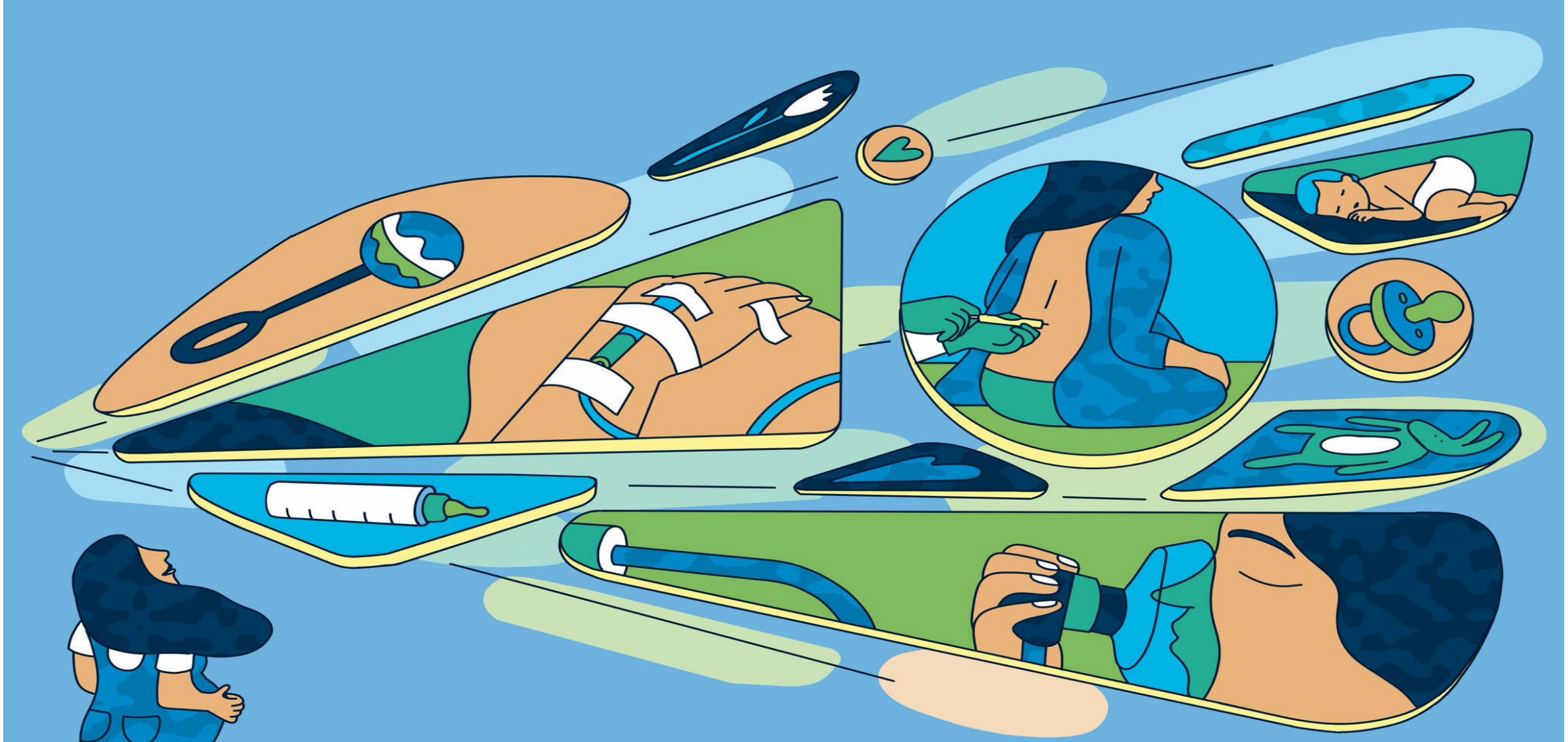
