Dexmedetomidine for the Prevention of Emergence Coughing

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Background

Emergence from General Anesthesia

The mechanisms responsible for unconsciousness are reversed

- Stage II occurs due to a rising sympathetic tone[1]
  - Airway reflexes return[1]
    - Exaggerated response to stimulation[1]

Potential Adverse Effects of Emergence Coughing in the Following Patient Populations:

- Reactive airway disease[4]
- Poor baseline pulmonary function[5]
- Decreased FRC
- Coronary artery disease[5]
- Thyroidectomy
- Carotid endarterectomy
- Laparotomy or hernia repair
- Vocal cord procedures

Adverse Effects of Emergence Coughing

Pharmacodynamics of Dexmedetomidine

α2 Adrenergic Receptor Agonist
- Presynaptic: inhibits release of norepinephrine (NE)[3]
- Postsynaptic: inhibits sympathetic activity[3]

Central Nervous System
- Concious Sedation[2]
- Anxiolysis[2]
- Reduce substance P release in the spinal cord[2]

Airway
- Reduce acetylcholine release[2]
- Attenuate C-fiber mediated contraction[2]

Cardiovascular
- Decreased heart rate[3]
- Decreased blood pressure[3]

Research Question

P In adult surgical patients requiring an awake endotracheal extubation,

I does intraoperative administration of dexmedetomidine in comparison

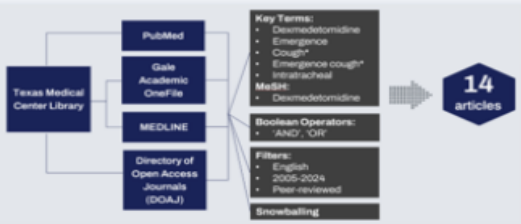
C to no administration of dexmedetomidine

O decrease the incidence of coughing

T during the emergence period?

Literature Review

Literature Search



Levels of Evidence[21]
Agency for Healthcare Research and Quality

Level I	Meta-analysis	1
Level II	Experimental design	13
Level III	Quasi-experimental design	
Level IV	Non-experimental design	
Level V	Case reports	

Strength of Evidence[22]
United States Preventive Services Task Force

A	Good evidence that intervention improves health outcomes	6
B	Fair evidence that intervention improves health outcomes	8
C	Balance of benefits and harms too close to recommend	
D	Fair evidence that an intervention is ineffective	
E	Evidence of efficacy is lacking or conflicting	

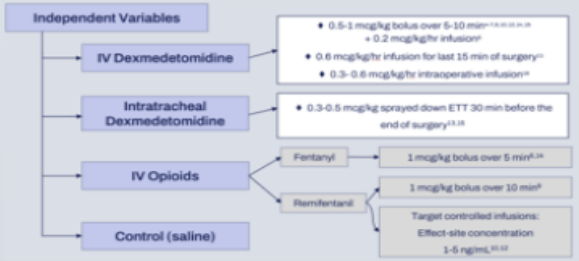
Summary of Findings

Study Design

Inclusion Criteria	Exclusion Criteria
Adult patients ≥ 18 years old[4-16]	Systemic diseases[4,6,7-13,15,16]
GETA[4-16]	Obesity[6,7,9,10]
ASA I-II[4,6,8-15] or I-III[5,7,16]	Potential for difficult airway[16-19]
Procedure duration ○ 1-4 hrs[5,7,16] or 1-2 hrs[9]	Cough inducing or suppressing medications[8,9,11,13] or sedatives[8,12,15]
Similar elective surgeries[4,6-8,10-12,15,16]	Conduction block on EKG[13,15]
	Chronic pain, taking analgesics[4,7,16]
	Chronic cough or respiratory disease[8-15]

Summary of Findings

Independent Variables



Primary Outcomes

Both IV and intratracheal DEX significantly decrease coughing during the emergence period

- IV DEX compared to placebo
- Intratracheal DEX compared to placebo
- DEX bolus vs Fentanyl bolus
  - Increased incidence of no coughing
  - Decreased incidence of severe coughing
- DEX bolus + Remifentanil infusion
  - Decreased incidence and severity of coughing
  - Fewer incidences of severe coughing
  - Less remifentanil required to prevent coughing
- Increasing doses of DEX further reduces coughing

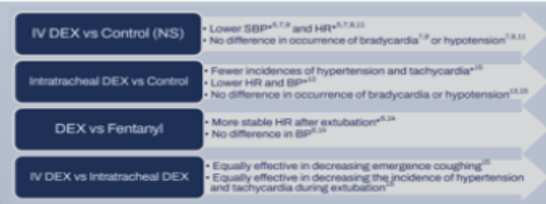
Smoothness of extubation was comparable

- DEX bolus vs Fentanyl bolus
  - Decreased response to laryngoscopy and suction

No difference in the mean number of coughs

- DEX bolus vs Remifentanil bolus

Secondary Outcomes



* $p < .05$

Summary of Findings

Secondary Outcomes

Recommendations for Practice

Patient	Timing	Dose
Ideal ◊ Adult ≥ 18 yrs ◊ ASA I-III ◊ Undergoing GETA **Avoid** ◊ Reduced cardiac function ◊ Hemodynamically unstable	**Emergence Bolus** ◊ Start bolus once maintenance agent is discontinued ◊ About 10 min before surgery completion	0.75-1 mcg/kg (LBW) bolus over 10 min
	Intraoperative Infusion ◊ Start infusion with induction of anesthesia	0.5-0.6 mcg/kg/hr (LBW)
	Intratracheal Dose ◊ Spray down ETT about 30 min before surgery completion	0.3-0.5 mcg/kg (LBW)

Limitations

- Small sample sizes
- Common comorbidities excluded
- Details unclear about administration timing
- Variable measurement scales of cough severity

Additional Findings

When administered via the intratracheal route, smaller doses may be required to decrease or prevent emergence coughing with less hemodynamic alterations.[13]

Intratracheal DEX (nebulized or added to transtracheal block) reduces coughing during awake nasal fiberoptic intubations and flexible bronchoscopy.[17-19]

In animal models, DEX not only decreased airway smooth muscle contraction by decreasing presynaptic acetylcholine release[20] but also directly relaxed airway smooth muscle that had been contracted with acetylcholine (acted as a bronchodilator).[2]

Future Research

- Alternative doses and timing of DEX administered via the intratracheal route
- ASA III and IV patients
- Patients with reactive airway disease
- Difference in adverse event occurrence with DEX vs alternative strategies

References

1. Cascella et al., 2020; 2. Mikami et al., 2017; 3. Yuki, 2021; 4. Singhu et al., 2022; 5. Aragaki et al., 2019; 6. Akou et al., 2009; 7. Bedi et al., 2023; 8. Elemary et al., 2019; 9. Jafarzadeh et al., 2022; 10. H. Y. Kim et al., 2021; 11. S. H. Kim et al., 2021; 12. Lee et al., 2015; 13. Nahar et al., 2023; 14. Rani et al., 2016; 15. Wang et al., 2018; 16. Wang et al., 2022; 17. Gu et al., 2019; 18. Mirdoraghi et al., 2017; 19. Sancheti et al., 2022; 20. Yamakage et al., 2008; 21. Agency for Healthcare Research and Quality [AHRQ], 2017; 22. U.S. Preventive Services Task Force [USPSTF], 2019

Institutional Review Board approval was not required for this research project.

A Multimodal Analgesic Approach to Attenuate Remifentanil-Induced Hyperalgesia (RIH)

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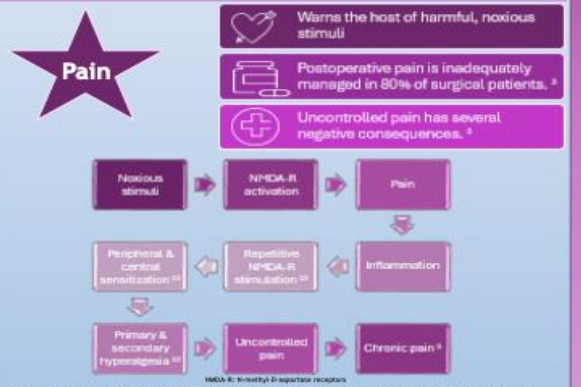
Learning Objectives

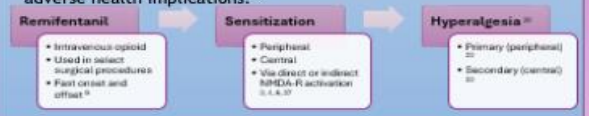
After the completion of this activity, the participant will be able to:

- explain how remifentanil alters the pain sensation process leading to RIH,
- describe the underlying mechanisms of hyperalgesia and its health implications,
- identify the multimodal analgesia alternatives that can be used to decrease RIH,
- Outline current recommendations for analgesic administration to manage RIH, and
- evaluate the risks and benefits of each multimodal analgesic medication as a preventive intervention for RIH.

Background

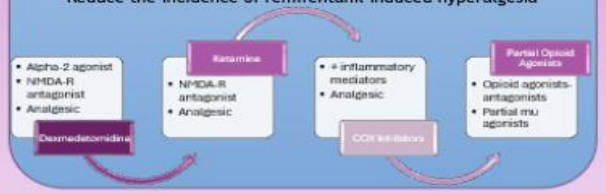


- Hyperalgesia is a heightened response to stimuli at the injury site, creating a more robust perception of nociception. [22]
- Uncontrolled postoperative pain can lead to increased opioid use, prolonged hospital stay, increased morbidity, decreased functional and quality of life, increased health care cost, chronic pain, and adverse health implications. [3]



Multimodal Analgesic Alternatives

Reduce the incidence of remifentanil induced hyperalgesia



Research Question

- **P** In adult patients who are receiving remifentanil infusions,
- **I** does the use of multimodal analgesics to attenuate remifentanil-induced hyperalgesia,
- **C** compared to no analgesics,
- **O** decrease the incidence of hyperalgesia
- **T** in the first 24 hours post remifentanil infusion?

Literature Search

TMC Health Sciences Resource Center
- EMBASE, PubMed, and The Cochrane Library

Filtered
- 2004-2024 and Type of Study

Keywords
- 'remifentanil,' 'hyperalgesia,' and 'analgesics'
- Boolean operator AND

Selected Articles
- Snowballing method
- 18 randomized controlled trials

Grading the Evidence

Level of Evidence [5]

- Level I: meta-analysis
- **Level II: experimental (18)**
- Level III: quasi-experimental
- Level IV: non-experimental
- Level V: clinical expertise

Strength of Evidence [18]

- A: Substantial net benefit; Strongly recommended
- B: Moderate net benefit; Recommended
- C: Small net benefit; Recommended selectively
- D: No net benefit; Recommend against
- I: Insufficient evidence; Evidence lacking or conflicted

Study Characteristics

Inclusion Criteria
- Cognitive capacity to make informed decisions
- Specified surgical procedure
- ASA physical status I-II
- Ages 18-75

Exclusion Criteria
- Inability to make informed decisions
- History of substance and drug use
- Significant medical disorder
- Allergy to medications used
- Current use of analgesics
- Psychiatric disorder
- Chronic pain
- Underweight
- Pregnancy
- Obesity

ASA: American Society of Anesthesiologists

Synthesis of Evidence

Dexmedetomidine [8, 12, 16, 19, 20, 23]
- ↓ primary hyperalgesia (4/6 articles) [8, 12, 16, 23]
- ↓ secondary hyperalgesia (2/6 articles) [8 & 23]
- ↑ time to first analgesic requirement (3/6 articles) [8, 12, 23]
- ↓ total analgesic consumption (4/6 articles) [8, 12, 16, 23]
- ↓ pain intensity (5/6 articles) [8, 12, 16, 20, 23]

Ketamine [1, 11, 21]
- ↓ primary hyperalgesia (2/3 articles) [1 & 21]
- ↓ secondary hyperalgesia (1/3 articles) [11]
- ↓ total analgesic consumption (2/3 articles) [1 & 21]
- ↓ pain intensity (2/3 articles) [1 & 21]

Flurbiprofen Axetil [23, 24, 25, 26]
- ↓ primary hyperalgesia (all articles) [23, 24, 25, 26]
- ↓ secondary hyperalgesia (all articles) [23, 24, 25, 26]
- ↑ time to first analgesic requirement (3/4 articles) [23, 24, 25]
- ↓ total analgesic consumption (3/4 articles) [23, 24, 25]
- ↓ pain intensity (all articles) [23, 24, 25, 26]

Parecoxib [13 & 17]
- ↓ secondary hyperalgesia (all articles) [13 & 17]

Butorphanol [10, 14, 24]
- ↓ primary hyperalgesia (1/3 articles) [24]
- ↓ secondary hyperalgesia (1/3 articles) [24]
- ↑ time to first analgesic requirement (1/3 articles) [24]
- ↓ pain intensity (all articles) [10, 14, 24]

Buprenorphine [15]
- ↓ primary hyperalgesia [15]
- ↑ time to first analgesic requirement [15]
- ↓ pain intensity [15]

Nalbuphine [7 & 26]
- ↓ primary hyperalgesia (all articles) [7 & 26]
- ↓ secondary hyperalgesia (all articles) [7 & 26]
- ↓ pain intensity (all articles) [7 & 26]

Side Effects

Respiratory Depression
- None of the analgesics produced respiratory depression

Nausea & Vomiting
- Ketamine: 1/3 articles had **increased** incidence [11]
- Butorphanol: 1/3 articles had **decreased** incidence [14]
- Dexmedetomidine: 2/3 articles had **decreased** incidence [16 & 20]

Awakening Time
- Ketamine: 1/3 articles had a **prolonged** awakening time [21]

Extubation time
- Ketamine: 1/3 articles had a **prolonged** extubation time [21]

Hemodynamics
- Dexmedetomidine: 2/6 articles had **increased** incidence in bradycardia and hypotension [12 & 16]

Sedation
- Ketamine: 2/3 articles had **increased** incidence [11 & 21]

Recommendations for Practice

- **Dexmedetomidine:**
  - Bolus dose: 0.2 - 1 mcg/kg over 10 minutes given before remifentanil
  - Continuous infusion dose: 0.2 - 0.7 mcg/kg/hr started before giving remifentanil
  - Bolus can be given with infusion; infusion should be stopped at procedure completion
  - Avoid in hemodynamically unstable patients
- **Ketamine:**
  - Bolus dose: 0.5 mg/kg given before remifentanil
  - Continuous infusion dose: 5 mcg/kg/min (start after bolus has been given; stop at skin closure)
  - Avoid in patients allergic to ketamine and patients with underlying conditions that can be exacerbated with ketamine (aortic dissection, aneurysms, uncontrolled hypertension, and myocardial infarction).
  - Use with caution in patients with schizophrenia, hemodynamic instability, intracranial hypertension, and a history of emergence delirium.
- **Flurbiprofen:**
  - Bolus dose: 0.5 - 1.5 mg/kg given before remifentanil
  - Avoid in patients with an allergy to NSAIDs or aspirin, have gastrointestinal bleeding, peptic ulcer disease, cerebrovascular bleeding, hemostatic dysfunction, pregnancy, and renal impairment.
- **Parecoxib**
  - Bolus dose: 40 mg infused over 10 minutes given before remifentanil
  - Avoid in patients with an allergy to NSAIDs, aspirin, or sulfa, and or have renal impairment.
- Partial Opioid Agonists
  - Butorphanol bolus: 20 mcg/kg given before remifentanil
  - Nalbuphine bolus: 0.1 - 0.2 mg/kg given before remifentanil
  - Buprenorphine infusion: 25 mcg/hr started before remifentanil and stopped 24 hours post-op
  - Avoid in patients with an allergy to butorphanol, nalbuphine, and buprenorphine and in patients with opioid addiction.
  - Use with caution in hemodynamically unstable patients.

