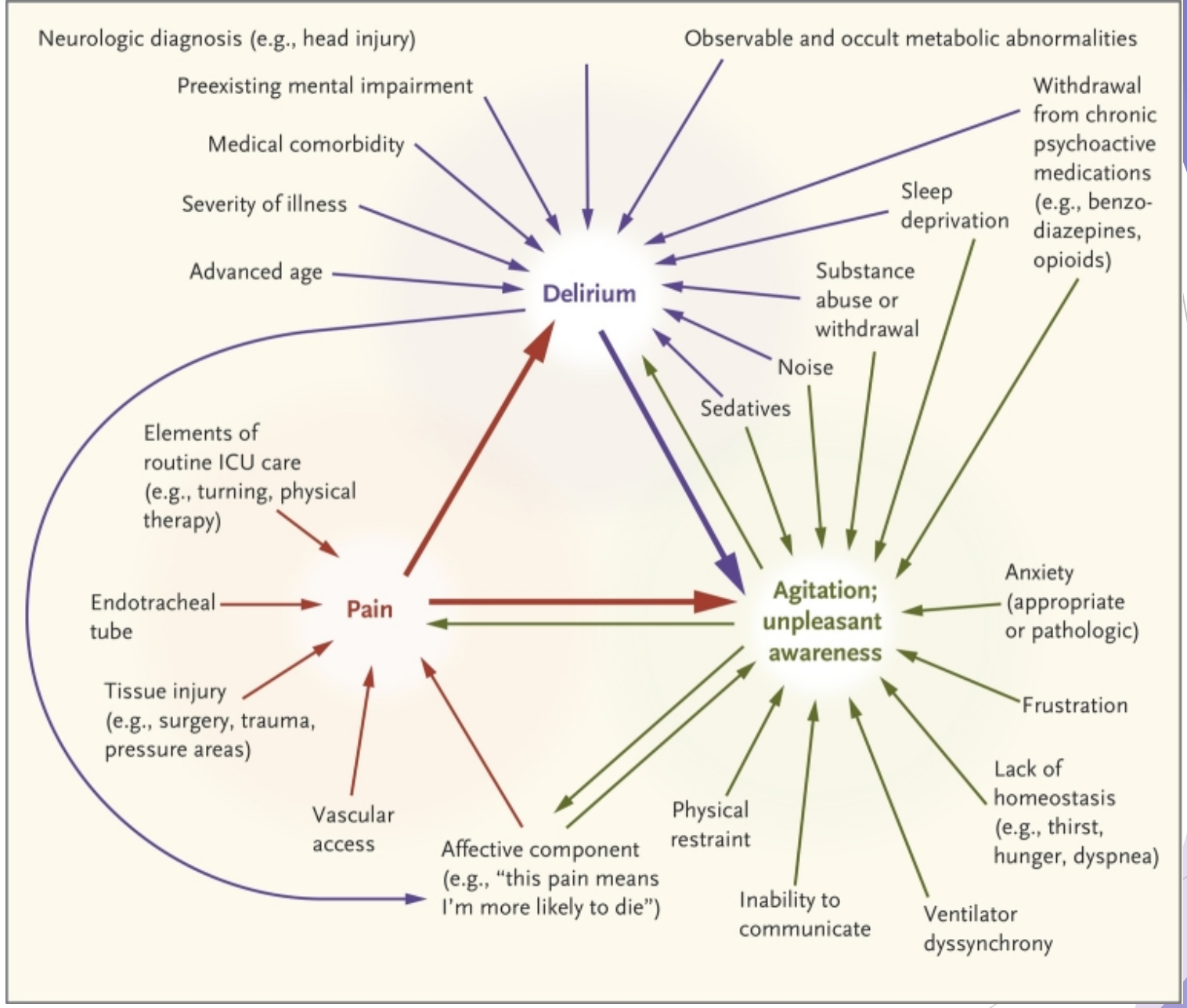
- The Patient ICU Experience:
  - Pain
  - Anxiety
  - Sedation
  - Delirium
- Pain control
- Sedation

The ICU Triad

- Pain
- Agitation / Unpleasant Awareness
- Delirium

Reade, M. C., & Finfer, S. (2014). Sedation and delirium in the intensive care unit. *New England Journal of Medicine*, *370*(5), 444-454.

The ICU Triad



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The ICU Experience

- How many people remember their stay in the ICU?

The ICU Experience

- How many people remember their stay in the ICU?