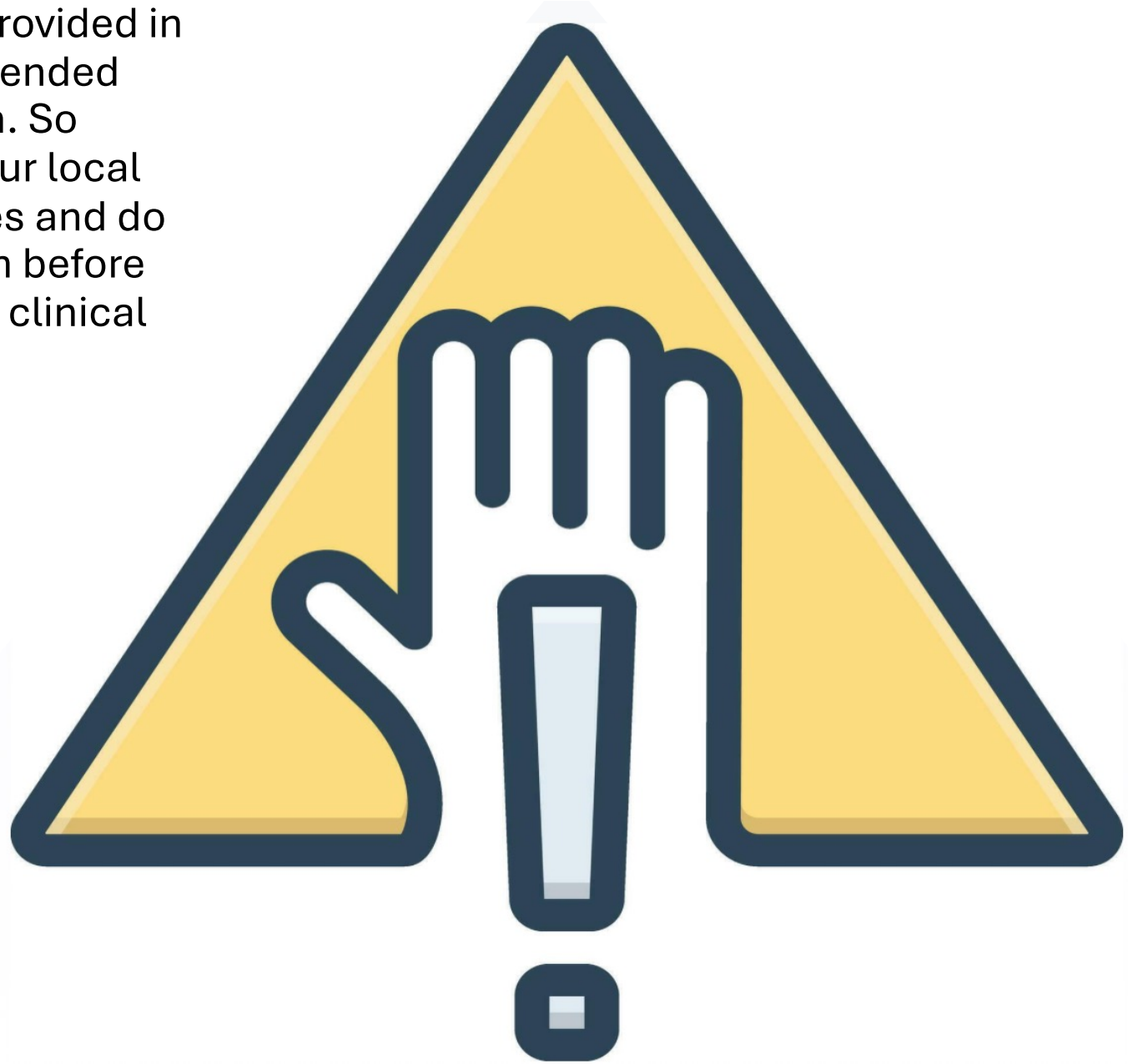