* recommendations are for patients with an ASA physical status I-II

Limitations

- Limited number of articles for each drug
- Moderate level of evidence; need for meta-analysis and systematic reviews
- Small sample sizes in some of the articles
- Variations in drug administration and timing
- Variations in hyperalgesia measurement techniques

References

1. Choi et al., 2015; 2. Fletcher & Martinez, 2014; 3. Gan, 2017; 4. Guntz et al., 2005; 5. Henriksen et al., 2005; 6. Horii et al., 2020; 7. Hu et al., 2020; 8. Jia et al., 2023; 9. Komatsu et al., 2007; 10. Kong et al., 2017; 11. Leal et al., 2015; 12. Lee et al., 2013; 13. Lenz et al., 2011; 14. Lv et al., 2016; 15. Mercieri et al., 2017; 16. Qiu et al., 2018; 17. Troster et al., 2006; 18. U.S. Preventive Services Task Force [USPSTF], 2012; 19. Wu et al., 2020; 20. Xia et al., 2020; 21. Yalcin et al., 2012; 22. Yam et al., 2018; 23. Yu et al., 2016; 24. Zhang et al., 2016; 25. Zhang et al., 2017; 26. Zhao et al., 2023; 27. Zhao & Joo, 2008

Intraoperative Methadone and Postoperative Pain Management in the Adult and Pediatric Population

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Background

- 80% of surgical patients experience postoperative pain
- 88% of these patients experience moderate to severe pain

Current practice includes administering intermittent boluses or infusions of short acting opioids which can have the following effects:

- Fluctuating blood level concentrations → respiratory depression, deep sedation, inadequate pain relief
- Opioid induced hyperalgesia → increased sensitivity to painful stimuli due to a lower pain threshold
- Acute tolerance → larger doses of opioids needed postoperatively

Properties of Methadone

potent mu agonist

N-methyl-d-aspartate antagonist

norepinephrine and serotonin reuptake inhibitor

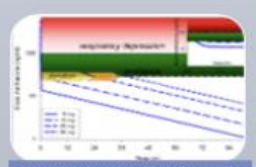
Elimination Half-Life: 24-36 hours

Metabolism: N-demethylation by CYP2B6

Rapid Equilibration: 4 minutes

Benefits of NMDA Antagonism:

- Opioid Induced Hyperalgesia
- Opioid Tolerance
- Chronic Postsurgical Pain



The duration of analgesia of methadone approximates its half life around doses of 15-20 mg. Due to rapid redistribution, respiratory depression is 30-45 minutes, even at higher single bolus doses.

Research Question

P In adult and pediatric surgical patients undergoing general anesthesia,

I does intraoperative intravenous methadone

C compared to traditional opioids such as fentanyl, morphine, sufentanil, or hydromorphone

O decrease postoperative pain

T during the first 24 hours after surgery?

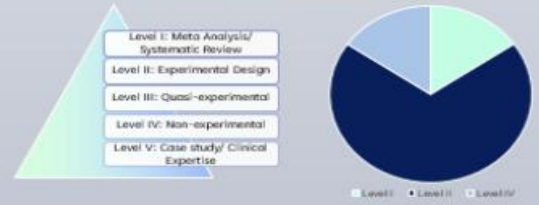
Literature Search

- Texas Medical Center Library: Medline Ovid, PubMed, Embase
- MeSH terms: 'methadone', 'pain, postoperative'
- Search terms: 'intraoperative methadone', 'postoperative pain'
- Boolean operators: 'AND'
- Snowballing technique
- Filters: English language, Peer reviewed, 2010-2024, Human subjects

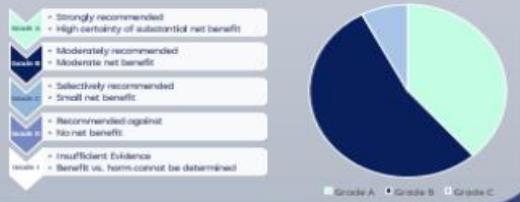
13 Articles selected for appraisal and review

Evidence Appraisal

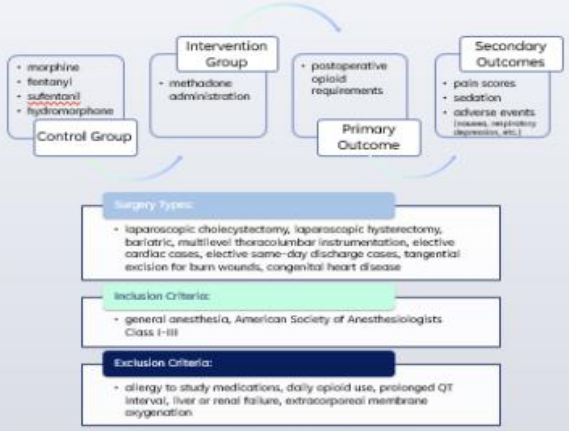
Agency for Healthcare Research & Quality



United States Preventive Services Task Force



Study Design



Synthesis of Evidence

Of 13 articles, 12 showed less postoperative opioid use in patients who received methadone versus those who received shorter acting opioids.

The administration of an intravenous methadone bolus during induction of general anesthesia resulted in:

statistically significant decreases in:

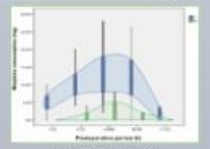
- postoperative opioid requirements in first 24 hours[1,3,4,10]
- postoperative opioid requirements at 48 and 72 hours[3]
- pain scores at rest[1-3]

Significantly lower incidences of nausea and vomiting[1,6,8]

No significant difference in opioid related side effects[2-5,7,9,10]

	Methadone	Fentanyl
Morphine (mg) First 24 hours	6 (4 to 12)	10 (6 to 22)
Level of pain with coughing First 12 hours	4 (3 to 5)	6 (4 to 8)

Murphy et al., 2015



Machado et al., 2018

Recommendations for Practice

Adult Population:

Pediatric Population:

Methadone may allow for decreased opioid consumption in the pediatric population.

However, due to limited randomized prospective studies, strong recommendations for intraoperative methadone use in the pediatric population cannot be made.

Study Limitations

- Heterogeneity in surgical procedures
- Heterogeneity in comparison drug of choice
- Variability in sample size and dosing
- Emergent cases not included
- Retrospective study designs in pediatric population

Future Research

- Prospective, randomized studies in pediatric population
- Larger sample sizes
- Longer follow up periods
- Consistent dosing regimens

References

1: Arriaza et al., 2021; 2: Friesgaard et al., 2023; 3:Gottschalk et al., 2011; 4: Kharasch et al., 2023; 5: Komen et al., 2019; 6: Machado et al., 2018; 7: Murphy et al., 2015; 8: Pontes et al., 2021; 9:Barnett et al., 2019; 10: Fons et al., 2023; 11: Azamfieri et al., 2023; 12: Carlson et al., 2022; 13: Robinson et al., 2020.

Applications of Machine Learning for Reduction in Intraoperative Hypotension

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Background

Hypotension

- Decrease in SBP > 20% from baseline[1]
- SBP < 80 mmHg[1]
- MAP < 65 mmHg for > 1 minute[2]

Key Points

- 313 million surgeries worldwide annually[3,4]
- Frequency of intraoperative hypotension is 88%[2]
- Brief episodes increase risk of acute kidney injury, myocardial injury, and mortality[5-8]
- Major cerebrovascular or cardiac events amplified by depth and duration of IOH[6,9]
- $1.2-$4.6 million in annual savings[10]

Monitoring Equipment

Non-invasive blood pressure cuff

- Based on oscillometry
- An indirect blood pressure measurement
- Systolic and diastolic pressures are calculated from point of maximal amplitude

Invasive arterial line

- Pressure transduced as harmonic waveform through incompressible fluid-filled tubing
- Pressure is then coupled with a Wheatstone bridge circuit
- A direct blood pressure measurement

The Hypotension Prediction Index (HPI)

- A commercially available machine learning-derived early warning system
- Provides unitless number from 0 to 100
- High priority alarm triggered when > 85
- Predicts hypotension 15 minutes before event[11,12]
- Sensitivity and specificity – 81% at 15 minutes[11]
- Improves to 88% and 87% within 5 minutes[12]

Acumen IQ Cuff ✓HPI compatible

Acumen IQ Sensor ✓HPI compatible

ClearSight Cuff ✗HPI compatible

https://www.edwards.com/healthcare-professionals/products-services/hemodynamic-monitoring

Research Question

- **P** – In adults undergoing general anesthesia,
- **I** – does the utilization of machine learning-derived early warning systems for the management of intraoperative hypotension,
- **C** – compared to standard goal-directed care,
- **O** – decrease the depth and duration of hypotension
- **T** – during the intraoperative period?

Literature Review

- **Texas Medical Center Library Online Portal**
- **Databases**
  - CINAHL, EMBASE, PubMed
- **Filters**
  - Peer-reviewed, English language, 2018-2024, article, full text, available online
- **Key & MeSH[c] Terms**
  - Machine learning, intraoperative hypotension, hypotension prediction, hypotension[c], general anesthesia, noninvasive, clearsight, computational intelligence, computer reasoning, artificial intelligence[c], intraoperative complication[c], perioperative complication, machine intelligence, HPI, hypotension prediction index
- **Aides**
  - TMC Librarian consultation, Yale MeSH analyzer, Boolean operators ('AND,' 'OR,' '*')

359 articles → Duplicates excluded; Reviewed for relevance; Snowballing technique → 16 articles

Levels & Grades of Evidence

Oxford Centre for Evidence Based Medicine[13]		United States Preventive Services Task Force[14]	
Level I	Meta-analysis	A	Strongly recommend; Substantial benefit
Level II	RCT	B	Highly recommend; Moderate benefit
Level III	Quasi-experimental	C	Selectively recommend; Small net benefit
Level IV	Non-experimental	D	Recommend against; No net benefit
Level V	Case report	I	Insufficient evidence; Evidence lacking or poor quality

Level II: 7 articles
Level III: 9 articles

Grade A: 10 articles
Grade B: 6 articles

Population Characteristics

Inclusion Criteria	Exclusion Criteria
≥ 18 years old[15-26]	Significant cardiac dysrhythmias[15-18,23,24,26,29]
≥ 45 years old[27-29]	Coagulation disorders[15,16,20-22]
General anesthesia[15-30]	Use of regional anesthesia[20]
Intraoperative MAP > 65 mmHg[15-29]	Severe aortic stenosis[15-18,23,24,26,29]
ASA physical status I-IV[21,28]	Cardiac defects or shunts[5,17,18,22-24]
I-III[16,18,20,23-26,30], II-III[22], II-IV[15,17,19]	Patients requiring hemodialysis[15,18,20,22-24,26,29]
III-IV[27,29]	Emergency surgery[15-18,21,23,26,29]
Surgical duration > 2 hr[15-29]	

Synthesis of Literature

When compared to standard goal-directed care with invasive or non-invasive blood pressure monitoring, the machine learning-derived early warning systems had:

Primary Outcomes

- Reduction in time-weighted average of intraoperative hypotension*[15,17-19,21-24,26,28]
- Reduction in area under hypotension threshold*[15, 22-24,26]
- Fewer incidences of intraoperative hypotension*[15,17-24,26,29]

* $p < .05$

Secondary Outcomes

Severe Hypotension

MAP < 60 mmHg	MAP < 55 mmHg	MAP < 50 mmHg
Decreased time-weighted average*[19]	Decreased time-weighted average*[19]	No difference in time-weighted average[15]
No difference in time-weighted average[29]	No difference in time-weighted average[29]	Decreased number of hypotensive events*[17,26]
		No difference in number of hypotensive events[15]

* $p < .05$

Intraoperative Fluids

Crystalloids	Colloids	Packed red blood cells
No difference[15,21-24,26]	No difference[15,22-24,26,29]	No difference[15,20-24,26,29]
Decreased total volume*[20,29]	Increased total volume*[20,21]	

Intraoperative Vasopressors

Ephedrine	Norepinephrine	Phenylephrine
No difference[15,20,21,23,24,26,29]	No difference[21,22,24,26,29]	No difference[21,24,26,29]
	Increased cumulative dose*[15]	Increased dose*[23]

* $p < .05$

Hypertension

MAP > 100 mmHg	MAP > 110 mmHg	MAP > 130 mmHg
Increase in time-weighted average*[23]	Increase in time-weighted average*[15]	No difference in time-weighted average[15]
Increased incidence of hypertension*[23]	Increased incidence of hypertension*[15]	No difference in incidence[15]
No difference in time-weighted average[29]		
No difference in incidence[29]		

* $p < .05$

Exploratory Outcomes

Length of Stay

Intensive Care	Hospital
No difference in length of stay[19,20,22]	Decreased length of stay*[21]
	No difference in length of stay[20,22,23,29]

* $p < .05$

Morbidity

Acute Kidney Injury	Myocardial Infarction	Cerebrovascular Event
No difference[19,21-23,29]	No difference[19,21-23,29]	No difference[19,21-23,29]

Cost-effectiveness

- Significant increased cost difference of $307 for HPI equipment*[30]
- No difference in hospital stay or ICU admissions[30]
- No difference in total cost[30]

* $p < .05$

Considerations & Limitations

- Treatment protocol variability
- Hawthorne effect
- Limited cost analysis information
- Lack of standardized timing of arterial line placement
- Provider experience

Recommendations

- **Who?**
  - Adult patients
  - ASA I-IV
- **When?**
  - Anticipated procedure duration > 2 hrs
  - Non-cardiac procedures
- **How?**
  - Begin monitoring 10 minutes before induction
  - Intervention consistency

Future Research

- More robust cost-effectiveness analysis
- Impact on long-term outcomes
- Inclusion of cardiac procedures and populations
- Utility and effectiveness in pediatric population

References

1. Awad et al., 2022; 2. Shah et al., 2020; 3. Meara et al., 2015; 4. Weiser et al., 2015; 5. Mascha et al., 2015; 6. Salmasi et al., 2017; 7. Sun et al., 2015; 8. Walsh et al., 2013; 9. Gregory et al., 2021; 10. Keuffel et al., 2019; 11. Davies et al., 2020; 12. Hatib et al., 2018; 13. OCEBM Levels of Evidence Working Group, 2011; 14. USPSTF, 2018; 15. Frassanito et al., 2023; 16. Frassanito et al., 2021; 17. Grundmann et al., 2021; 18. Murabito et al., 2022; 19. Runge et al., 2023; 20. Schneck et al., 2019; 21. Solares et al., 2022; 22. Sribar et al., 2023; 23. Tsoumpa et al., 2021; 24. Wijnberge et al., 2020; 25. Wijnberge et al., 2022; 26. Yoshikawa et al., 2024; 27. Maheshwari et al., 2020; 28. Maheshwari et al., 2018; 29. Maheshwari et al., 2020; 30. Frassanito et al., 2023

Institutional Review Board approval was not required for this research project.