The majority of patients remember their ICU stay	The majority of patients don't remember their ICU stay

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The majority of patients remember their ICU stay

The majority of patients <u>don't</u> remember their ICU stay

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- How many people remember their stay in the ICU?

The majority of patients remember their ICU stay

The majority of patients don't remember their ICU stay

The ICU Experience

- How many people remember their stay in the ICU?
  - 20 – 40% of people report no recollection of their ICU stay
- How many people experience pain or discomfort while in the ICU?

The ICU Experience

- How many people remember their stay in the ICU?
  - 20 – 40% of people report no recollection of their ICU stay

- How many people experience pain or discomfort while in the ICU?

Less than half of patients report pain	More than half of patients report pain

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The ICU Experience

- How many people remember their stay in the ICU?
  - 20 – 40% of people report no recollection of their ICU stay
- How many people experience pain or discomfort while in the ICU?
  - 50 – 80% of patients report pain

The ICU Experience

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- How many people experience pain or discomfort while in the ICU?
  - 50 – 80% of patients report pain
    - Painful procedures
    - Turning
    - Suctioning

The ICU Experience

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  - 30 – 50% of patients have pain at rest

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    - Turning
    - Suctioning
  - 30 – 50% of patients have pain at rest
  - 25% of patients who report stressful ICU experiences show symptoms of PTSD four years out from discharge

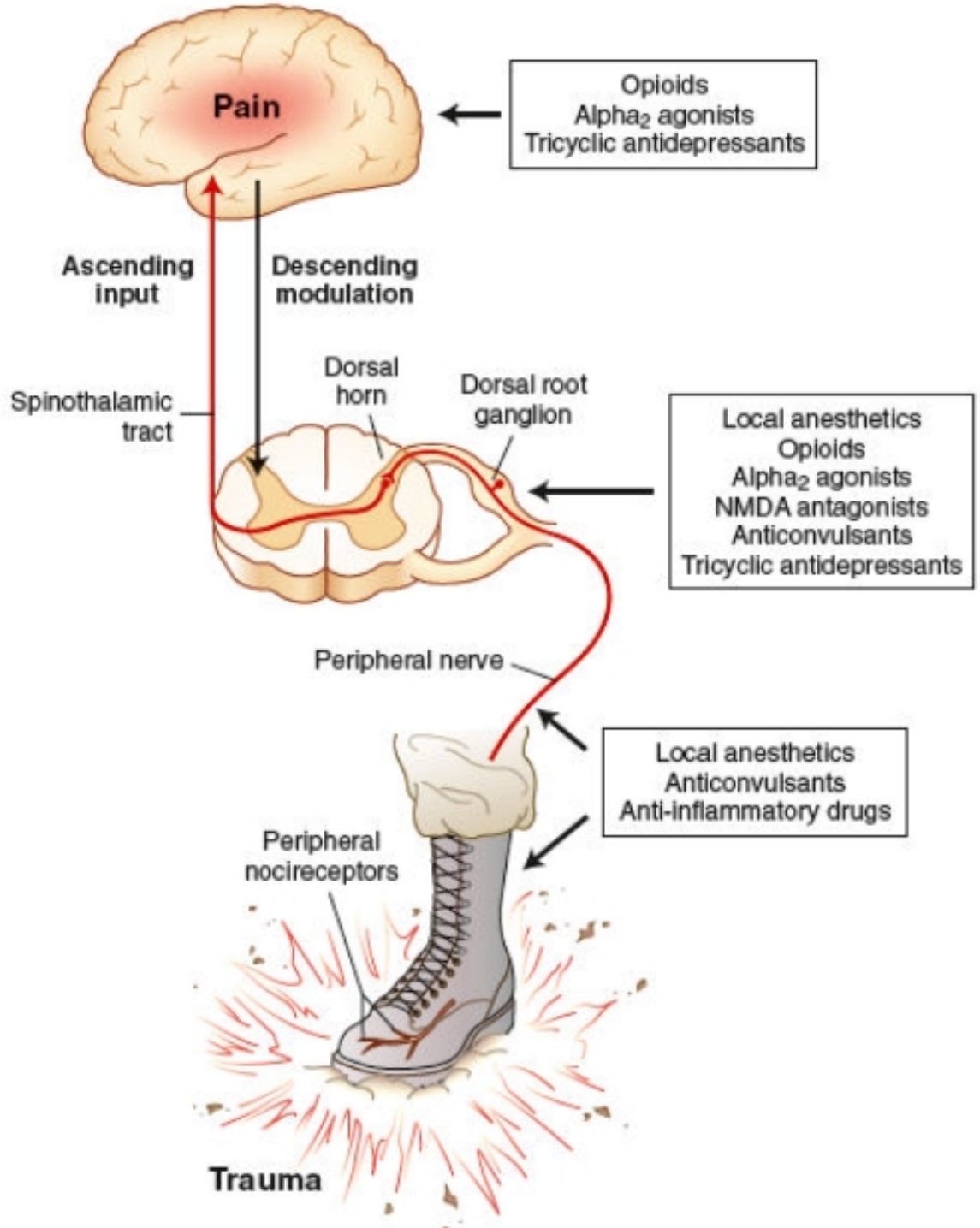
Anesthesia?