Dexmedetomidine – Magic or Myth

Han Lu (Fellow)

The information provided in this podcast is intended only for education. So please consult your local practice guidelines and do your own research before applying it to your clinical practice.

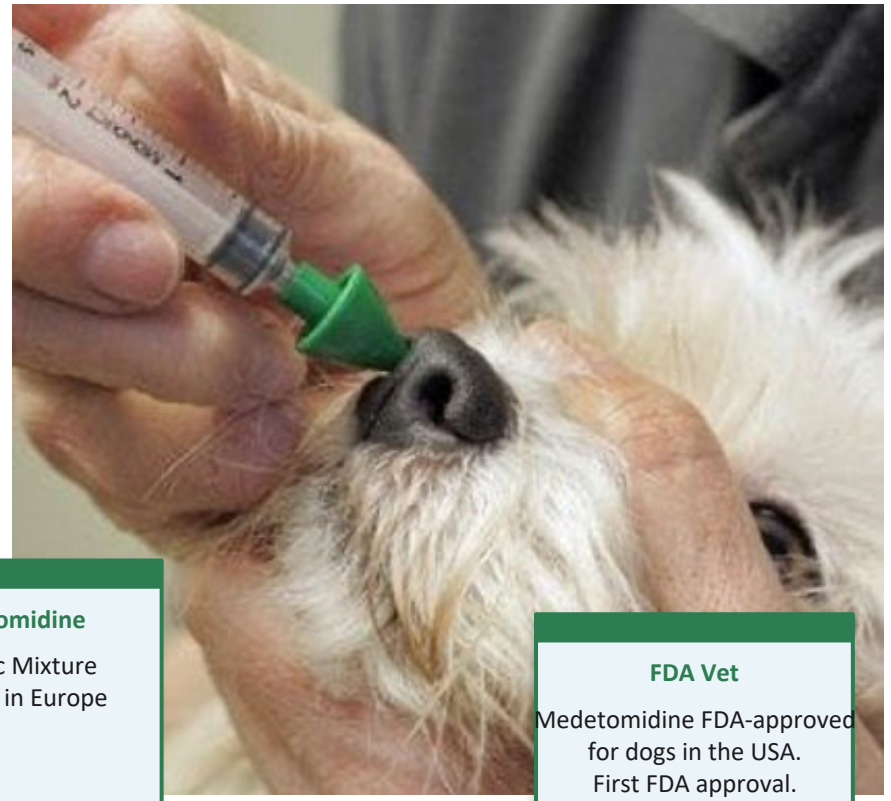


Objective

- History of α2 agonist
- Pharmacology
- Dosing
- Roles / indications
  - Premed
  - Opioid Sparing
    - ERAS
    - Bariatric
  - Post Operative Cognitive Dysfunction (POCD) Reduction
  - Blunting Surgical Stress inflammation
  - Regional anesthesia
  - Obstetric medicine
- Conclusion

VI

VENDREDI – Après la visite Opérations.



1962

Xylazine

1st α2 agonist.
Human antihypertensive.
Too sedating for people
Vets adopted

1966

Clonidine

1st human α2 agonist.
Approved for hypertension.