Neuraxial Dexmedetomidine in Labor Analgesia

Disclosure: The use of dexmedetomidine via neuraxial route is considered "off-label".

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Neuraxial dexmedetomidine results in:

- a longer duration of action of analgesia.
- a quicker onset of analgesia.
- decreased maternal pruritis.
- no worse maternal nausea and vomiting.
- no adverse fetal/neonatal outcomes.

Background

Stages of Labor

Stage One
- Visceral pain → not well localized
- "dull", "ache"
- Cervical dilation, stretching of lower uterine segment
- T10-L1 spinal segments
- Unmyelinated C fibers

Stage Two
- Somatic Pain → well localized
- "sharp"
- Compression and stretching pelvic floor, perineum, and vagina
- S2- S4 spinal segments
- Pudendal nerves

Dexmedetomidine

- Selective alpha-2-adrenergic agonist
  - Inhibits release of norepinephrine
- Highly lipophilic
  - Minimal placental transfer
- Brain and spinal cord
- Anxiolysis, sedation, analgesia, sympatholytic
- Cytochrome P450 metabolism
- 2-3 hour elimination half-life

Literature Search

- Identification of a clinical need and research question:
  In adult patients receiving neuraxial analgesia for labor, does the addition of dexmedetomidine to a local anesthetic, compared to opioids, shorten the onset and lengthen the duration of action of analgesia?
- Healthcare databases accessed using the Texas Medical Center Health Sciences Resource Center (library.tmc.edu).
- Using Boolean operators and snowballing, terms searched included 'dexmedetomidine,' 'labor, obstetrics,' 'epidural,' 'spinal,' 'labor analgesia,' 'epidural,' and 'neuraxial.'
- After filtering results, the search yielded 11 relevant articles.

Grading the Evidence

Study Characteristics

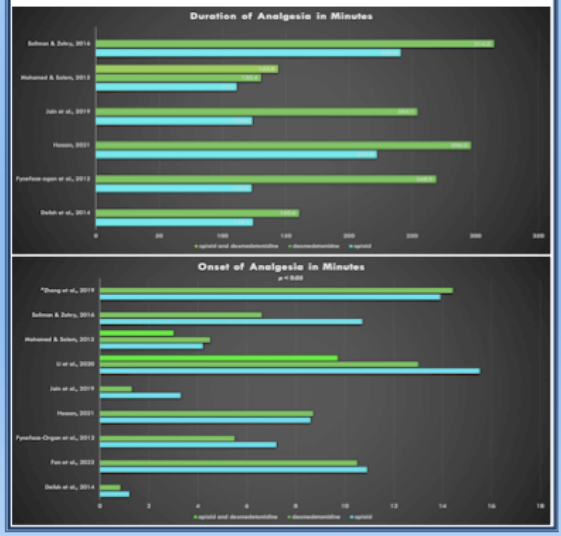
Outcomes Measured
1. Duration of analgesia
2. Onset of analgesia
3. Maternal bradycardia & hypotension
4. Degree of motor blockade
5. Nausea & Vomiting
6. Pruritis
7. Fetal/Neonatal outcomes

Inclusion
- >18 years old
- Full Term
- Single uterine pregnancy
- Cephalic presenetaion
- Healthy fetus
- Active labor
- Standard vaginal delivery
- ASA I or II

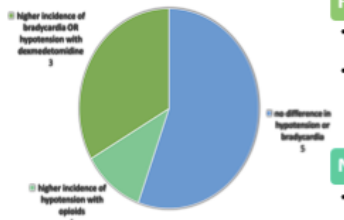
Exclusion
- Does not meet inclusion criteria
- Maternal CV disease
- Fetal abnormalities
- Maternal contraindications to neuraxial
- Cesarean section
- ASA III or IV

Synthesis of Evidence

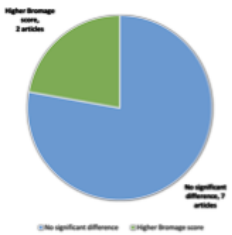
Duration and Onset of Analgesia



Hypotension and Bradycardia (1,3-4,6-7,9,12,14)



Motor Blockade (1-4,6-8,12-14)



Fetal/Neonatal Outcomes

- No statistically significant differences in fetal/neonatal outcomes groups (2-3,6-7,9,12)
- Outcomes measured varied between studies
  - Including bradycardia, APGAR scores, oxygenation, and acidosis

Nausea and Vomiting

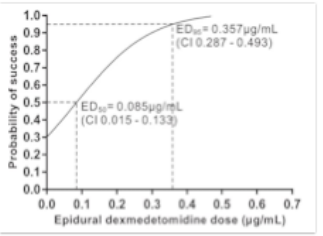
- Five studies compared nausea and vomiting between the dexmedetomidine and opioid groups (3-4,6,9,12)
- All studies found less nausea and vomiting with dexmedetomidine (3-4,6,9,12)
  - However, this finding was only clinically significant ($p<0.05$) in one study (12)

Pruritis

- Four studies assessed for pruritis (2,6,9,12)
- Two studies found insignificant differences (6,9)
- Two studies found statistically significant worse pruritis when an opioid was used compared to dexmedetomidine (2,12)

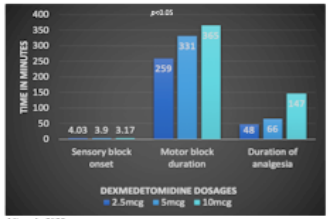
Dexmedetomidine Dosage

Epidural



- No statistically significant ($p>0.05$) increase in secondary outcomes with 0.1-0.5mcg/ml[10,15]
- Motor blockade occurred with dosages >0.75mcg/ml[15]

Intrathecal



Ni et al., 2022

- Level of sedation higher with 5mcg compared to 2.5mcg ($p<0.001$)[5]
- Secondary outcomes were not significantly ($p>0.05$) different with 2.5, 5, or 10mcg dexmedetomidine [5,11]

Recommendations for Practice

Neuraxial administration safe for use in:
- ASA I or II
- >18 years old
- No maternal cardiovascular history
- Healthy, full-term fetus

Add dexmedetomidine to epidural or intrathecal space for laboring parturient
- Can be in place of or in addition to opioids

Bupivacaine or Ropivacaine dosage should be made on an individual patient basis

Dexmedetomidine Dosage:
- Intrathecal 2.5 mcg for standard vaginal deliver (SVD) or 10 mcg for cesarean section (CS)
- Epidural 0.3 mcg/ml for SVD or 0.75 mcg/ml for CS

Future Research

- ASA III & IV
- Cardiovascular issues
- Comparison of neuraxial technique utilized
- Use of dexmedetomidine for cesarean section
- Dosage of dexmedetomidine
- Comparison of fentanyl vs sufentanil vs dexmedetomidine
- Multi-gestational pregnancies
- Fetal anomalies

References

1. Cheng et al., 2019; 2. Delish et al., 2014; 3. Fan et al., 2022; 4. Fyneface-Ogan et al., 2012; 5. Gupta et al., 2016; 6. Hassan, 2021; 7. Jain et al., 2019; 8. Li et al., 2020; 9. Mohamed & Salem, 2015; 10. Ni et al., 2022; 11. Shaikh & Dattani, 2016; 12. Soliman & Zohry, 2016; 13. Wang et al., 2022; 14. Zhang et al., 2019; 15. Zhang & Ming, 2017

Ultrasound-guided Paratracheal Pressure as a Safer Alternative to Traditional Cricoid Pressure

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Nurse Anesthesia · Baylor College of Medicine · DNP · Doctor of Nursing Practice · Lifelong Learning · Integrity · Excellence · Service · Advocacy

Learning Objectives

Upon completion of this activity, the participant will be able to:

- Identify complications of cricoid pressure,
- demonstrate an understanding of pertinent US Anatomy,
- examine the differences between cricoid and paratracheal pressure,
- compare paratracheal pressure to cricoid pressure,
- evaluate the benefits of paratracheal pressure in pulmonary aspiration prevention, and
- formulate plants to incorporate paratracheal pressure into current practice.

Background

Pulmonary aspiration
- Incidence rate is 0.5%[8,11]
  - Higher incidence in high-acuity settings (e.g. ER, ICU)[1]
- Rare & serious cause of perioperative adverse events[18,20]

Cricoid Pressure
- Varied Support in the Literature[2,18]
- Inconsistent use in clinical practice
- Aspiration events noted despite cricoid pressure (CP) application[7]

Paratracheal Pressure
- Quantitative Esophageal closure[11]
- Decreased gastric insufflation[11,17]
- Less susceptible to external manipulation[26]

Research Question

(Population) In adult patients requiring rapid sequence induction

(Intervention) does the application of paratracheal pressure

(Comparison) compared to cricoid pressure

(Objective) decrease the incidence of pulmonary aspiration of gastric contents

(Time) during the induction of general anesthesia?

Literature Search Method

DATABASES SEARCHED:
- TMC Library, PubMed, CINHAL, Cochrane Library, Clinical Key, Medline

Accessed via Texas Medical Center Library Health Resource Center

Publication Requirements:
- Published within the last 15 years
- Articles must be published in English

MeSH Terms
- 'Intubation'
- 'Intratracheal'
- 'Rapid sequence induction'
- 'Cricoid Cartilage'
- 'Aspiration'
- 'Adult'
- 'Human'
- 'Respiratory aspiration of gastric contents'

Key Terms
- Sellick maneuver
- Cricoid pressure
- Left paratracheal pressure
- Rapid sequence induction
- Pulmonary aspiration

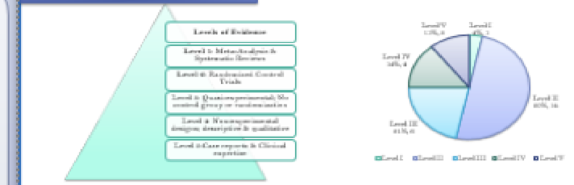
Inclusion Criteria
- Adults aged 18 – 75
- Perioperative setting
- Surgery requiring General Anesthesia (GA)
- Rapid sequence induction (RSI)

Snowballing
- Articles gathered from citations of meta-analysis and systematic reviews

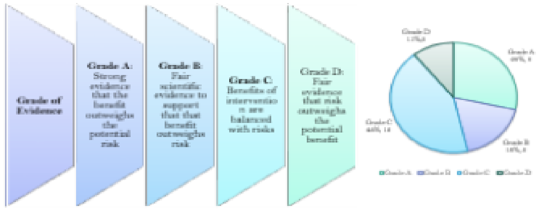
Exclusion Criteria
- Special populations – Pediatrics, Obstetrics settings, i.e., ICU or ER

Boolean Operators
- 'AND' to narrow the search
- 'OR' to expand search

Evidence Appraisal



Based on the Agency for Healthcare Research and Quality (AHRQ)



Based on the US Preventive Services Task Force (UPSTF) Grading scale

In Total, 28 Articles met the inclusion and Review Criteria

Study Designs

Major Variables:
- Age, BMI, ASA status, Mallampati score, presence of full stomach, NPO Status
- Patients undergoing **general anesthesia with rapid sequence induction**
- Presence of a nasogastric tube before induction
- **Risk factors for aspiration**: Gastroparesis, GERD, Hernia, ileus, Diabetes Mellitus

Inclusion and exclusion criteria:
- *Inclusion:* Male or female patients 18–75 years of age, **ASA I-II**
- *Exclusion:* Patient refusal, pregnancy, pediatrics, **patients with predicted difficult airway**, & emergency procedures

ASA I-II | Adequate NPO times | Mallampati I-II | Special populations omitted | No superiority trials

Complications of Cricoid Pressure

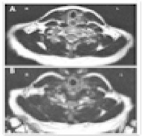
Misidentification leads to incorrect application[6,16,29]
- 30.2% of nurse anesthesia students had formal training ($p < .001$)[29]
- Knowledge gap from lack of formalized training[16,29]
- Cricoid cartilage fracture & esophageal rupture from excessive force[6,16,22,29]

How does Cricoid pressure esophageal intubation?
- Higher Cormack-Lehane Grade during glottic visualization[7,9,15]
- Increased time to intubation with decreased first-attempt success rate[7,16,18,28,29]

Cricoid pressure decreases lower esophageal sphincter (LES) tone[4,6]
- Decrease in LES proportionate to applied force[4,21,24]
- Nullifies compensatory increase of LES tone from succinylcholine[4,21,24]
- Return of LES tone occurs with removal of cricoid pressure[21]

Anatomical Variation and Cricoid Pressure

MRI scans show significant variation:
- 52.6% of patients have lateral displacement before CP[24]
- Esophagus deviates to left before C5 ($p = .004$)[24]
- Lateralization increased to 90.5% after CP ($p = .015$)[7]
- Prevents closure against vertebral bodies[24]



Smith et al., 2003

CP pressure is ineffective in 50% of patients when the esophagus is left of the midline.[7]

Is it time for a left shift?