Anesthesia?

- Anesthesia: Greek for “without sensation”:
  state of controlled, temporary loss of sensation or awareness
  - Amnesia: loss of memory
  - Analgesia: relief of pain
  - Paralysis: muscle relaxation

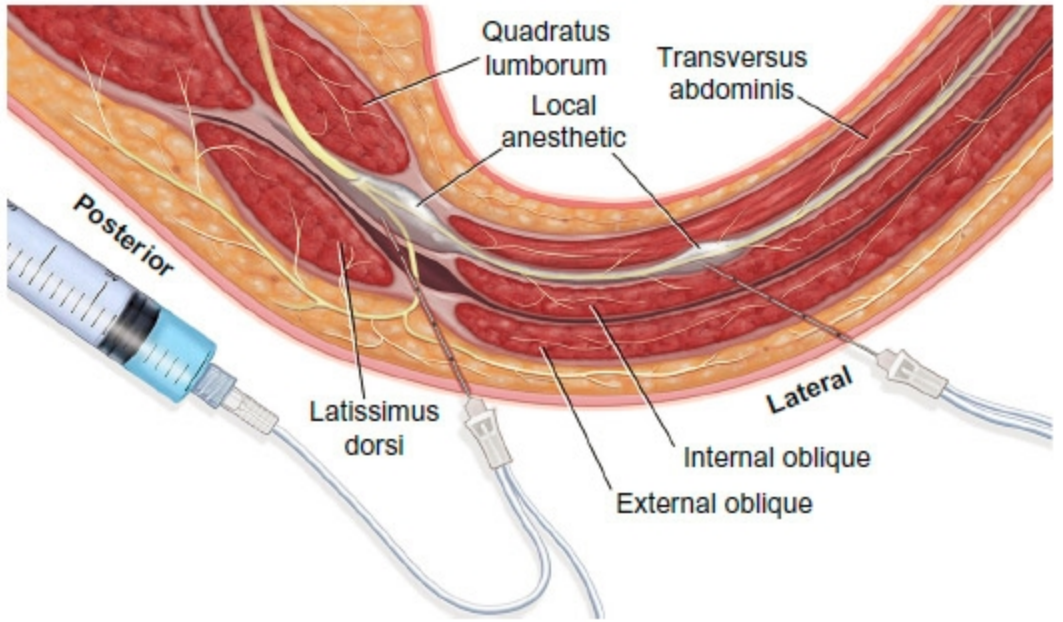
Pain Control

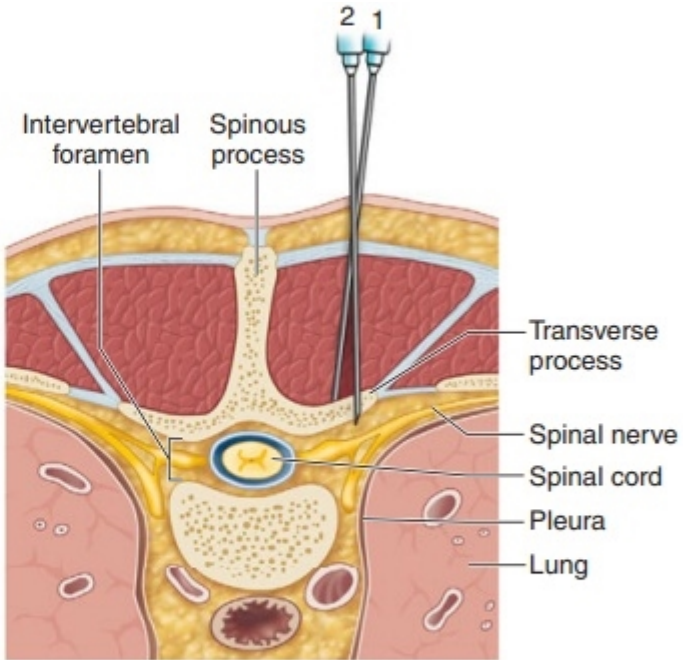
- Painful stimulus received by peripheral nocireceptor
- Afferent nerves (Aδ and C) carry signal to the spinal cord
- Afferent nerves synapse within the dorsal horn and are carried to the brain via the spinothalamic tract
- Interpretation of pain occurs once pain signal reaches the cerebral cortex