1981

Mechanism

α2 mechanism elucidated

1986

Discovery

Finland isolates
dexmedetomidine
α2: α1 = 1620:1

1987

Medetomidine

Racemic Mixture
launched in Europe

1988

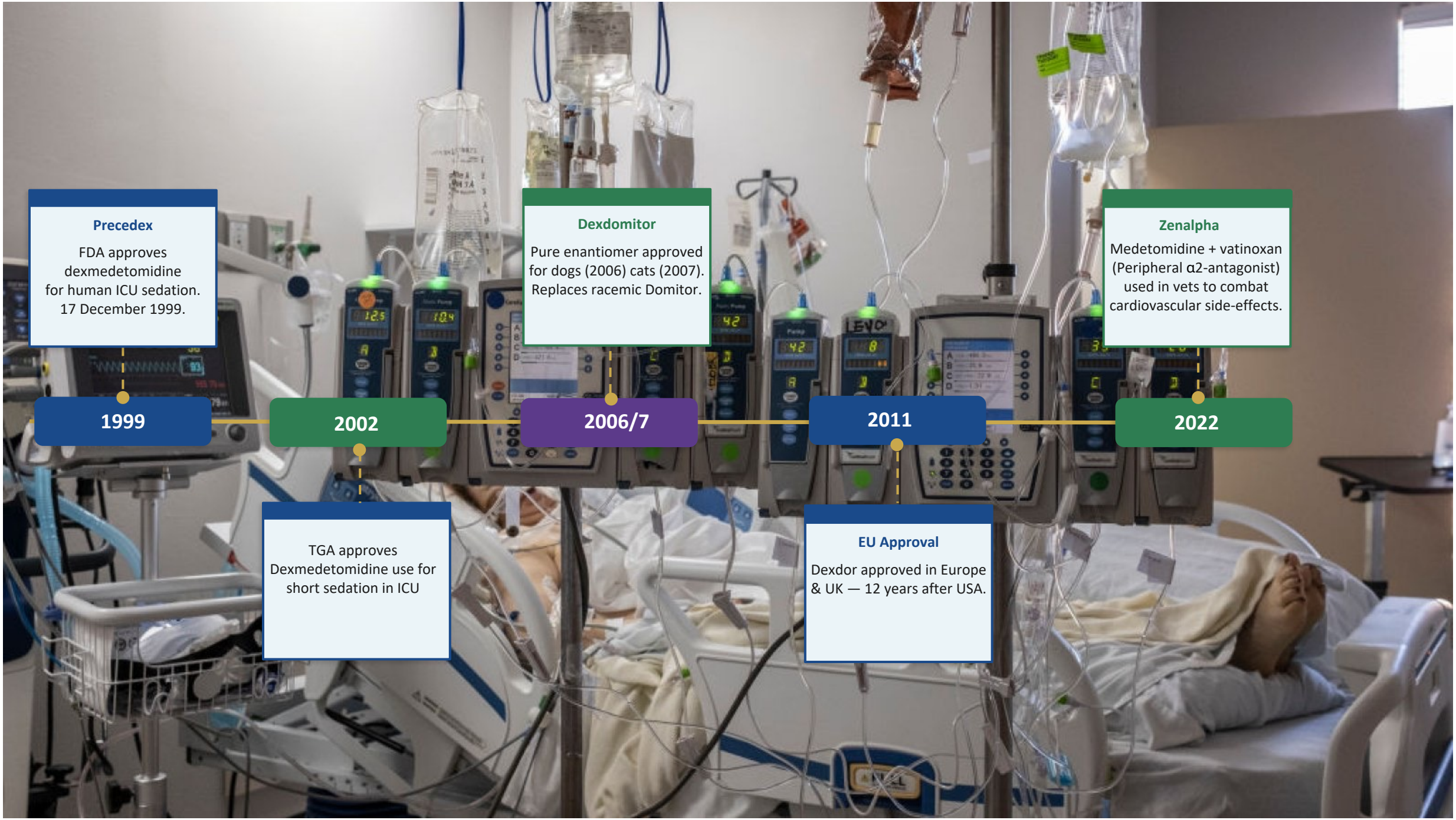
Segal & Maze

Standord
Dexmedetomidine
enantiomer
reduces halothane MAC.
Levomedetomidine = inactive.

1996

FDA Vet

Medetomidine FDA-approved
for dogs in the USA.
First FDA approval.


Precedex
FDA approves dexmedetomidine for human ICU sedation. 17 December 1999.
1999
2002
TGA approves Dexmedetomidine use for short sedation in ICU
Dexdomitor
Pure enantiomer approved for dogs (2006) cats (2007). Replaces racemic Domitor.
2006/7
2011
EU Approval
Dexdor approved in Europe & UK — 12 years after USA.
Zenalpha
Medetomidine + vatinoxan (Peripheral α2-antagonist) used in vets to combat cardiovascular side-effects.
2022


Pharmacology

- Dexmedetomidine: active S-Enantionmer of Medetomidine

- Central α2 agonists

- α2:α1 ratio
  - Clonidine 200:1
  - Dexmedetomidine 1620:1

- Centrally
  - α2 in presynaptic membrane of noradrenergic neurons
  - Agonism -> inhibition of noradrenaline release

- Peripheral
  - α2 agonism causes vasoconstriction

- Sedation / Anxiolysis
  - α2 agonism - locus coeruleus of the pons causing dose-dependent inhibition of norepinephrine release
  - Preserved muscle tone + ventilation
  - Awakening to external stimuli -> patients are cooperative and can obey simple instructions.
  - (EEG shows dexmedetomidine mimic stage 2 NREM sleep)

- Analgesia
  - Likely by modulating descending pain pathways
  - Spinal cord - α2-receptors agonism in substantia gelatinosa of the dorsal horn causes interneuron hyperpolarisation and reduces release of nociceptive neurotransmitters (Substance P / glutamate)

- Cardiovascular
  - Biphasic response
  - HTN -> α2β receptors on vascular smooth muscle
  - Hypotension + Bradycardia -> centrally mediated inhibition of SNS outflow

- Respiratory
  - Minimal ventilation effect -> case reports even with 10x maximum dose.
  - MRI studies have shown airway remain patent