Paratracheal pressure allows for complete esophageal closure:
- Applied cephalad to the **left clavicle**[11]
- Thumb or ultrasound probe applies force[11]
- Compresses the esophagus directly **below cricoid level**[15]
- Quantitively view esophageal closure[11,15]

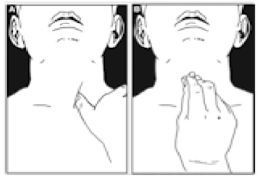
How is my view during laryngoscopy?
- Does not compress hypopharyngeal space[11,15]
- **Less susceptible** to external laryngeal manipulation[26]
- Increased expiratory tidal volume during mask ventilation ($p < .001$)[17,23]

Is Paratracheal Pressure protective against Gastric Insufflation?
- **Early air detection in esophagus and gastric antrum**[17]
- Real-time assessment allows modification of maneuver[17]
- Decreased gastric insufflation risk ($p < .001$; $p < .001$)[11,17]

How many Newtons do I need?
- 30 Newtons(N) of force with thumb or US probe[5,23]
- Measurement of esophageal AP Diameter[11]
- Visualization of esophageal compression[11]

Paratracheal Pressure V.S. Cricoid Pressure

Cricoid Pressure	Paratracheal Pressure
Lower percentage of glottic opening (POGO)[28]	Higher success rate for LMA & ETT insertion ($p = .077$)[7,26]
Decreased first-pass success rate[28]	Lower rates of difficult intubation[7]
Increased time to intubation[28]	Decreased gastric insufflation ($p < .001$)[11]
Higher rates of airway obstruction ($p < .001$)[26]	Easier mask ventilation ($p < .008$)[26]



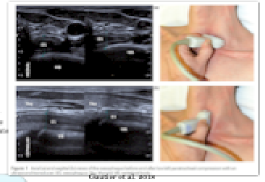
Gautier et al. 2018

Ultrasound-Guided Paratracheal Pressure

Position: Supine or Semi-fowlers
Probe: Linear 17-5 MHz or Hockey Stick Probe 15 -7 MHz[11]
Placement: Left side of the neck; axial or sagittal plane
Target: Esophagus
Landmarks: Thyroid, vertebral body, Sternocleidomastoid, Cricoid Cartilage[11]

Paratracheal Step-By-Step

1. Place the US probe on the left side of the neck, cricoid level.
2. Identify the esophagus
   - Esophagus may be unidentifiable in 13% of patients at cricoid level[7]
3. Scan caudal, following esophagus natural lateralization
4. Apply 30 N of force immediately cephalad to left clavicle
   - Measure AP Diameter, can be reduced by up to 40%[1,11]
   - AP diameter compression not affected by neck circumference or gender[7]



Gautier et al. 2018

Practice Recommendations

USG-Paratracheal Pressure:
- Quantitative evaluation of esophageal closure
- Real-time visualization of air entering esophagus
- Decreased gastric insufflation
- Utilize with masses/vascular injury on anterior neck surface

Adjuncts for Pulmonary Aspiration Prevention

Omit pre-curarization dose of NDNMB in RSI
- May prevent protective increase in Lower esophageal tone with Succinylcholine[6,10]

Utilize pre-operative Gastric Pocus in high-risk individuals
- Full stomach with >1.5 ml/kg of fluid or solid in gastric antrum[27]

Pre-operative nasogastric tube placement
- ~~Empty stomach and remove prior to induction~~[10,18]

References

1. Achar & Shetty, 2022, 2. Ahlstrand et al., 2011, 3. Ajmal, 2016, 4. Algie et al., 2015, 5. Andruszkiewicz et al., 2026, 6. Bham & Markham, 2019, 7. Birenbaum et al., 2019, 8. Butt & Hoda, 2019, 9. Dunn, 2022, 10. Eriksson et al., 2011, 11. Gautier et al., 2018, 12. He et al., 2022, 13. Hwang & Yoon, 200, 14. Hurr et al., 2021, 15. Kim et al., 2022, 16. Kopka & Robinson, 2016, 17. Li et al., 2021, 18. Mittal et al. 2023, 19. Noll et al., 2019, 20. Parson & Duke, 2018, 21. Salem et al., 2008, 22. Salem et al., 2017, 23. Seol et al. 2023, 24. Smith et al., 2003, 25. Tsaousi et al., 2022, 26. Thapa et al. 2023, 27. Van de Putte et al., 2017, 28. Won et al., 2021, 29. Yahaya et al., 2016

Truncal Blocks: Effect on Postoperative Opioid Consumption

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BACKGROUND

Local Anesthetics (LAs)

- **Mechanism of Action:**
  - Uncharged LA diffuses across the lipid bilayer[1]
  - Charged LA binds to cytoplasmic Na+ channels[1]
  - Depolarization (open state) promotes binding[1]
  - Prevention of further Na+ activity[1]
- **Avoid LAST** (perioral numbness, tinnitus, seizures, CV collapse)[2,3]
- **Treatment**[2]: 20% lipid emulsion
  - Bolus[2]: 1.5 mL/kg + Infusion: 0.25 mL/kg/min

Dexmedetomidine (DEX)

- **Mechanism of Action:**
  - Alpha-2 adrenoreceptor agonist at locus coeruleus[4]
  - Sympatholytic effects[4]
  - Causes peripheral vasoconstriction[4]
- Prolongs block duration and accelerates block onset[5]
- **Adverse Effects**[4]:
  - Bradycardia, hypotension, hypertension, and drowsiness

ULTRASOUND

- Visualize structures to directly target fascial planes between muscles
- LA spreads through fascial plane to anesthetize surrounding nerve fibers
- Use an in-plane needling technique

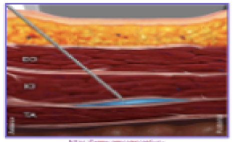
Approach	Probe
TAP Block	linear
QL Block	curvilinear

TAP BLOCKS

- Targets pain pathways in the abdominal wall
- Clinically easier to place
- Only blocks **somatic** pain
- Leaves visceral pain receptors sensitized to the effects of surgical manipulation

Three approaches:

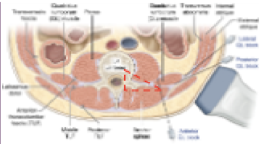
- Oblique subcostal approach (T6 – L1)
  - Pain **above** the umbilicus
- Lateral approach (T10 – T12)
  - Pain **below** the umbilicus
- Posterior approach (T9 – T12)
  - Lateral & posterior pain below umbilicus



QL BLOCKS

- A derivative of the TAP block
- Blocks **somatic pain and visceral pain** receptors
- Thoracolumbar fascia surrounds the quadratus lumborum muscle
- Thoracolumbar fascia contains many nociceptors
  - A-fibers, C-fibers, mechanoreceptors

Approach	Target Nerves	Additional Contributions
Anterior	T10 – L3	Lumbosacral nerve plexus
Lateral (QL1)	T6 – L1	Paravertebral dorsal rami, sympathetic nerve fibers, middle and posterior thoracolumbar fascial layers
Posterior (QL2)	T6 – L1	



RESEARCH QUESTION

- **P**: In adult patients undergoing major abdominal surgery,
- **I**: does the administration of a QL block
- **C**: in comparison to TAP block
- **O**: reduce rescue analgesia consumption
- **T**: during the first 24 hours postoperatively?

LITERATURE REVIEW

Texas Medical Center
- Librarian consultation
- Databases: PubMed, Embase, Web of Science

MeSH & Key Terms
- General anesthesia (MeSH), general anaesthesia
- TAP block, QL block
- Transversus Abdominis Plane block
- Quadratus Lumborum block

Boolean Operators
- AND
- OR
- Asterisk (*)

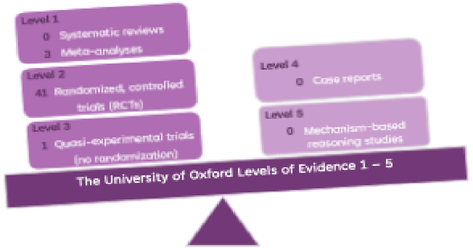
Snowballing

Filters
- English
- Within 10 years

Exclusion
- Pediatrics

45 articles

GRADES AND LEVELS OF EVIDENCE



Grade A	Grade B	Grade C	Grade D	Grade I
Highly recommended	Moderately recommended	Neither recommended for nor against	May cause harm	Recommendation lacks quality and strength
30	10	4	1	0

United States Preventive Services Task Force (USPSTF)

SYNTHESIS OF EVIDENCE

Inclusion Criteria	Exclusion Criteria
Age 18 – 80 years	Patient refusal
BMI: 15 – 40 kg/m²	Coagulopathy or signs of infection
ASA I – III	LA allergy
Major abdominal surgery	Pediatric patients
General anesthesia	Chronic pain, opioid tolerance, or alcohol abuse
Spinal anesthesia	
Obstetrical	

PROCEDURES
- Hernia repair
- Gynecological/Obstetric
- Kidney removal/transplant
- Laparoscopic
  - Appendectomy
  - Cholecystectomy
  - Colorectal
  - Gastrectomy
- Liver resection
- Varicocelectomy
- Unspecified

PRIMARY ANESTHETIC
- General with ETT
- Spinal anesthesia42–52

INJECTATE SOLUTION
- LA only
- LA + DEX

PRIMARY RESCUE ANALGESIA
- Fentanyl
- Meperidine
- Morphine
- Sufentanil
- Tramadol
- Non-opioid

ANALGESIC REGIMEN
- Multimodal approach
  - Acetaminophen
  - NSAIDs
  - Opioids
- PCA infusions
  - Basal rate + demand
  - Demand bolus only
- Opioids only
- Oral Medications only

BLOCK PLACEMENT
- Preoperative holding
- Before induction
- After induction
- At the end of surgery
- An unspecified time

Local Anesthetic
- Bupivacaine
- Ropivacaine
- Levo-Bupivacaine

Local Anesthetic Concentration
- Variable: 0.2 – 0.75%
- Most common:
  - 0.25%
  - 0.375%

Local Anesthetic Volume
- Standard: 20 mL
- Weight-based: 0.2 – 3 mL/kg

Dexmedetomidine
- Standard: 20 mcg
- Weight-based: 0.5 – 1 mcg/kg

OUTCOMES

Primary Outcomes

Cumulative Opioid Consumption
- QLB < TAPB*
  - QLB: 52.1 ± 11.6 mg
  - TAPB: 81.3 ± 16.4 mg
  - IV sufentanil
- QLB = TAPB

Block Duration
- LA: QLB > TAPB*
  - QLB: 8.05 h
  - TAPB: 5.59 h
- LA + DEX: QLB > TAPB*
  - QLB: 10.2 h
  - TAPB: 6.45 h

Postoperative Pain Scores (rest and movement)
- QLB < TAPB*
- QLB = TAPB

Secondary Outcomes

Sensory Dermatomal Level
- QLB > TAPB*
  - TAPB: 6 segments
  - QLB: 8 segments

Time to first analgesic request
- LA: QLB > TAPB*
  - TAPB: 8 h
  - QLB: 17 h
- LA + DEX: QLB > TAPB*
  - TAPB: 14 h
  - QLB: 21 h

Patient Satisfaction
- QLB > TAPB*
  - QLB: 80% satisfaction
  - TAPB: 60% satisfaction

*$p < .05$

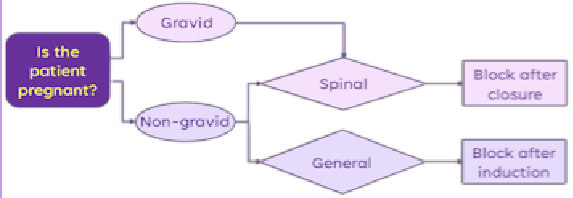
LIMITATIONS

- No ASA IV or V patients
- Few publications assessed sensory levels
- No dry needling as control group
- Basal PCA infusions mask block duration
- Intermittent rescue analgesia may mask interval pain scores

RECOMMENDATIONS FOR FUTURE PRACTICE

Patient Demographics	Age 18 – 80; ASA I – III; BMI 15 – 40 kg/m²
QL Block	Place with ultrasound guidance: **GA:** after induction and before surgical incision; **Spinal:** after surgical closure
Local Anesthetic(s)	Bupivacaine or ropivacaine; **Concentration:** 0.25 – 0.375%; **Volume:** 20 mL
Dexmedetomidine	20 mcg or 0.5 – 1 mcg/kg

- Use truncal blocks with other multimodal therapies
- Use dexmedetomidine to prolong block duration
- Integrate QLBs into ERAS protocols



FUTURE RESEARCH

- Assess QLB efficacy in ASA IV – V patients
- QL1 v. QL2 on postoperative opioid consumption
- Dry needling to control for placebo effect
- Assess dermatomal level recession during recovery
- Eliminate basal PCA opioid infusions
- Determine truncal block efficacy in the pediatric population
- Compare different additive effects on opioid consumption

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Institutional Review Board approval was not required for this research project.

Dexmedetomidine for Preventing Postoperative Nausea and Vomiting

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Background

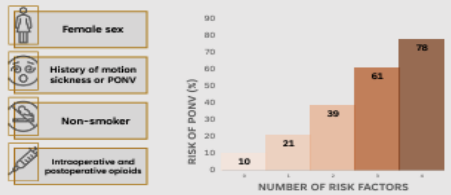
Postoperative Nausea and Vomiting (PONV)

Definition: Nausea, retching, or vomiting within 24 hours postoperatively[7]

Incidences:
- No risk factors: one-third of surgeries[2]
- High-risk populations: 70–80% of surgeries[2,25]

Consequences:
- Patient dissatisfaction[7]
- Prolonged post-anesthesia care unit (PACU) stay[7]
- An increase in unexpected hospital admissions and costs[7]

Apfel Score[3]



Dexmedetomidine

Mechanism of Action[34]

Highly selective centrally acting alpha-2-adrenoreceptor agonist

- → Anxiolytic
- → Sedative
- → Sympatholytic
- → Analgesic
- → Anesthetic sparing

Pharmacodynamics[34,35]
- Sedative effects from locus coeruleus
- Minimal respiratory depression

Adverse Effects[36]
- Hypotension
- Bradycardia
- Transient hypertension with loading dose

The anti-emetic mechanism of action of dexmedetomidine is yet to be elucidated

The hypothesized mechanisms of action:
- → Decreases use of inhaled anesthetic and opioids[7]
- → Inhibition of locus coeruleus[15]
- → Decreased sympathetic tone[7,15]

Research Question

- **P** In adult surgical patients undergoing general anesthesia,
- **I** does the use of intravenous (IV) dexmedetomidine
- **C** versus no dexmedetomidine
- **O** decrease the incidence of postoperative nausea and vomiting
- **T** during the first 24 hours postoperatively?