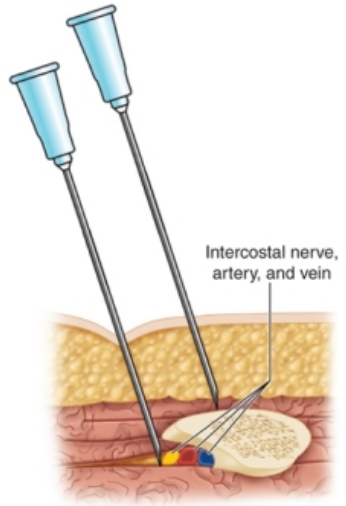


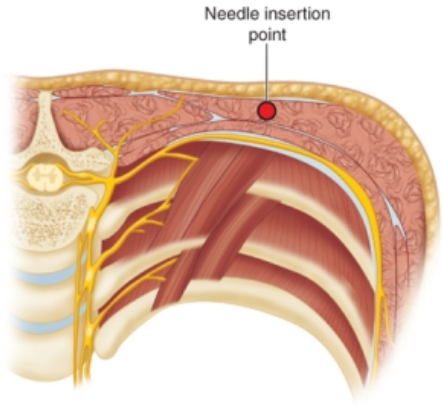
Pain Control

- Regional Anesthesia
  - Spinal Anesthesia
  - Epidural Anesthesia
  - Peripheral Nerve Blocks
- Local Anesthetics: dose dependent blockade of Na+ current within nerve fibers