CNS

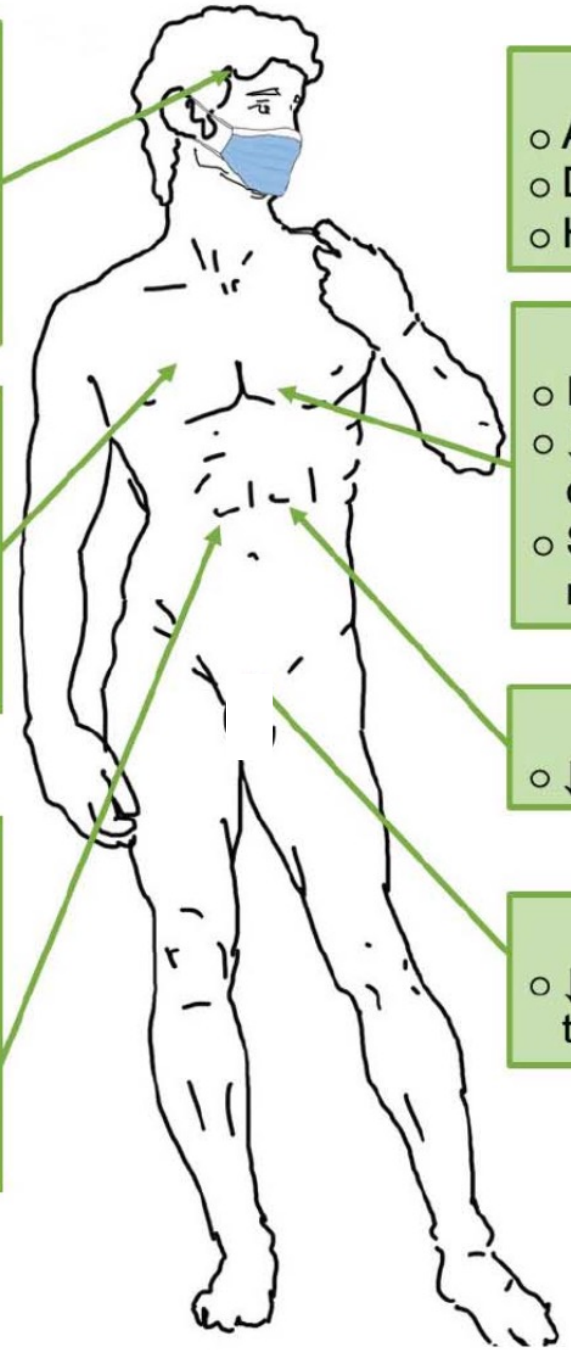
- Rousable sedation resembling natural sleep, with preserved muscle tone and ventilation
- Analgesia
- ↓ cerebral blood flow and $CMRO_2$

Respiratory

- Minimal change in ventilatory function
- Mild ↑ RR
- Mild ↓ tidal volume
- Maintained hypercapnic drive and airway reflexes

Endocrine

- Theoretical risk of adrenal suppression due to imidazole structure (not clinically significant)
- ↓ renin release
- ↓ insulin release (not clinically significant)



Other

- Anti-sialogogue
- Decongestant
- Hyperthermia

Cardiovascular

- Initial ↑ BP and ↓ HR , followed by ↓BP
- ↓ cardiac output (due to ↓ HR, no effect on SV)
- Severe bradycardia and asystole reported

GI

- ↓ bowel motility

Renal

- ↓ ADH activity on the distal convoluted tubule causing diuresis

- **Bioavailability**
  - 16% PO
  - 65% Nasally
  - 82% Buccally

- Readily crosses BBB to exert central CNS effects.
- Readily crosses the placenta