Literature Review

The Texas Medical Center Library Health Sciences Resource Center

Databases	Search Terms and Filters
❑ PubMed ❑ EMBASE ❑ Medline (Ovid) ❑ The Cochrane Library	❑ MeSH terms: • "Dexmedetomidine" • "Postoperative nausea and vomiting" ❑ Boolean Operators: "AND" & "OR" ❑ Filters: • English language • 2013 – 2024 • Peer-reviewed • Adult population • Human subjects

32 articles

Levels and Grades of Evidence

Agency for Healthcare Research and Quality[1]		United States Preventive Services Task Force[33]	
Level I: Meta-Analysis	1 article	Grade A: Strongly recommend	19 articles
Level II: Experimental	31 articles	Grade B: Moderately recommend	13 articles
Level III: Quasi-Experimental		Grade C: Selectively recommend	
Level IV: Non-Experimental		Grade D: Recommend against	
Level V: Case Reports		Grade I: Insufficient evidence	

Study Designs

Inclusion Criteria
- ✓ Adult (18+ years old)
- ✓ Undergoing general anesthesia
- ✓ BMI < 35 kg/m²
  - Included > 35 kg/m²[27]
- ✓ ASA physical status I–II
  - Included ASA III[25,27]

Exclusion Criteria
- ✗ Allergy to study medications
- ✗ Severe organ dysfunction
- ✗ Severe cardiac arrhythmias
- ✗ Uncontrolled hypertension or diabetes
- ✗ Drug or alcohol abuse
- ✗ Pregnancy or lactation
- ✗ Preoperative use of anti-hypertensive, opioid, or anti-emetic medications

Surgery Types
- ❑ Laparoscopic[5–7,9,12–13,16,18,23,25–27,29,34–35,37]
- ❑ Thoracic[6,11,24]
- ❑ Major or immediate non-cardiac[8,21,22,30–31]
- ❑ Gynecological[10]
- ❑ Abdominal[14,17]
- ❑ Neurosurgery[19,28,36]
- ❑ Ears, nose, throat (ENT)[15,20]

Intervention Groups
- ❑ Control (0.9% normal saline)[4,6,8–12,14,17,21–26,28,30–31,34,35–36]
- ❑ Comparison drugs
  - ❑ Opioids
    - ❑ Fentanyl[5,28]
    - ❑ Sufentanil[26]
    - ❑ Remifentanil[8,12,15,18,20,27]
  - ❑ Dexamethasone[7,16]
  - ❑ Lidocaine[37]
  - ❑ Dexmedetomidine[29]

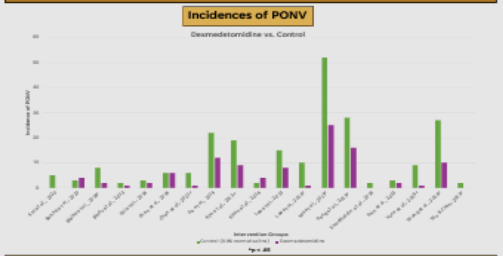
Initiation Time
- ❑ Before induction[5,11–14,18–20,23,25,29–31,34,36]
- ❑ With induction[8,15,22,26,36]
- ❑ After induction[4,6–8,10,16–17,21,24,27–28,33,34,35]

Maintenance of Anesthesia
- ❑ Total intravenous anesthesia[5,13–14,17–19,25,35–36]
- ❑ Volatiles
  - ❑ Nitrous oxide[10,16,22,31,34]
  - ❑ Sevoflurane[4,7,9,11,12,15,20–21,26,35]
  - ❑ Desflurane[8,22–24,27–31,35]
  - ❑ Isoflurane[4,6,16,34,35]

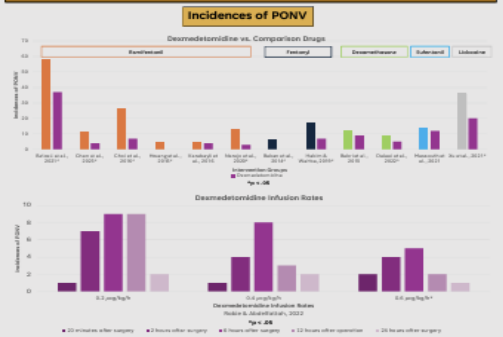
Administration Methods
- ❑ Single dose
  - ❑ 0.2 – 1.0 μg/kg[10,21]
  - ❑ 1 μg/kg[13,25,31,36]
- ❑ Continuous infusion
  - ❑ With loading dose[4–6,11–15,18–20,22–24,26,34–35,37]
  - ❑ Without loading dose[8–9,17,27,28–29]
  - ❑ Dose ranges: 0.2 – 1.0 μg/kg/h

Outcomes

Control (0.9% normal saline)



Comparison Drugs



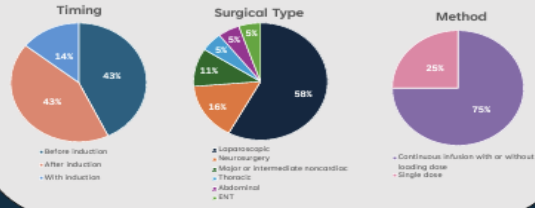
Summary of Findings

32 articles reviewed (100%)

29 articles showed decreased incidences of PONV (91%)

19 articles revealed statistically significant fewer incidences of PONV (59%)

Statistically Significant Articles by:



Recommendations for Practice

Consider the following recommendations for dexmedetomidine intraoperative use to prevent PONV:

Patient Population

- Adult patients (> 18 years old)
- ASA I–III
- Laparoscopic surgeries

Method, Dose, and Timing

If using as a:

Single Dose
- ❑ 0.5 μg/kg after induction
- ❑ 1.0 μg/kg over 10–15 minutes before induction or after induction

Continuous Infusion
- ❑ 0.2–0.7 μg/kg/hr with or without loading dose used before, with or after induction

Monitoring Parameters

Hemodynamics[34,36]
- Heart rate
- Blood pressure

PACU Length of Stay

A systematic review and meta-analysis covering 33 RCT studies with a total of 2,676 patients revealed that the postoperative recovery after intraoperative dexmedetomidine use in adults results in[32]:

- ❑ PONV
- ❑ Emergence agitation
- ❑ Cough
- ❑ Pain
- ❑ Shivering

↑ ❑ Hypotension

No clinically significant effect on:
- ❑ Length of PACU stay
- ❑ Time to extubation
- ❑ Residual sedation
- ❑ Bradycardia

Limitations

- Heterogeneity of the literature
- Differences in intervention groups
- Sample size
- Variability in timing and administration
- Single-institution

Future Research

- Larger-scale randomized controlled trials
- Consensus on dosage, timing, and method of administration
- Assessment of baseline PONV risk
- Standardized PONV assessment tool

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Tracheal Intubation Using Remifentanil Instead of Neuromuscular Blocking Agents

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Key Points

- NMBAs may be contraindicated in certain patient populations or cause prolonged neuromuscular blockade following extubation
- Remifentanil sidesteps risks associated with NMBAs
- Remifentanil boluses produce adequate intubating conditions

Background

Remifentanil

- Mu-opioid receptor agonist
- 1-minute onset of action
- 10-minute half-life
- May cause bradycardia and hypotension

NMBAs

- Depolarizing (succinylcholine) or non-depolarizing (rocuronium)
- Ineffective in patients with neuromuscular conditions
- May cause MH or anaphylaxis

Research Question

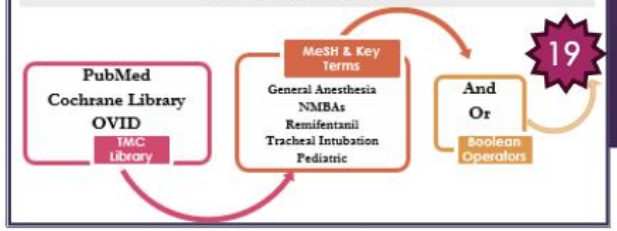
P In patients requiring endotracheal intubation

I does remifentanil,

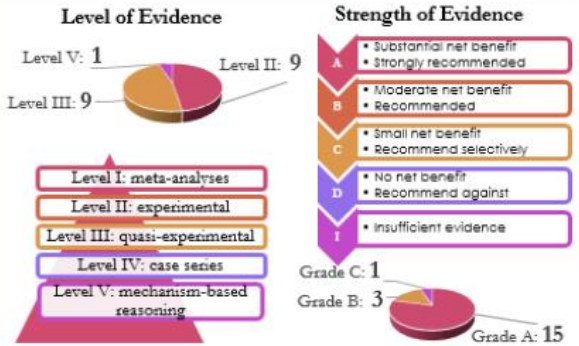
C compared to NMBAs,

O produce adequate intubating conditions?

Literature Search



Grading the Evidence



Study Population

Inclusion Criteria	Exclusion Criteria
Adults ≥ 18 year	Suspected difficult airwa
Pediatrics < 18 year	History of difficult intubatio
ASA 1 or	Cormack-Lehane grade ≥ 2
Elective intubatio	Reactive airway diseas
	Vocal cord patholog

Measured Outcomes

1. Intubating conditions **(primary outcome)**
2. Hemodynamic Tolerance
3. Airway Trauma
4. Muscle Rigidity

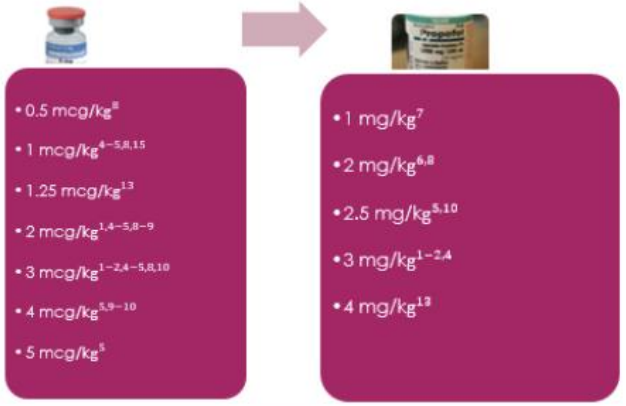
Intubating Conditions[6]

Variables	Acceptable		Not acceptable
	Excellent	Good	Poor
Ease of laryngoscopy (jaw relaxation)	Easy	Fair	Difficult
Vocal cord position	Abducted	Intermediate	Closed
Vocal cord movement	None	Moving	Closing
Airway reaction (coughing)	None	Slight	Sustained (>10 s)
Movement of the limbs	None	Slight	Vigorous

Overall intubating conditions were defined as Excellent: All variables are excellent, Good: One or more variable good, no quality poor, Poor: The presence of a single variable listed under poor

Induction Variations

- Articles examined remifentanil boluses[1–2,4–10,12–15,17–19] or infusions[3,11,16]
- Co-administration of propofol[1–10,13–14,16], sevoflurane[11–12,17,19], or ketamine[2]
- NMBAs used as a rescue agent in cases of failed intubation[6,8–13,15]
- Remifentanil boluses yielded clinically acceptable intubating conditions ($p < .05$)[1–2,4–10,12–15,17–19]



Additional Adjuncts

Benzodiazepines → Vasopressors → Anticholinergics

Recommendations for Practice

- **Assess ASA status** → 1 – 3
- **Assess surgery type** → elective, requiring general anesthesia, neuromuscular blockade not warranted
- **Premedicate with benzodiazepines** to prevent muscle rigidity
- **Perform tracheal intubation at peak effect of remifentanil**

Limitations

- Exclusion of ASA 4 or 5 patients
- Unknown timing of Cormack-Lehane assessment
- Unclear if propofol contributes to acceptable intubating conditions more than remifentanil

Future Research

- Examine efficacy in obstetric patients
- Cost effectiveness of remifentanil versus NMBAs
- Cost effectiveness of remifentanil versus insufficient neuromuscular blockade reversal
- Determine suitability for suspected difficult airway

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Norepinephrine for Spinal Anesthesia-Induced Hypotension in Parturients

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Spinal Anesthesia-Induced Hypotension

Undesired repercussion[1,2]
- SNS predominates in pregnancy[3]
- SNS and PNS imbalance[4]

Exaggerated sympatholytic effects[4]
- Acute vasomotor blockade of sympathetic nerves[1,2]
- Activation of cardioinhibitory receptors[1,2]
- Pooling of up to 20% of blood volume[3]

Parturients undergoing cesarean section
- SAIH incidence 7.4% to 74.1%[4]

Maternal and Neonatal Adverse Effects

- Altered consciousness and decreased cardiac output[1,4]
- Splanchnic hypoperfusion leads to emetogenic serotonin release[1]
- Decreased cerebral perfusion and oxygenation stimulate vomiting[4,5]
- Decreased placental and fetal perfusion[4]
- Oxypurines and lipid peroxides found in umbilical blood[4]
- Acidosis and depressed Apgar scores[1]

2018 International Consensus Statement

Recommendations
- PE is the drug of choice for SAIH[1]
- More data is needed to recommend NE[1]
- Infusions are superior to bolus injections[1,6]

Norepinephrine vs. Phenylephrine

Norepinephrine
- **Potent** α1-agonist[7]
- **Mild** β1-agonism[8]
  - Oppose baroreflexive bradycardia and decreased CO
- Cardiac index increases with limited increase in HR or MVO_2[9]

Phenylephrine
- **Potent** α1-agonist[10]
- **Lacks** β-agonism[11]
  - No direct chronotropic or inotropic effects
- Effects on cardiac output are complex[12]
- Dosing, volume status, HR, sympathetic tone

Research Question

P In parturients receiving SA for cesarean section,

I how do intravenous norepinephrine infusions

C compared to intravenous phenylephrine infusions

O affect SAIH and related adverse effects

T during the intraoperative period?