Pain Control

- Regional Anesthesia
  - Spinal Anesthesia
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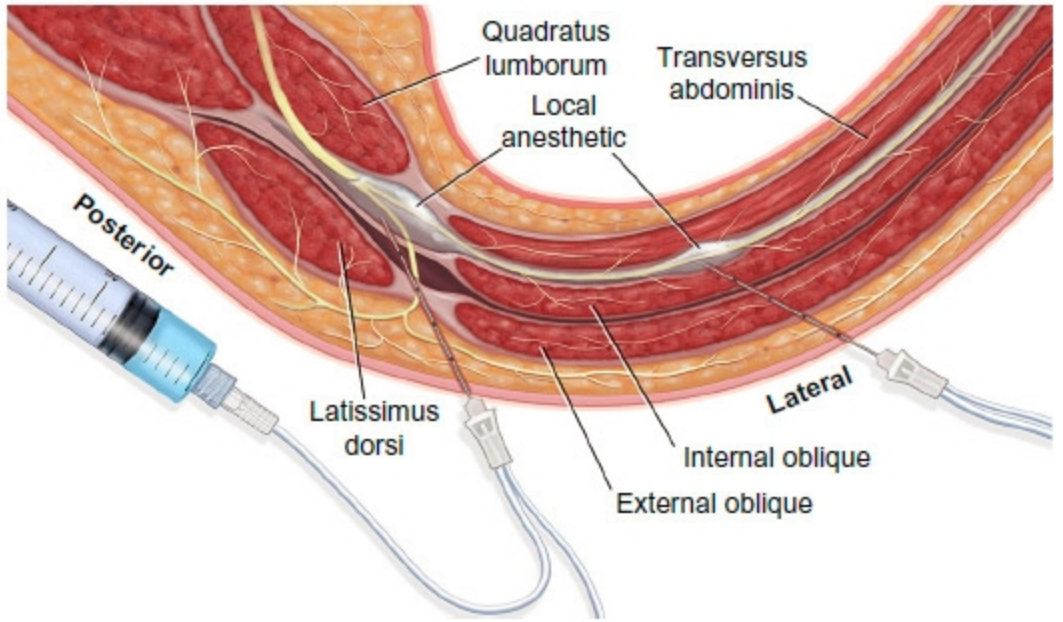
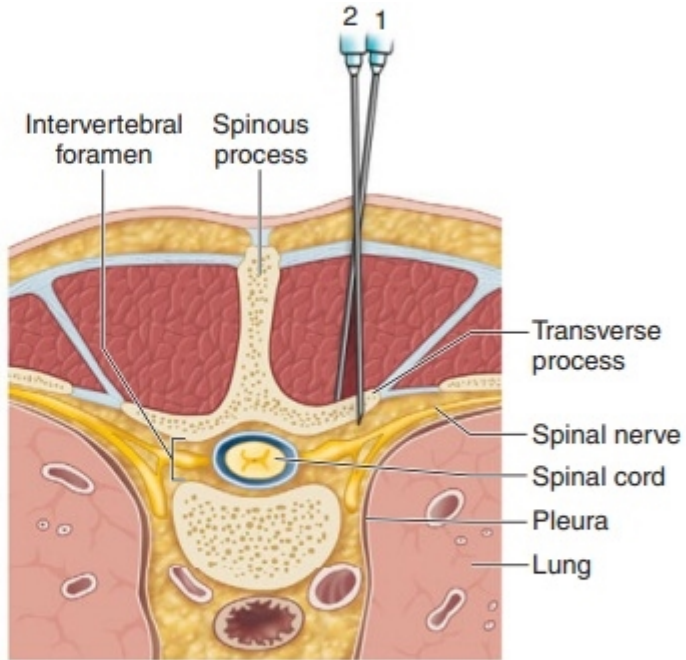
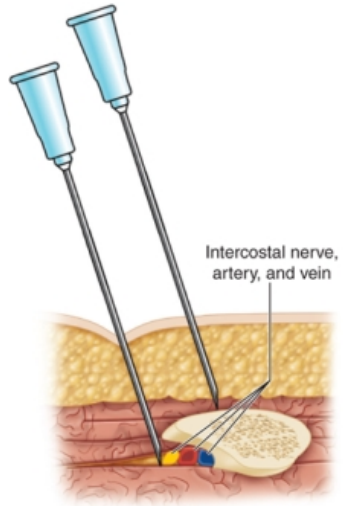
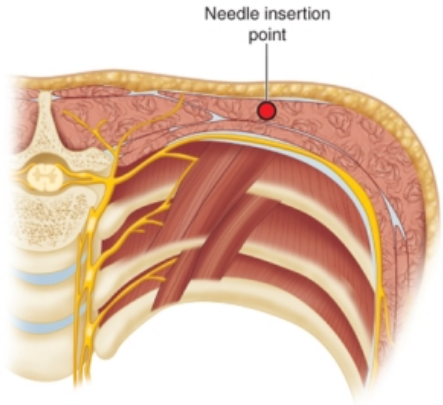
- Local Anesthetics: dose dependent blockade of Na+ current within nerve fibers
  - Mepivacaine → Carbocaine
  - Chloroprocaine → Nesacaine
  - Lidocaine → **Xylocaine**
  - Ropivacaine → Naropin
  - Bupivacaine → **Marcaine**
  - Procaine → **Novocaine**









Pain Control

- Regional Anesthesia
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  - Peripheral Nerve Blocks
- Local Anesthetics: dose dependent blockade of Na+ current within nerve fibers
  - Esters
    - Chloroprocaine (0.5-1 hr)
    - Procaine (1-1.5 hr)
  - Amides
    - Lidocaine (1-3 hr) Max: 5 mg/kg; 7 mg/kg with epi
    - Mepivacaine (1-3 hr) Max: 5 mg/kg; 7 mg/kg with epi
    - Bupivacaine (3-6 hr) Max: 3 mg/kg without epi
    - Ropivacaine (3-6 hr) Max: 3 mg/kg without epi

Pain Control - Opioids

- Bind to opioid receptors in the CNS and peripheral tissues
- Receptors: μ_1(supraspinal), μ_2, δ (spinal), κ (spinal), ε, and σ receptors

- Fentanyl
- Hydromorphone (Dilaudid)
- Morphine
- Oxycodone
- Hydrocodone
- Codeine

Pain Control

- Opioids
  - Bind to opioid receptors in the CNS and peripheral tissues
  - Receptors: μ_1(suprspinal), μ_2, δ (spinal), κ (spinal), ε, and σ receptors

- Fentanyl → fastest onset; no histamine; no renal adjustment; no metabolites
- Dilaudid → slower onset; no histamine; no renal adjustment; (+) metabolites
- Morphine → slowest onset; hypotension d/t histamine; renal adjustment; metabolites can cause seizures
- Oxycodone
- Hydrocodone
- Codeine

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Alvimopan (Entereg)

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Alvimopan (Entereg)
oral, peripherally-acting mu-opioid receptor antagonist