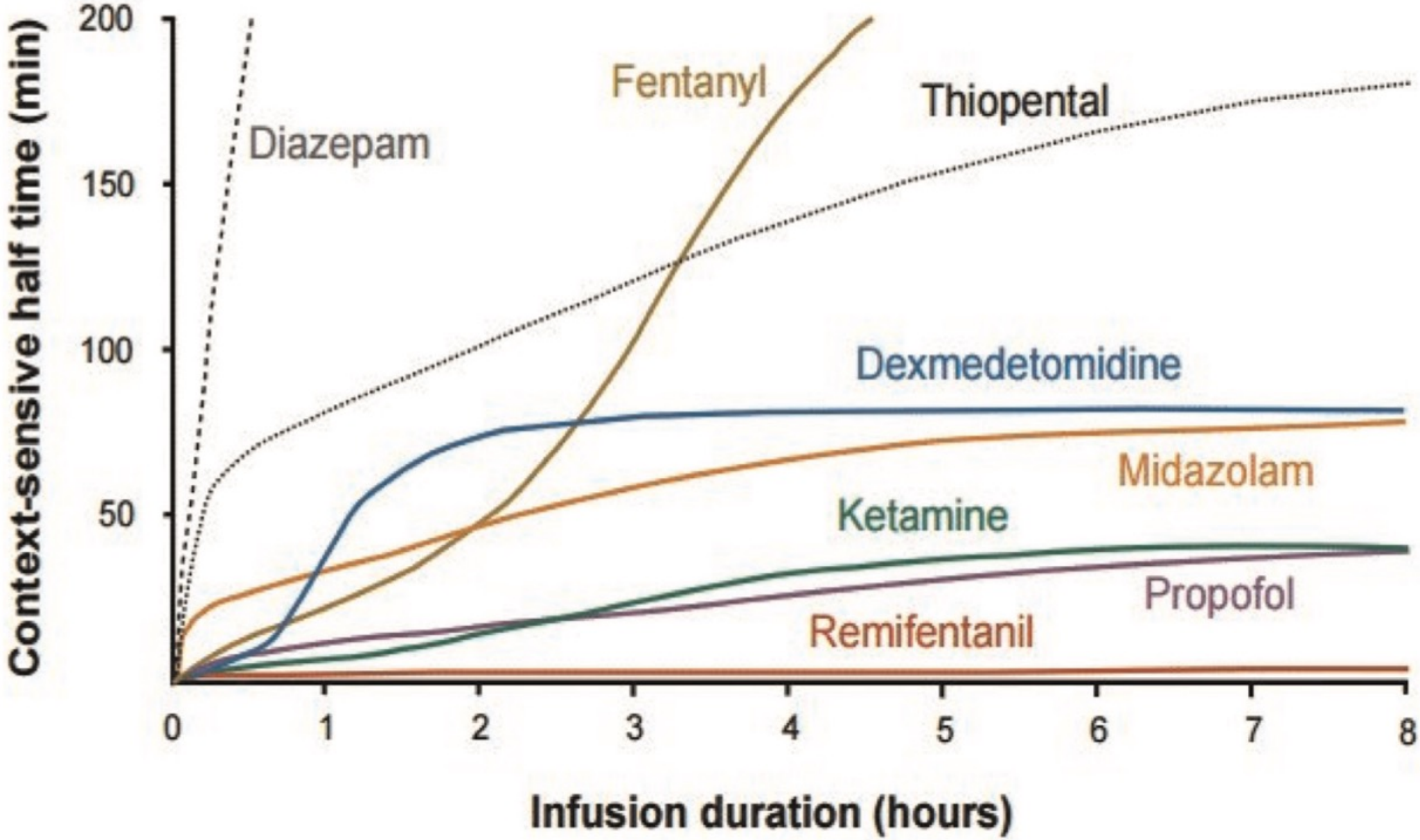
- T1/2 α – 6 min
- T1/2β
  - Clonidine 9 – 18 hours
  - Dexmedetomidine 2 hours

- **Protein binding** - 94%

- Metabolism – Hepatic glucuronidation, hydroxylation, and N-methylation to inactive metabolites

- **<u>Dose reduction in hepatic disease due to decreased protein / metabolism</u>**

- **Excretion** – Renal – **<u>No adjustment in renal failure</u>**


Context-sensitive half time (min)
200
150
100
50
0
1
2
3
4
5
6
7
8
Infusion duration (hours)
Diazepam
Fentanyl
Thiopental
Dexmedetomidine
Midazolam
Ketamine
Propofol
Remifentanil

Dosing

- Loading
  - Up to 1 mcg/kg over 10 min (LBW)
  - Reduce to 0.5 mcg/kg over 10 min (LBW) for >65 yo + less invasive procedures (e.g. ophthalmic)
- Infusion
  - 0.6 mcg/kg/hr titrated to the clinical effect -> 0.2 - 1.0 mcg/kg/hr

- No guideline for cessation. Longer cases cease at least > 30 minutes before extubation
- Discontinuation Syndrome
  - Clonidine: rebound agitation / hypertension / tachycardia after prolonged clonidine infusion
  - Dexmedetomidine: Occasionally reported

- Contraindications
  - Uncontrolled Hypotension
  - 2^{nd} / 3^{rd} Heart Block
  - Acute cerebrovascular conditions – Decreased CBF (but in some studies flow-metabolism coupling seems maintained)

Anaesthesia for Patients Living with Obesity

Society for Obesity and Bariatric Anaesthesia

Pre-operative Evaluation

Red Flags

- Poor functional capacity
- Abnormal ECG
- Uncontrolled BP, CCF or IHD
- SpO_2 <94% on air
- If bicarbonate >27, OHS likely
- Previous DVT/PE
- STOP-BANG ≥ 5
- OS-MRS >3
- Metabolic Syndrome