Literature Review

- **Texas Medical Center Library Online Portal**
  - PubMed, EMBASE, Cochrane Library, CINAHL, Ovid MEDLINE
- **Filters**
  - 2013-2024, Humans, English language, randomized controlled trial, article
- **Aides**
  - Boolean operator 'AND,' snowballing technique
- **MeSH* & Key Terms**
  - Norepinephrine*, phenylephrine*, hypotension*, spinal anesthesia*, obstetrics*

15 randomized controlled trials

Levels and Grades of Evidence

Oxford Centre for Evidence-Based Medicine[13]		United States Preventive Services Task Force[14]		
Level 1	Systematic review	A	High certainty of net benefit	5
Level 2	RCTs	B	Benefit in eligible patients	10
Level 3	Non-RCTs	C	No recommendation for or against	
Level 4	Case series	D	Routine use not recommended	
Level 5	Mechanism based reasoning	I	Insufficient evidence	

Population

Inclusion Criteria
- ASA score < III[6,8,15-27]
- ≥18 years old[6,8,15-27]
- Term[6,8,15-17,19-21,23-27]
- Singleton[6,8,15-18,20-27]
- SA for CS[6,8,15-27]

Exclusion Criteria
- Pre-eclampsia[22]
- > 32 weeks[18,22]
- Twins[8,16,18,19]
- Non-elective[8,15]
- Pre-eclampsia[6-8,15-21,23-27]
- Cardiovascular disease[6,8,15-27]
- Coagulation disorders[6,8,15-27]

Study Design

Local Anesthetic
- 7.5-15 mg of 0.5% bupivacaine[6,8,15-18,20-27]
- 12 mg of 0.5% ropivacaine[19]

Drug Adjuncts
- 2.5-5 mcg sufentanil[16,19]
- 100-200 mcg PF morphine[14,27]
- 10-25 mcg fentanyl[8,15,21,23-27]
- No adjunct[6,17,18,22]

Crystalloid Co-load
- 10 - 20 mL/kg[17,20,23,26]
- 0.5 - 1 L[15,16,19,27]
- ≤ 2 L[6,8,21,24]
- No co-load[18,22,25]

NE-to-PE Potency
- 5:1 to 13:1[16,18,19,20,22,27]
- 15:1 to 20:1[6,8,15,17,21-26]
- (Dose at which two different drugs are equipotent)[28]

Norepinephrine vs. Phenylephrine Drips
- 0.05 mcg/kg/min NE vs. 0.1-0.75 mcg/kg/min PE[15,16,20,22,23,27]
- 2.5-6 mcg/min NE vs. 40-100 mcg/min PE[6,8,16,17,19,22,23]
- Started at the time of spinal or immediately after[6,8,15-24]

Approach to Treating Hypotension
- Titration of drips[8,16,21,23,24]
- 50-100 mcg PE or 5-15 mg ephedrine based on HR[16,23,27]
- 2.5-8 mcg NE vs. 25-100 mcg PE[6,8,15,17-22,24-26]

Outcomes

Maternal

Hypotension
- No difference[6,8,15,19-23,26]
- Higher in PE group*[16,17,25]
- Higher in NE group*[18]
- Rescue bolus requirements
  - No difference[6,8,15,16,18,21-23,27]
  - Higher in PE group*[17,25]

Bradycardia
- Higher in PE group*[6,8,15,18-22,24,26]
- No difference[16,17,23,25,27]
- Rescue atropine requirements
  - No difference[6,15-18,25]

Reactive Hypertension
- No difference[6,18,19,21-23]

Vomiting
- No difference[6,8,16-26]
- Higher in PE group*[15,27]

Cardiac Output
- No difference[19,20,27]
- Higher in NE group*[24]

Systemic Vascular Resistance
- No difference[19,20,27]
- Higher in PE group*[24]

*$p < .05$

Neonatal

Apgar Scores
- No difference[6,8,15-27]

Lactate Levels
- No difference[16,18,20,24,26]

Umbilical Artery Blood Gas
- No difference in pH, pO_2, pCO_2[6,8,15,16,18,20,22-26]
- Base deficit higher in NE group*[26]

Glucose Levels
- No difference[16,20]
- Higher in NE group*[18,24]

*$p < .05$

Potency Equivalency & Dose-Finding

Phenylephrine vs. Norepinephrine Dose Equivalency

ED	Phenylephrine	Norepinephrine	Potency
ED 50[29]	137 mcg*[29]	10 mcg*[29]	13.1:1[29]
ED 90[30]	90.9 mcg*[30]	8 mcg*[30]	11.4:1[30]

Norepinephrine (mcg/kg)[31]

ED 50	ED 95
0.067 mcg/kg*	0.121 mcg/kg*

Norepinephrine (mcg/kg/min)

ED 50	ED 80*/ED90*	ED 95
0.042 mcg/kg/min*[32]		0.097 mcg/kg/min*[32]
0.029 mcg/kg/min*[33]	0.080 mcg/kg/min◊*[33]	
0.029 mcg/kg/min*[34]	0.068 mcg/kg/min†*[34]	0.105 mcg/kg/min*[34]

*95% CI, SAIH during cesarean section

Limitations

- Single-center studies[6,8,15-27] → difficult to generalize
- Elective cesarean section[6,16-21,23-27]
- Gravid patients without severe comorbidities[6,15-21,23-27]
- NE and PE doses may not have been equipotent[18,22,27]

Recommendations

For adult parturients undergoing cesarean section requiring SA

Crystalloid Bolus	• Pre-load or co-load • 500-1,000 mL
NE Infusion Dose	• 0.05 mcg/kg/min or 2.5-3.5 mcg/min • Titrate to SBP within 90-110% of baseline
Initiation of Infusion	• Time of SA injection • Discontinue based on adequate BP
Acute Hypotension	• Additional 3-10 mcg NE boluses

Future Research

- NE use in patients with pre-eclampsia
- Application to other surgeries requiring SA
- NE benefits in non-gravid populations
- Potency equivalencies between NE and PE

References

1. Kinsella et al., 2018; 2. Ferré et al., 2020; 3. Brislane et al., 2023; 4. Šklebar et al., 2019; 5. Hirose et al., 2019; 6. J. Singh et al., 2022; 7. Adda et al., 2021; 8. Ngan Kee et al., 2020; 9. Russell et al., 2021; 10. West-Ward Pharmaceuticals, 2012; 11. Habib, 2012; 12. Richards et al., 2023; 13. OCEBM Levels of Evidence Working Group, 2011; 14. USPSTF, 2018; 15. Ali & Bajaj, 2023; 16. Belin et al., 2023; 17. Berawala et al., 2021; 18. Chen et al., 2022; 19. Du et al., 2022; 20. Feng et al., 2020; 21. Goel et al., 2021; 22. Guo et al., 2022; 23. Hasanin et al., 2019; 24. Ngan Kee et al., 2015; 25. Pauline et al., 2023; 26. A. Singh et al., 2022; 27. Vallejo et al., 2017; 28. Tallarida & Rafa, 2010; 29. Ngan Kee, 2017; 30. Guo et al., 2023; 31. Wang et al., 2020; 32. Xu et al., 2021; 33. Fu et al., 2020; 34. Wei et al., 2020

Institutional Review Board approval was not required for this research project.

Intravenous Dexmedetomidine for the Treatment of Neuraxial Shivering

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Learning Objectives

By the end of this presentation, the learner will be able to:

- describe potential disadvantages of neuraxial anesthesia induced shivering,
- recall the pharmacology behind dexmedetomidine, tramadol, and meperidine,
- compare the effectiveness of dexmedetomidine to tramadol, and meperidine based on current literature,
- evaluate the risks and benefits of using dexmedetomidine as a treatment for post neuraxial shivering, and
- summarize recommendations for future research.

FDA Disclosures

- Off label use of intravenous dexmedetomidine
- Intravenous tramadol is pending FDA approval
- Meperidine boxed warning

Neuraxial Shivering

- Occurs in approximately half of patients receiving neuraxial anesthesia[6]
- Core heat is redistributed to periphery[10]
- Impaired autonomic thermoregulation below level of the block → vasodilation and heat redistribution[6]
- Can lead to increased oxygen requirements, CO_2 production, and cardiac output[6]
- Patient discomfort and issues with vital sign monitoring

Pharmacology

Dexmedetomidine

- Centrally acting alpha-2 adrenergic agonist[12]
  - Possesses antihypertensive, analgesic, anxiolytic, and sedative properties
  - Minimal effects on respiratory drive
- Decreases the shivering threshold through modulation of the central thermoregulatory system[25]
- Side effects: bradycardia and hypotension

Meperidine (Pethidine)

- Phenylpiperidine synthetic opioid[28]
- Modulation of the central thermoregulatory system + kappa agonism[2]
- Side effects: nausea, vomiting, somnolence, and respiratory depression[10]

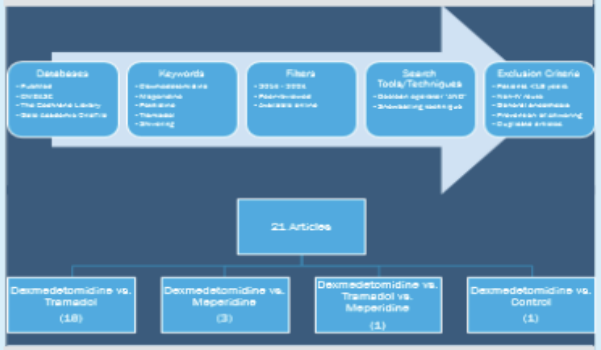
Tramadol

- Synthetic opioid[28]
- Blocks the reuptake of serotonin and norepinephrine[28]
- Side effects: nausea and vomiting

Research Question

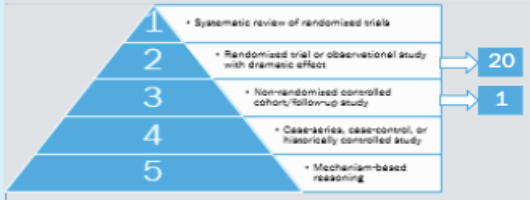
P	In adult patients undergoing neuraxial anesthesia
I	does the use of intravenous dexmedetomidine
C	compared to the use of intravenous tramadol and meperidine
O	more effectively reduce shivering
T	in the perioperative period?

Literature Review



Levels and Grades of Evidence

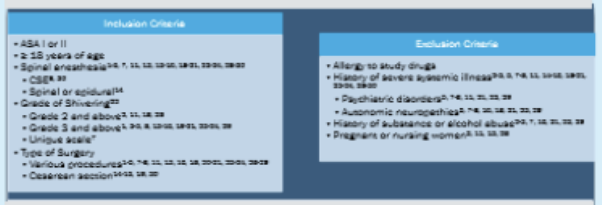
Oxford Centre for Evidence-Based Medicine[17]



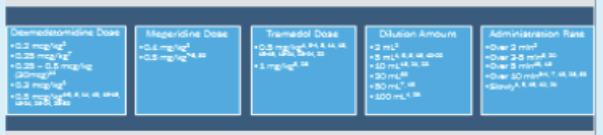
United States Preventive Services Task Force[27]

Grade A	Recommended due to high certainty of net benefit
Grade B	Recommended due to moderate certainty of net benefit
Grade C	Selectively recommends
Grade D	Recommended against the intervention
Grade I	Insufficient evidence for recommendation

Synthesis of Literature



Intervention Administration



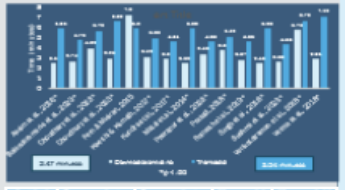
Outcomes

Primary Outcome: Time for Cessation of Shivering

Mean Time for Cessation of Shivering

- The dexmedetomidine group was significantly* faster when compared to tramadol[1, 3-5, 11, 13, 16, 18-19, 21, 23-24, 28-29]
- The dexmedetomidine group was significantly* faster when compared to meperidine[2]
  - Dexmedetomidine dose of 0.5 mcg/kg and 0.3 mcg/kg
- The dexmedetomidine group was significantly* faster when compared to normal saline[14]

*p < .05



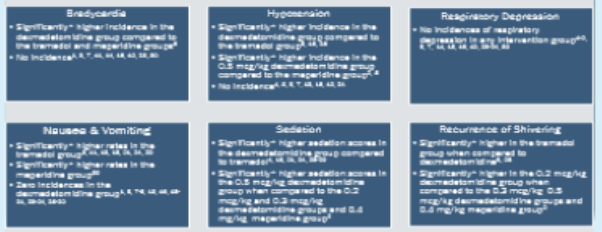
Article	Dexmedetomidine Dose	Dexmedetomidine Mean Time (min)	Meperidine Dose	Meperidine Mean Time (min)
Abdel-Ghaffar et al., 2016	0.5 mcg/kg 0.3 mcg/kg 0.3 mcg/kg	1.62 1.67 1.89	0.4 mg/kg	2.36
Dixit et al., 2022	0.25 mcg/kg	2.0	0.5 mg/kg	2.52
Fern & Misiran, 2015	0.5 mcg/kg	7.2	0.5 mg/kg	8.3

Response Rate: cessation of shivering within a certain time frame

Dexmedetomidine vs. Tramadol	Dexmedetomidine vs. Meperidine	Dexmedetomidine vs. Control
• Significantly* higher response rate in the 0.5 mcg/kg dexmedetomidine group at 5 min[22] and 15 min[8, 20, 28]	• Significantly* higher in the 0.3 mcg/kg and 0.5 mcg/kg dexmedetomidine group at 10 min[3]	• Significantly higher in the 30 mcg dexmedetomidine group at 5, 10, and 15 min[26]

*p < .05

Secondary Outcomes



*p < .05

Results Recap

Dexmedetomidine

- Significantly* faster than tramadol by approximately 2 minutes
- Not inferior to meperidine
- Less nausea and vomiting
- Less recurrence of shivering
- Higher sedation scores
- Higher incidence of bradycardia and hypotension

*p < .05

Recommendations for Practice

- Dexmedetomidine dose 0.25 - 0.5 mcg/kg
- Administer over at least 5 minutes
- Administer once neuraxial shivering is identified
- Administer after cord clamping in the parturient
- Caution in patients who have bradycardia or hypotension
- Sedation pros and cons

Limitations

- Small sample sizes n = 50 - 120
- Variations in dilution and administration
- Exclusion of patients with severe comorbidities

Future Research

- Cost comparison
- Comparison to other interventions
- Superior route investigation
- Use in general anesthesia
- Additional dose-finding trials
- Sample population expansion

References

1. Aasim et al., 2016; 2. Abdel-Ghaffar et al., 2016; 3. Balasubramanian et al., 2023; 4. Choudhary et al., 2022; 5. Choudhury et al., 2023; 6. Crowley & Buggy, 2008; 7. Dixit et al., 2022; 8. Fern & Misiran, 2015; 9. Hospira, 2016; 10. Hynson et al., 1991; 11. Keerthi & Kamath, 2017; 12. Khan et al., 1999; 13. Kundra et al., 2017; 14. Lamontagne et al., 2019; 15. Manhas et al., 2023; 16. Mittal et al., 2014; 17. OCEBM Levels of Evidence Working Group, 2011; 18. Peerapur et al., 2023; 19. Prasad, 2018; 20. Ranjha et al., 2023; 21. Ramesh et al., 2019; 22. Singh et al., 1993; 23. Singh et al., 2016; 24. Sushma et al., 2023; 25. Talke et al., 1997; 26. Tsai & Chu, 2001; 27. United States Preventative Services Task Force, 2018; 28. Venkatraman et al., 2018; 29. Verma et al., 2018; 30. Yu et al., 2019.

International Review Board approval was not required for this research project.

The Perioperative Use of Cefazolin in Patients with a Penicillin Allergy

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Background

- Surgical site infections (SSI) make up 20% of healthcare acquired infections, resulting in healthcare costs of $3 billion and a 3% mortality rate[1].
- Prevention of SSI is one of The Joint Commission's National Patient Safety Goals[2].
- Prophylactic antibiotics vary by procedure type and are typically administered by anesthesia providers to ensure timeliness[3].