Acetaminophen

- MOA incompletely understood
- May selectively inhibit or reduce COX in the brain
- Does not appear to inhibit COX enzyme activity outside of the CNS and therefore is not considered an anti-inflammatory
- May modulate the cannabinoid system

NSAIDs

- Inhibits COX enzyme activity, reducing prostaglandins that act directly on nociceptors

- Ibuprofen (Motrin)
- Ketorolac (Toradol)
- Celecoxib (Celebrex): selective COX-2 inhibitor

ORIGINAL ARTICLE

Ketorolac Use and Postoperative Complications in Gastrointestinal Surgery

Meera Kotagal, MD, MPH, Timo W. Hakkarainen, MD, MS,* Vlad V. Simianu, MD,* Sara J. Beck, MS,† Rafael Alfonso-Cristancho, MD, PhD, MSc,* and David R. Flum, MD, MPH**

Objective: To study the association between ketorolac use and postoperative complications.

Background: Nonsteroidal anti-inflammatory drugs may impair wound healing and increase the risk of anastomotic leak in colon surgery. Studies to date have been limited by sample size, inability to identify confounding, and a focus limited to colon surgery.

Methods: Ketorolac use, reinterventions, emergency department (ED) visits, and readmissions in adults (≥18 years) undergoing gastrointestinal (GI) operations was assessed in a nationwide cohort using the MarketScan Database (2008–2012).

Results: Among 398,752 patients (median age 52, 45% male), 55% underwent colorectal surgery, whereas 45% had noncolorectal GI surgery. Five percent of patients received ketorolac. Adjusting for demographic characteristics, comorbidities, surgery type/indication, and preoperative medications, patients receiving ketorolac had higher odds of reintervention (odds ratio [OR] 1.20, 95% confidence interval [CI] 1.08–1.32), ED visit (OR 1.44, 95% CI 1.37–1.51), and readmission within 30 days (OR 1.11, 95% CI 1.05–1.18) compared to those who did not receive ketorolac. Ketorolac use was associated with readmissions related to anastomotic complications (OR 1.20, 95% CI 1.06–1.36). Evaluating only admissions with ≤3 days duration to exclude cases where ketorolac might have been used for complication-related pain relief, the odds of complications associated with ketorolac were even greater.

Conclusions: Use of intravenous ketorolac was associated with greater odds of reintervention, ED visit, and readmission in both colorectal and noncolorectal GI surgery. Given this confirmatory evaluation of other reports of a negative association and the large size of this cohort, clinicians should exercise caution when using ketorolac in patients undergoing GI surgery.

Keywords: adverse events, gastrointestinal surgery, ketorolac, medication use, post-operative complications

(*Ann Surg* 2015;00:1–5)

Received: 23 April 2019 | Revised: 18 September 2019 | Accepted: 22 October 2019

DOI: 10.1002/ags3.12300

SYSTEMATIC REVIEW ARTICLE

AGSurg Annals of Gastroenterological Surgery WILEY

Postoperative non-steroidal anti-inflammatory drugs and anastomotic leakage after gastrointestinal anastomoses: Systematic review and meta-analysis

Supaschin Jamjittrong[1,2] | Akihisa Matsuda[1] | Satoshi Matsumoto[1] | Tunyaporn Kamonvarapitak[1,2] | Nobuyuki Sakurazawa[1] | Youichi Kawano[1] | Takeshi Yamada[3] | Hideyuki Suzuki[1] | Masao Miyashita[1] | Hiroshi Yoshida[3]

[1]Department of Surgery, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan

[2]Department of Surgery, Queen Savang Vadhana Memorial Hospital, Sri Racha, Thailand

[3]Department of Gastrointestinal Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Tokyo, Japan

Correspondence
Akihisa Matsuda, Department of Surgery, Nippon Medical School Chiba Hokusoh Hospital, 1715 Kamagari, Inzai, Chiba 270-1694, Japan.
Email: a-matsu@nms.ac.jp

Abstract

Aim: Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used to control postoperative pain; however, their postoperative use has been associated with anastomotic leakage after gastrointestinal surgery. This systematic review and meta-analysis aimed to determine the correlation between the use of NSAIDs and anastomotic leakage.

Methods: We conducted a comprehensive electronic literature search up to August 2018 to identify studies comparing anastomotic leakage in patients with and without postoperative NSAID use following gastrointestinal surgery. We then carried out a meta-analysis using random-effects models to calculate odds ratios (OR) with 95% confidence intervals (CI).