Yes →

Consider:

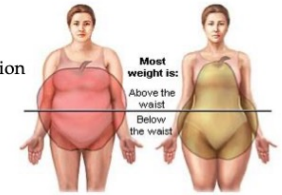
- Preoperative CPAP
- Blood Gases / Sleep Studies
- Echocardiogram
- Cardiorespiratory referral
- Experienced Anaesthetist
- Book HDU Bed

No →

- May be suitable for day-case surgery

Central Obesity
(waist > half height)

- Difficult airway/ventilation more likely
- Greater risk of CVS disease/thrombosis
- Higher risk of metabolic syndrome



Peripheral Obesity
(Fat outside body cavity)

- Less co-morbidity
- Lower risk

OS-MRS Calculator

tools.farmacologiaclinica.info

SOBA App

https://apps.apple.com/gb/app/soba-uk-app/id1549542383

STOPBANG Calculator

www.stopbang.ca

Intra-operative Management

Airway Equipment:

- Device or equipment for ramping
- Step for anaesthetist
- Difficult airway equipment
- Videolaryngoscope

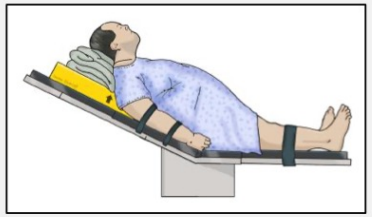
Theatre Equipment:

- Suitable bed/trolley and operating table
- Gel padding
- Wide strapping and foot plates
- Table extensions/arm boards
- Hover mattress or equivalent
- Appropriately sized calf compression devices
- Sufficient staff to move patient

Other Anaesthesia Equipment:

- Ventilator capable of PEEP & pressure modes
- Long spinal, regional and vascular needles
- Ultrasound machine
- Forearm cuff or large BP cuff
- Depth of anaesthesia monitoring (EEG/BIS)
- Neuromuscular monitoring

Ramping



- Tragus level with sternum
- Reduces risk of difficult laryngoscopy
- Improves ventilation and pre-oxygenation

Induction:

- Self-position on operating table
- Consider premed antacid & analgesia
- Consider CPAP and/or HFNO
- Preoxygenate and intubate in ramped/sitting position
- Tracheal intubation recommended
- Caution with SAD in BMI >40
- Minimal induction to ventilation time

Intra-Op:

- DVT prophylaxis
- Commence maintenance promptly
- Increased risk of visceral injury when prone
- Avoid spontaneous ventilation, use PEEP
- Use short-acting inhalationals or TIVA
- Short-acting opioids & multimodal analgesia
- Think pressure areas

Extubation:

- Ensure full NMB reversal
- Extubate and recover sitting up

Lean Body Weight: This exceeds ideal body weight in patients with obesity and plateaus at:

- ≈100kg for a man
- ≈70kg for a woman

Ideal Body Weight: Broca formula

- Men: height (in cm) - 100
- Women: height (in cm) - 105

Adjusted Body Weight: Ideal plus 40% extra

If in doubt, titrate and monitor effect*

Suggested dosing for anaesthetic drugs

Lean Body Weight	Adjusted Body Weight	Total Body Weight
•Propofol induction •Thiopentone •Fentanyl and Alfentanil •Morphine •Non-depolarising NMBDs •Paracetamol •Local Anaesthetics	•Propofol Infusion •Neostigmine (max 5mg) •Sugammadex (read pack insert) •Antibiotics	•Suxamethonium •LMWHs (titrate dose with Xa levels)

Single Agent GA

- Dexmedetomidine only GA has been reported…
- 5–10 mcg/kg/hr to be adequately anaesthetised

- Two cases
  - Laser ablation of a tracheal stenosis
  - Tracheal debridement + stenting and bronchopulmonary lavage
- One patient required a chin lift, but maintained ventilation / airway patency.
- ??No haemodynamic compromise in this small group of patients.

ANZCA
FPM

Question 15 **Pass Rate: 49.7%**

At the end of a case under general anaesthesia, you inadvertently administer 200 mcg of dexmedetomidine instead of 200 mg sugammadex intravenously.