Cefazolin

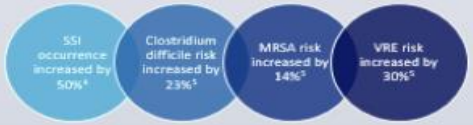
- First-line antibiotic for a majority of surgical procedures[3].
- Beta-lactam and 1st generation cephalosporin antibiotic[3].
- Inhibition of cell wall synthesis with coverage against common skin bacteria[3].

Penicillin

- First antibiotic discovered, part of the beta-lactam family.
- Most common drug allergy, 10% of patients report penicillin allergy[4].
- Allergy is over-reported, and sensitivity is known to decrease over time[4].

Penicillin Allergy Implications

- Penicillin-allergic patients have worse outcomes than those without allergy., directly correlated to administration of second-line antibiotics

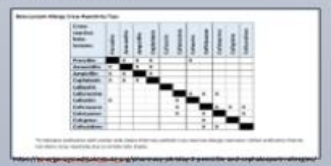


Historical Impact

- Penicillin was discovered by in 1928 and widely in use by the mid-1940s.
- Cross-reactivity concerns began in the 1960s when cephalosporins were introduced, initially thought to be related to beta-lactam ring[6].
- Penicillin-allergic patients were known to have increased reactivity to structurally unrelated drugs[7].
- Theorized that early data showing increased cross-reactivity was secondary to contamination of cephalosporins by penicillins[6].

Chemical Structure

- IgE mediated cross-reactivity among beta-lactam antibiotics is determined by R1 sidechain, not the beta-lactam ring[6].
- Sidechains are not related to cephalosporin generation, common misconception that all 1st generation cephalosporins are cross-reactive.
- Cefazolin has unique sidechain.



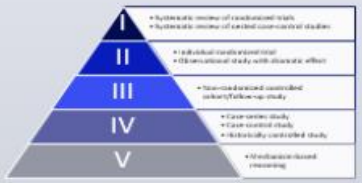
Research Question

PICOT

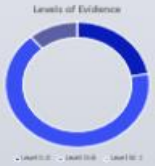
- In surgical patients with a documented penicillin allergy,
- how does the administration of cefazolin
- compared to second-line antibiotics
- affect the incidence rate of hypersensitivity response
- within the perioperative period?

Literature Search

Levels and Strength of Evidence

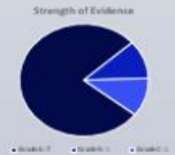


Oxford Centre for Evidence-Based Medicine, 2011



Grade A	Strongly recommended – Apply to practice
Grade B	Recommended - Apply to practice
Grade C	May be applicable in certain circumstances
Grade D	Recommend against
Grade I	Insufficient evidence

United States Preventive Services Task Force, 2018



Study Design

Primary Outcome: HSR to antibiotic

All observational cohort studies

- Six retrospective[8-13]
- One prospective[14]
- One with retrospective and prospective components[15]
- One systematic review of case reports[16]

Inclusion Criteria	Exclusion Criteria
Cefazolin first-line for procedure type[10]	Missing or uninterpretable data[12,15]
Documented penicillin allergy[8,9,11,12,14,16]	Other antibiotic courses[10,11,13]
Any patient receiving antibiotic prophylaxis[13]	Antibiotics during study transition period[12]
History of anaphylaxis[13,16]	Not enrolled in study[12,14]
Penicillin skin-testing[14]	Primary cephalosporin allergy[9]

Variables

Findings

Cefazolin	3,961 administrations[8-11,13-15]	11 HSRs (0.3%)
Clindamycin	2,749 administrations[8-11,13-15]	33 HSRs (1.2%)

Kaiser Permanente Regional Comparison Study[12]

- New antibiotic allergy higher in penicillin-allergic patients
- Penicillin allergy associated with higher morbidity and mortality

Drug allergy 2022: Practice Parameter Update[17]

Cefazolin is a non-cross-reactive cephalosporin.

Routinely administer with history of anaphylaxis to penicillin.

Limitations

Practice Recommendations

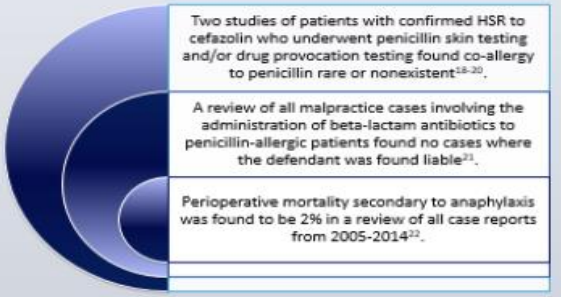
Administer cefazolin to penicillin-allergic patients with history of:

- ✓Any IgE-mediated HSR, including anaphylaxis.
- ✓All other HSR, except type II or III.

Limited evidence to support cefazolin administration:

- History of type II or III HSR to any beta-lactam antibiotic.
- Further evaluation of patient history as recommended by CDC

Considerations

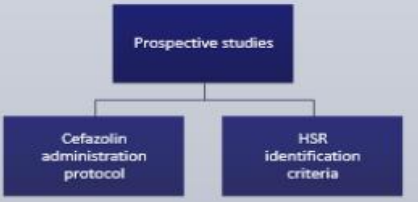


Two studies of patients with confirmed HSR to cefazolin who underwent penicillin skin testing and/or drug provocation testing found co-allergy to penicillin rare or nonexistent[18-20].

A review of all malpractice cases involving the administration of beta-lactam antibiotics to penicillin-allergic patients found no cases where the defendant was found liable[21].

Perioperative mortality secondary to anaphylaxis was found to be 2% in a review of all case reports from 2005-2014[22].

Future Research



References

1. Centers for Disease Control, 2023 2. Agency for Healthcare Research and Quality, 2019
3. Bratzler et al., 2013 4. Blumenthal et al., 2017 5. Macy et al., 2014 6. Vorobeichik et al., 2018 7. Moellering & Swartz, 1976 8. Anstey et al., 2021 9. Beltran et al., 2015 10. Dong et al., 2023 11. Fosnot et al., 2021 12. Macy et al., 2021 13. Norvell et al., 2023 14. Macy & Ho, 2011 15. Grant et al., 2021 16. Harper et al., 2018 17. Khan et al., 2022 18. Kuhlen et al., 2016 19. Pedersen et al., 2024 20. Pipet et al., 2011 21. Jeffries et al., 2018 22. Gonzalez-Estrada et al., 2021

O-Mg: Perioperative Utility of Magnesium Sulfate

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Background

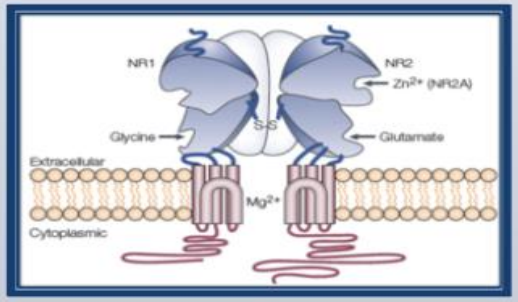
Postoperative pain is costly yet still frequently undertreated.

Opioids are still the mainstay of postoperative pain control but have many adverse effects.

Healthcare reimbursement is moving towards value-based payments.

Magnesium sulfate is a safe, cost-effective, non-opioid analgesic agent.

Magnesium sulfate has numerous beneficial effects for surgical patients in addition to its demonstrated analgesic benefits.



(Witt et al., 2004)

PICOT Question

In adult patients undergoing general anesthesia, does the administration of intravenous magnesium sulfate compared to no administration of magnesium sulfate decrease opioid consumption in the perioperative period?

Literature Review

TMC Research Portal	MeSH and Key Terms	Filters
• Medline OVID • Cochrane Database • Cumulative Index for Nursing and Allied Health Literature (CINAHL)	• **Analgesia** • **Magnesium Sulfate** • Intravenous magnesium sulfate • Opioid • Pain • **Pain, Postoperative/Drug Therapy** • Surgery	• Published within the last 10 years • Randomized controlled trials (RCTs) • Intravenous magnesium vs. no administration • Opioid consumption as a measured variable • Patients undergoing general anesthesia

Results

19 Articles

All level II evidence
- High-quality experimental designs (RCTs)

Graded for strength according to USPSTF criteria
- One article assigned Grade A
- Fifteen articles assigned Grade B
- Three articles assigned Grade C

Study Criteria

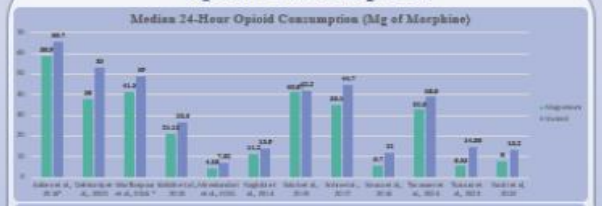
Inclusion criteria
- ASA I-III
- Adult Patients

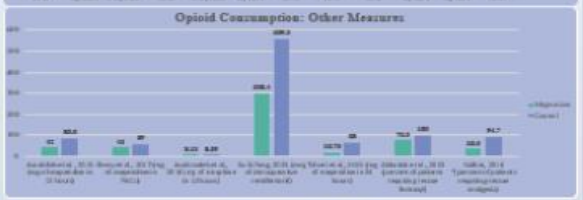
Exclusion criteria
- Allergy to study drugs
- Severe cardiovascular, hepatic, renal, or neuromuscular disorders
- Opioid or drug abuse
- Calcium channel blocker therapy

Limitations

- Significant heterogeneity in the literature
- Lack of data regarding optimal dosing / timing
- Lack of data regarding use in ASA class IV or chronic pain patients
- Uncertainty about precise analgesic mechanism

Opioid Consumption





Other Findings

Dosing strategies	• Boluses from 20-50 mg/kg over 10-30 minutes • Infusions ranging from 2-20 mg/kg/hr typically stopped once skin closure begins
Pain Score	• Significantly (p <.05) decreased postoperative pain scores in adults • Reduces pain scores for 12-48 hours
Hypermagnesemia	• Adverse effects of elevated magnesium not seen in any studies • Serum magnesium levels increased, but remained within therapeutic range
Recovery Time	• No prolongation in emergence / extubation time / length of PACU stay • One study showed a significantly (p <.05) shorter length of PACU stay
Miscellaneous	• Decreases emergence delirium • No increase in operative blood loss • No adverse hemodynamic effects • Improves postoperative respiratory function • Decreases vasodilator requirements

Recommendations

- 20-50 mg/kg bolus dose of magnesium sulfate after induction
- Avoid in patients with severe renal or hepatic disease or with high-degree heart block
- In longer procedures (> 4 hours), consider magnesium infusion at 2-20 mg/kg/hr
- Consider in procedures where avoiding hypertension is desirable (e.g., sinus surgery)
- Consider for patients at risk of arrythmias, cerebral ischemia, or bronchospasm
- No preoperative serum level needed, unless renal dysfunction present

Future Research

- Optimal dose-finding studies
- Timing of administration
- Use in ASA class IV patients
- Analgesic correlation with serum magnesium levels
- Utility in patients with chronic pain

References

Neuromuscular Monitoring and Residual Neuromuscular Blockade

Christian Terrazas, B.S.N., S.R.N.A.; Jessica Gaines, D.N.P., CRNA, CHSE

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Background

Physiology[1]

- Action potential travels from the nerve to muscle
- Increased [Ca^{2+}] leads to acetylcholine (Ach) exocytosis
- ACh interacts with postsynaptic nicotinic receptors
- Influx of Na^{+} ions → action potential in the muscle
- Acetylcholinesterase catabolizes ACh in the synaptic cleft

Pharmacology

Neuromuscular Blocking Agents

- **Depolarizing[2]**
  - Succinylcholine
- **Non-Depolarizing[3]**
  - Rocuronium
  - Vecuronium
  - Cisatracurium

Neuromuscular Blockade Reversal Agents

- **Selective Relaxant Biding Agent[4]**
  - Sugammadex
- **Cholinesterase Inhibitors[5]**
  - Neostigmine
  - Edrophonium
  - Pyridostigmine
  - Physostigmine

Monitoring Sites[6]

Ulnar Nerve: Adductor Pollicis

Facial Nerve: Orbicularis Oculi, Corrugator Supercilii

Posterior Tibial Nerve: Flexor Hallucis Longus

Quantitative Neuromuscular Monitoring

Acceleromyography (AMG)

Electromyography (EMG)

Kinemyography (KMG)

- **Provides a train-of-four ratio (TOFR)**
- **Use supported by:**
  - European Society of Anaesthesiology and Intensive Care[7]
  - American Society of Anesthesiologists[8]
  - 2018 expert consensus statement[9]
- **Only 17% of providers use neuromuscular monitoring[10]**
  - 11% of these providers use quantitative monitoring[10]
- **Low compliance attributed to:**
  - Cost, equipment availability, and lack of provider education[11]

Devices

TOF-Watch
Most used monitor in 2017[12]

Datex-Ohmeda NMT
Only EMG available until 2018[13]

TwitchView
Available in 2018[13]

Background

Qualitative Neuromuscular Monitoring

- **Visual or tactile train-of-four stimulation[15]**
- **Clinical Assessment:[15]**
  - Head lift
  - Hand grip strength
  - Spontaneous breathing
  - Ability to cough
- **4/4 twitches may still represent:**
  - 75-80% receptor blockade[16]

Residual Neuromuscular Blockade (RNMB)

- **RNMB is defined as TOFR < 0.9[17]**
- **Associated with:[18]**
  - Poor outcomes
  - Increased incidence of complications
- **Complications:[18]**
  - Upper respiratory obstruction
  - Respiratory depression
  - Increased risk for aspiration

Research Question

P For adult surgical patients receiving a non-depolarizing neuromuscular blocking agent

I does the utilization of intraoperative quantitative neuromuscular monitoring

C in comparison to qualitative neuromuscular monitoring

O reduce the incidence of residual neuromuscular blockade

T in the first hour after tracheal extubation?