Results: Twenty-four studies were included in this meta-analysis, including a total of 31 877 patients. Meta-analysis showed a significant association between NSAID use and anastomotic leakage (OR 1.73; 95% CI = 1.31-2.29, $P < .0001$). Subgroup analyses showed that non-selective NSAIDs, but not selective cyclooxygenase-2 inhibitors, were significantly associated with anastomotic leakage. However there was no significant subgroup difference between selective and non-selective NSAIDs.

Conclusion: Results of this meta-analysis indicate that postoperative NSAID use is associated with anastomotic leakage following gastrointestinal surgeries. Caution is warranted when using NSAIDs for postoperative analgesic control in patients with gastrointestinal anastomoses.

KEYWORDS

anastomotic leakage, cyclooxygenase inhibitor, gastrointestinal surgery, meta-analysis, non-steroidal anti-inflammatory drugs

Alpha Agonists

- Clonidine
  - Alpha-2 agonists may produce analgesia by inhibiting norepinephrine release from prejunctional alpha-2 receptors, which triggers a sympatholytic effect
- Dexmedetomidine (Precedex)
  - Alpha-2 adrenergic receptor agonist
- Guanfacine
  - Alpha-2A adrenergic receptor agonist

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Phenylephrine (NeoSynephrine)
Alpha-1 Agonist which induces contraction of smooth muscle

Other Pain Adjuncts

- Dextromethorphan
  - Uncompetitive N-methyl-D-aspartate (NMDA) glutamate receptor antagonist
- Ketamine
  - NMDA receptor antagonist, prevents central sensitization in dorsal horn neurons, preventing pain transmission to the spinal cord

- Gabapentin (Neurontin) and Pregabalin (Lyrica)
  - Inhibits α2δ subunit of voltage dependent calcium channels in the posterior horn, reducing hyperexcitability
  - Despite their name, gabapentin and pregabalin do NOT bind to GABA receptors

Other Pain Adjuncts

Ice Packs Reduce Postoperative Midline Incision Pain and Narcotic Use: A Randomized Controlled Trial

Ammara A Watkins, MD, Timothy V Johnson, MD, Adam B Shrewsberry, MD, Paymon Nourparvar, MD, Tarik Madni, MD, Colyn J Watkins, MD, Paul L Feingold, MD, David A Kooby, MD, FACS, Shishir K Maithel, MD, FACS, Charles A Staley, MD, Viraj A Master, MD, PhD, FACS

BACKGROUND: Postoperative pain is an unavoidable consequence of open abdominal surgery. Although cryotherapy, the application of ice to a surgical wound site, has been shown to be effective in reducing postoperative pain in orthopaedic, gynecologic, and hernia operations, it has not been assessed in patients who undergo major open abdominal operations. We hypothesized that patients who receive cryotherapy would report lower pain scores as a primary outcomes measure.

STUDY DESIGN: Patients undergoing abdominal operations with midline incisions were randomized to receive cryotherapy for a minimum of 24 hours in time intervals dictated by patient preference vs no cryotherapy. The primary outcome of pain relief was assessed with visual analog pain scores (VAS). The study was powered to detect a clinically significant difference in VAS between the control and cryotherapy group. Comparisons between groups were measured by Student's *t*-test or Mann-Whitney U test for parametric and nonparametric data, respectively.

RESULTS: There were 55 patients randomized: 28 to the control group and 27 to the cryotherapy group. For the primary measure, mean postoperative pain score on postoperative days (PODs) 1 and 3 after surgery was significantly lower between the control and cryotherapy groups on the visual analog pain scale ($p < 0.005$). Narcotic use was decreased in the cryotherapy group on POD 1 by 3.9 morphine equivalents ($p = 0.008$). No statistically significant difference was found between the 2 treatment groups with respect to length of hospital stay, pulmonary complications, and wound infection rate in terms of secondary measures.

CONCLUSIONS: Ice packs are a simple, cost-effective adjuvant for decreasing postoperative pain and narcotic use in patients undergoing major abdominal operations. (J Am Coll Surg 2014;219: 511–517. © 2014 by the American College of Surgeons)

Sedation

RASS	SAS
+4 Combative Combative, violent, immediate danger to staff	**7 Dangerous Agitation** Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, trashing side-to-side
+3 Very Agitated Pulls to remove tubes or catheters; aggressive	**6 Very Agitated** Requiring restraint and frequent verbal reminding of limits, biting ETT
+2 Agitated Frequent non-purposeful movement, fights ventilator	**6 Very Agitated** Requiring restraint and frequent verbal reminding of limits, biting ETT
+1 Restless Anxious, apprehensive, movements not aggressive	**5 Agitated** Anxious or physically agitated, calms to verbal instructions
0 Alert and Calm Spontaneously pays attention to caregiver	**4 Calm and Cooperative** Calm, easily arousable, follows commands
-1 Drowsy Not fully alert, but has sustained awakening to voice - eye opening and contact >10 seconds	**3 Sedated** Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
-2 Light Sedation Briefly awakens to voice - eyes open and contact <10 seconds	**3 Sedated** Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
-3 Moderate Sedation Movement or eye opening to voice - no eye contact	**3 Sedated** Difficult to arouse but awakens to verbal stimuli or gentle shaking, follows simple commands but drifts off again
-4 Deep Sedation No response to voice, but movement or eye opening to physical stimulation	**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
-5 Unarousable No response to voice or physical stimulation	**1 Unarousable** Minimal or no response to noxious stimuli, does not communicate or follow commands

Sedation

Richmond Agitation-Sedation Scale

	Target RASS Value	RASS Description
+4	Combative	Combative, Violent, Immediate Danger to Staff
+3	Very Agitated	Pulls or Removes Tube(s) or Catheter(s); Aggressive
+2	Agitated	Frequent non-Purposeful Movement, Fights Ventilator
+1	Restless	Anxious, Apprehensive but Movements are not Aggressive or Vigorous
0	Alert and Calm	
-1	Drowsy	Not Fully Alert, but has Sustained Awakening to Voice (Eye Opening & Contact >10sec)
-2	Light Sedation	Briefly Awakens to Voice (Eye Opening & Contact <10sec)
-3	Moderate Sedation	Movements or Eye Opening to Voice (BUT NO Eye Contact)
-4	Deep Sedation	No Response to Voice, BUT has Movement or Eye Opening to Physical Stimulation
-5	Unarousable	No Response to Voice or Physical Stimulation

Benzodiazepines

- Examples: midazolam (Versed), lorazepam (Ativan)
- Mechanism: depressant that enhances the effect of the neurotransmitter GABA
- Outcome:
  - Sedation
  - Hypnosis
  - Anxiolysis
  - Muscle relaxation
  - Anticonvulsant
- Advantages: amnestic and sedative effect; treats seizures and withdrawal
- Disadvantages: accumulates delaying ICU awakening; delirium

Propofol

- Mechanism: Activates GABA receptors (different subunit than benzodiazepines) and cannabinoid receptors
- Outcome:
  - Decreased consciousness, sedative
  - Amnesia
- Advantages: rapid arousal, reduced ICP
- Disadvantages: respiratory depression, hypotension, anaphylactic reaction, hypertriglyceridemia
  - Propofol Infusion Syndrome: bradycardic heart failure, lactic acidosis, rhabdomyolysis, renal failure

Dexmedetomidine (Precedex)

- Mechanism: alpha-2 receptor agonist
- Outcome:
  - Sedative
  - Amnestic
  - Mild analgesic properties
- Advantages: no respiratory depression, closer to natural sleep, less delirium
- Disadvantages: decreased heart rate, blood pressure, and circulating NE, high risk bradyarrhythmias in patients with heart failure or conduction defects

Chandrasekhar, R., Hughes, C. G., Pun, B. T., Orun, O. M., Ely, E. W., & Pandharipande, P. P. (2020). Statistical analysis plan for the maximizing the efficacy of sedation and reducing neurological dysfunction and mortality in septic patients with acute respiratory failure trial. *Critical Care and Resuscitation*, *22*(1), 63-71.

Antipsychotics

- Example: Haloperidol (Haldol), Seroquel, Zyprexa
- Mechanism: blocks dopamine receptors in the CNS
- Outcome:
  - Sedative
  - Antipsychotic
- Advantages: no respiratory depression, no hypotension
- Disadvantages: extrapyramidal side effects, Neuroleptic Malignant Syndrome, ventricular tachycardia (prolonged QT) or Torsades

One Final Case

“Did you reverse her?”

“Oh, no. Figured let her wake up slowly.”

Paralytics

- Depolarizing neuromuscular blockade: succinylcholine
- Non-depolarizing neuromuscular blockade: rocuronium
  - Reversible:
    - Neostigmine and glycopyrrolate
    - Sugammadex

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  - If you choose not to reverse the paralytic...

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  - If you choose not to reverse the paralytic...

SEDATION

Train of Four

Questions?

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