Literature Search

Databases were accessed via the Texas Medical Center Library

PubMed | EMBASE | Cochrane | CINAHL | Medline (Ovid)

Search Terms:
- Residual neuromuscular blockade
- Residual neuromuscular curarization
- Quantitative monitoring
- Acceleromyography
- Electromyography

MeSH Terms:
- Neuromuscular monitoring
- Delayed emergence from anesthesia

Boolean Operator:
- 'AND'

Filters:
- Last 10 years
- Human
- English

Snowballing Technique

→ **13 Articles**

Levels and Grades of Evidence

Oxford Centre for Evidence-Based Medicine Guidelines[19]

Level 1	Systematic reviews or meta-analyses	
Level 2	Randomized control trials (RCT)	3
Level 3	Non-randomized studies	10
Level 4	Case-control and case-series studies	
Level 5	Mechanism-based reasoning studies	

U.S. Preventive Services Task Force (USPSTF)[20]

Grade A	Strongly recommended High certainty of net benefit	7
Grade B	Recommended Moderate certainty of net benefit	4
Grade C	Selectively recommended	2
Grade D	Recommended against	
Grade I	Insufficient evidence, poor quality Conflicting results	

Summary of Findings

Inclusion

- Adults (≥18 years)[21-27]
  - Ages 18-60 years[28]
- General anesthesia[21-28]
- Elective surgery[21-28]
- ASA-PS I-III[21-28]
- Administration of NDNMBA[21-28]

Exclusion

- Pre-existing neuromuscular, renal, or cardiac diseases[21-25,27,28]
- Lack of access to ulnar nerve[21-25,27,28]
- Postoperative ICU admission[21-25,27,28]
- Emergency surgery[21-25,27,28]
- BMI > 35 kg/m² [21-25,27,28]

Neuromuscular Blockade Reversal Methods

- Reversal method decided by providers[21,22, 23,24,26]
- Standardized reversal method[25,27,28]
- Neostigmine only[21,22,25,26,27,28]
- Neostigmine and sugammadex available[23,24]
- Reversal administered to all patients[21,22,26]
- Reversal agent not administered to all patients[23,24,25,27,28]

Measurements

- All monitored the adductor pollicis muscle

AMG[21-25,27,28]
- TOF-Watch SX[22,24,25,27,28]
- Phillips IntelliVue NMT Module (intraoperative) and TOF Watch SX (PACU)[23]

EMG[26]
- Datex-Ohmeda ElectroSensor[26]

Primary Outcomes

Residual Neuromuscular Blockade (RNMB)

Qualitative
- Increased incidence of RNMB*[21,23-27]
- Incidence of RNMB: 30.5% to 66.7%[21-25,28]
- Mean TOFR on admission to PACU:
  - 0.858 to 0.88*[25-27]

Quantitative
- Decreased incidence of RNMB*[21,23-27]
- Incidence of RNMB: 1.6% to 22.2%[21-25,28]
- Mean TOFR on admission to PACU:
  - 0.939 to 0.98*[25-27]

Factors Affecting RNMB and TOFR

Female Gender	Increased incidence of RNMB*[21,24]
Female: 29.8% to 76.9%[21,24] **Male:** 22.4% to 35.3%[21,24]	
Older Age	Lower TOFR on PACU admission*[22]
Shorter Surgery Duration	Lower incidence of RNMB*[22]
ASA-PS and BMI	No difference in incidence of RNMB[21]

Qualitative Neuromuscular Monitoring

- **Qualitative clinical assessments for detecting RNMB:[22,25]**
  - Sustained head lift
  - Hand grip strength
  - Ability to cough

	Chetty et al., 2020	Murphy et al., 2011
Sensitivity	80%	43.5%
Specificity	20%	94%

Secondary Outcomes

- **RNMB increased the incidence of:**
  - Critical respiratory events and reintubation*[21,24]
- **Critical respiratory events were associated with higher BMI*[21]**

	Incidence of PACU reintubation*[24]	Average SpO_2 on PACU arrival*[21]
With RNMB	1.06%	91%
Without RNMB	0%	96%

*p < .05

Summary of Findings

Secondary Outcomes Cont.

- **TOFR at extubation:[27]**
  - Quantitative monitoring: 0.94*
  - Qualitative monitoring: 0.86*
- **No significant difference in:[27,28]**
  - Anesthetic duration
  - Total dose of rocuronium
  - Frequency of rocuronium administration
  - Total dose of neostigmine

AMG vs. EMG

- AMG overestimates TOFR compared to EMG by 10% to 17.6%[29-33]
- Significantly more AMG TOFR values >1.0 (23%) compared to EMG (2%)*[29]
- EMG relative intraobserver variability is lower compared to AMG*[29]
  - EMG (2.0%) vs. AMG (3.2%)
- EMG devices are more reliable and consistent than AMG[29]
- TOFR of 1.0 using AMG could not exclude RNMB[32]
- AMG and EMG recordings of TOFR cannot be used interchangeably[33]

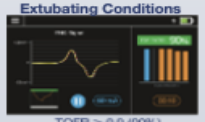
Practice Recommendations

- Quantitative neuromuscular monitoring should be used any time a NDNMBA is administered to an adult surgical patient
- EMG technology is preferred over AMG due to more reliable and consistent results
- Neuromuscular blockade reversal should be guided by quantitative monitoring
- Qualitative monitoring can be used when quantitative monitors are not available

Intubating Conditions

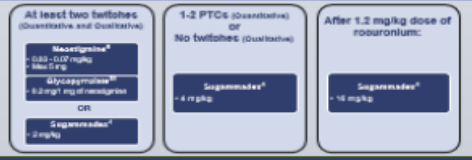
TOF count = 0

Extubating Conditions



TOFR ≥ 0.9 (90%)

Neuromuscular Blockade Reversal



Limitations and Future Research

Limitations

- Small sample sizes
- Lack of randomization
- Single center studies
- Limited availability of equipment

Future Research

- Evaluate new EMG technology (TwitchView and TetraGraph)
- Research and development for new technology to be used at the orbicularis oculi and corrugator supercilii muscles
- Explore reasons for low quantitative monitor utilization

References

1.Omar et al. 2023; 2.Hager & Bumes, 2023; 3.Cook & Simons, 2023; 4.Chandrasekhar et al., 2023; 5.Neely et al., 2023; 6.Naguib et al., 2016; 7.Fuchs-Bader et al., 2023; 8.Thilen et al., 2023; 9.Naguib et al., 2018; 10.Philips et al., 2013; 11.Brull & Kopman 2017; 12.Soderstrom et al., 2017; 13.Lee, 2021; 14.Weigel et al., 2022; 15.Motamed, 2023; 16.Foster et al., 2002; 17.Murphy et al., 2010; 18.Murphy et al., 2008; 19.Howick et al., 2011; 20.USPSTF, 2018; 21.Alenezi et al., 2021; 22.Chetty et al., 2020; 23.Domench et al., 2019; 24.Errando et al., 2016; 25.Murphy et al., 2011; 26.Todd et al., 2014; 27.Ziemann-Gimmel et al., 2018; 28.Wardhana et al., 2019; 29.Bowdle et al., 2019; 30.Giudici et al., 2021; 31.Kopman et al., 2005; 32.Liang et al., 2013; 33.Viela et al., 2008; 34.Howard et al., 2017

Institutional Review Board approval was not required for this research project.

Dexamethasone and Diabetes: The Current Evidence

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Postoperative Nausea and Vomiting

Patient-feared complication[13]

Affects one-third of the surgical population

Can result in increased[13]:

- Health care costs
- Hospital length of stay
- Hospital re-admission

Apfel Score[13]:

Risk Factors	Risk of PONV
0	10%
1	20%
2	40%
3	60%
≥ 4	80%

Risk Factors[13]:

Female sex · Non-smoker · History of PONV · History of motion sickness · Intraoperative & postoperative opioid use

Diabetes Mellitus (DM)

- **Type 1[6]** → Pancreatic beta cell destruction → Insulin dependence
- **Type 2[6]** → Most prevalent → Disease of insulin-resistance

Dexamethasone

Glucocorticoid Class[12]

- Family of steroid hormones

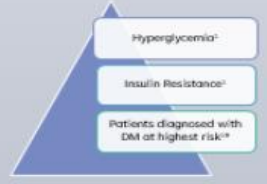
Pharmacology[12]

- Most potent glucocorticoid
- **Onset:** 10-30 minutes
- **Duration of action:** 34-72 hours
- **Typical Adult Dosing:** 4-10 mg IV

Most common uses[12]

- Anti-emetic & anti-inflammatory

Limitations



Anti-emetic[10]:

Research Question

- **P** In adult diabetic patients undergoing general anesthesia,
- **I** does the administration of intraoperative dexamethasone,
- **C** compared to no dexamethasone administration,
- **O** increase blood glucose levels,
- **T** during the first 24-hours of the postoperative period?

Literature Review

- **Texas Medical Center Library Health Research Center**
- **Databases:** PubMed, Medline (OVID), CINAHL
- **MeSH Terms:** "Dexamethasone" and "Diabetes"
- **Key terms:** "postoperative nausea and vomiting", "diabetic hyperglycemia", "intraoperative dexamethasone", "efficacy", and "dose comparison"
- **Boolean operator:** "AND"
- **Snowballing technique**

225 Articles → Filtered for relevance, language, article type, and publication date within 10 years → 17 Total articles

Grades and Levels of Evidence

Agency for Healthcare Research & Quality[2]	United States Preventive Services Task Force[22]
Level 1: Meta-Analysis	**Grade A:** Strongly recommend
Level 2: Experimental	**Grade B:** Moderately recommend
Level 3: Quasi-Experimental	**Grade C:** Recommend selectively
Level 4: Non-Experimental	**Grade C:** Recommend against
Level 5: Case Study/Clinical Expertise	**Grade I:** Insufficient evidence
Level I: 1 **Level II:** 8 **Level III:** 8	**Grade A:** 11 **Grade B:** 5 **Grade I:** 1

Synthesis of Literature

Inclusion Criteria	Exclusion Criteria
≥ 18 years old	< 18 years old
Active diagnosis of diabetes mellitus (DM)	ASA class V
Type-2 DM[1,3-4,11,14,17,18,22]	Receiving preoperative steroid therapy
Receiving treatment for DM[1,11,22]	Received preoperative insulin[4,5,18-19,21]
ASA class I–IV	Multiple dexamethasone doses[4,5,18-19,21]
Undergoing elective surgery	Allergic to dexamethasone
General anesthesia	Undergoing emergent surgery
Postop hospital stay of ≥ 24 hours[5,7,11,13,18,22]	Missing baseline or postoperative values[18]

Study Designs

Dexamethasone Dose:

- 4 mg[4,7,11,17-18,20,24]
- 8 mg[1,3,4,18,20,21]
- 10 mg[5,14,18]
- Not specified[16,23]

Route:

- Intravenous (IV)

Timing of Administration

- Intraoperative period
  - Pre-incision
- Preoperative period[1,3]

Timing of Assessment

- End of surgery
- 24 hours postoperatively

Primary Outcomes

- Incidence of postoperative hyperglycemia
- Postoperative insulin administration
- Low-dose dexamethasone efficacy

Outcome Measurements

- Postoperative serum glucose testing
- Number of units of insulin administered postoperatively[1,3,11,14-16,17-18,22]
- Visual Analogue Scale (nausea)[3,7,11,24,26]

Secondary Outcomes

- Postoperative pain
- PONV
- Postoperative surgical site infection
- Postoperative hospital readmission

Outcome Measurements

- Numerical Rating Scale (NRS) (pain)[11,26]
- Visual Analogue Scale (pain)[3,7,11,24,26]
- Electronic Medical Record[4-5,16]

Findings

When administered to diabetic patients, dexamethasone resulted in:

Postoperative Hyperglycemia:
- Not statistically significant[1,3,11,16-18]
- Statistically significant difference*[4,14,16,18-19,21-22]

Maximum 24-hour postoperative glucose level:
- < 200 mg/dL[14,16,18-19,21-22]
- > 200 mg/dL*[24]

Postoperative Insulin Administration:
- No significant increase in number of units[1,17]
- Significant increase in number of units*[3,14,22]

Low-dose dexamethasone efficacy:
- Prevention of PONV*[4,7,26]
- Decreasing severity of postoperative pain*[7]

Incidence of Hyperglycemia: Lab data
- Elevated baseline HgbA1c*[3,11,15,18,24]
  - 6.5%[11,15,18,24]
  - 6.8%[3]
- Elevated baseline serum glucose levels
  - >180 mg/dL[4,18,24]

Incidence of PONV:*[16,24]
- Decreased additional antiemetic requirements

Severity of Postoperative Pain:*[7, 11,18, 26]
- Improvement in NRS pain scores
- 4 vs. 6 in control[11]

Surgical Site Infections:[16]
- No significant increase in incidence

Hospital Readmissions:[16]
- No significant increase in incidence

4 mg of Dexamethasone Postoperative Findings	8 mg of Dexamethasone Postoperative Findings
Serum glucose increase – 20 mg/dL[18]	Serum glucose increase – 20- 40 mg/dL[16-19]
174 mg/dL maximum serum glucose[18]	191 mg/dL maximum serum glucose[18]
↓ incidence of hyperglycemia*[11,14,18]	Increased incidence of hyperglycemia*[11,16,18]
↓ insulin administration*[3,14,22]	Increased insulin administration*[3,14,22]
4.3 u of insulin[3,14,22]	9.2 u of insulin[3,14,22]

*p < .05

Limitations

- Variability in sample size and dose administered
- Retrospective study designs
- Inconsistent administration of dexamethasone by anesthesia providers
- Emergent cases not studied
- Cardiac and obstetric cases not included

Recommendations for Practice

The benefits of Dexamethasone may outweigh the potential risks

Dexamethasone Dose:

In adult diabetic patients:
- 4 mg administered intravenously
- The dose should be administered intraoperatively, prior to incision

Ideal Patient Population:

- Age ≥ 18 years old
- ASA I – IV
- **If Type-2 diabetic:**
  - Tight preoperative glycemic control
    - *Hemoglobin A_{1c} < 6.5%*
    - *Serum glucose < 180 mg/dL*

Avoid Use In:

- **Preoperative findings:**
  - Hemoglobin A_{1c} : > 6.5 %
  - Serum glucose > 180 mg/dL
- Allergic Hypersensitivity
- Preoperative steroid therapy

Future Research

- Larger sample sizes
- Studies including emergent, type-1 diabetic, cardiac, and obstetric patients
- Dose and administration standardization within the study
- A focus on comparing dexamethasone doses

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1: Abdelmalak et al., 2023; 2: Agency for Healthcare Research and Quality, 2013; 3: Allen et al., 2020; 4: Arumugam et al., 2020; 5: Backes et al., 2013; 6: Bailes, 2002; 7: Barros et al., 2013; 8: Black & Grodzinsky, 2019; 9: Center for Disease Control and Prevention, 2023; 10: Chu et al., 2014; 11: Corcoran et al., 2021; 12: Coutinho & Chapman, 2011; 13: Dimmen et al., 2020; 14: Egan et al., 2019; 15: Godshaw et al., 2019; 16: Harding et al., 2021; 17: Huffman et al., 2023; 18: Low et al., 2015; 19: Mohammed et al., 2020; 20: Peacock, 2019; 21: Purushothaman et al., 2018; 22: Tien et al., 2016; 23: United States Preventive Services Task Force, 2018; 24: Wastie et al., 2021; 25: Wang et al., 2013

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