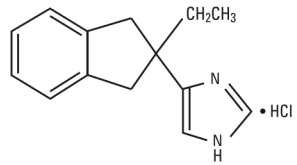
a) Describe your immediate clinical management of the consequences of this drug error. (50%)
b) Outline measures used to minimise the risk of look-alike, sound-alike (LASA) medication errors. (50%)

ANTISEDAN®
(atipamezole hydrochloride)

Sterile Injectable Solution - 5.0 mg/mL
Dexmedetomidine and Medetomidine Reversing Agent
For intramuscular use in dogs only

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: ANTISEDAN (atipamezole hydrochloride) is a synthetic α_2-adrenergic antagonist.
The chemical name is 4-(2-ethyl-2,3-dihydro-1H-inden-2-yl)-1H-imidazole hydrochloride.
The molecular formula is $C_{14}H_{16}N_2 \bullet HCl$ and structural formula is:



Each mL of ANTISEDAN contains 5.0 mg atipamezole hydrochloride, 1.0 mg methylparaben (NF), 8.5 mg sodium chloride (USP), and water for injection (USP).

INDICATIONS: ANTISEDAN is indicated for the reversal of the sedative and analgesic effects of DEXDOMITOR (dexmedetomidine hydrochloride), and DOMITOR (medetomidine hydrochloride) in dogs.

DOSAGE AND ADMINISTRATION: ANTISEDAN is administered intramuscularly (IM) for reversal of sedation and analgesia regardless of the route used for DEXDOMITOR or DOMITOR. The atipamezole dose for the reversal of IV DEXDOMITOR or DOMITOR is 3750 mcg/m^2. The atipamezole dose for the reversal of IM DEXDOMITOR or DOMITOR is 5000 mcg/m^2.

The dosage of ANTISEDAN is calculated based on body surface area. Use the following tables to determine the correct injection volume or the correct ANTISEDAN dosage on the basis of kilograms of body weight.

Note that the mcg/kg dosage decreases as body weight increases.

Table 1: Atipamezole dosing for reversal of IV dexmedetomidine- or medetomidine-induced sedation/analgesia:

Dose table for ANTISEDAN (3750 mcg/m^2) when dexmedetomidine or medetomidine is given IV			
For # lbs	**For # kg**	**dose = mcg/kg**	**volume = mL ANTISEDAN**
4-7	2-3	300	0.1
7-9	3-4	250	0.15
9-11	4-5	230	0.2
11-22	5-10	200	0.3
22-33	10-15	170	0.4
33-44	15-20	150	0.5
44-55	20-25	140	0.6
55-66	25-30	130	0.7
66-81	30-37	120	0.8
81-99	37-45	110	0.9
99-110	45-50	105	1.0
110-132	50-60	100	1.1
132-143	60-65	95	1.2
143-165	65-75	93	1.3
165-176	75-80	91	1.4
>176	>80	90	1.5

Table 2: Atipamezole dosing for reversal of IM dexmedetomidine- or medetomidine-induced sedation/analgesia:

Dose table for ANTISEDAN (5000 mcg/m^2) when dexmedetomidine or medetomidine is given IM			
For # lbs	**For # kg**	**dose = mcg/kg**	**volume = mL ANTISEDAN**
4-7	2-3	400	0.15

PRECAUTIONS:

1. Handling: ANTISEDAN can produce an abrupt reversal of sedation; therefore, dogs that have recently received ANTISEDAN should be handled with caution. The potential for apprehensive or aggressive behavior should be considered in the handling of dogs emerging from sedation, especially in dogs predisposed to nervousness or fright. Also, avoid situations where a dog might fall.

2. Sedation relapse: While atipamezole does reverse the clinical signs associated with medetomidine or dexmedetomidine sedation, complete physiologic return to pretreatment status may not be immediate or may be temporary, and dogs should be monitored for sedation relapse. Sedation relapse is more likely to occur in dogs that receive an alpha$_2$-agonist by the IV route, compared to dogs that are sedated using the IM route. Animals should be monitored closely for persistent hypothermia, bradycardia, and depressed respiration, until signs of recovery persist.

3. Analgesia reversal: Atipamezole reverses analgesic effects as well as sedative effects. Additional procedures for the control of pain may be required.

4. Debilitated dogs: The safety of atipamezole has not been evaluated in dogs with compromised health. Geriatric, debilitated, and ill dogs are more likely to experience adverse reactions associated with the administration of alpha$_2$-antagonists (as well as alpha$_2$-agonists). Dogs with abnormalities associated with the cardiovascular system are especially at risk.

5. Breeding dogs: ANTISEDAN has not been evaluated in breeding dogs; therefore, the drug is not recommended for use in pregnant or lactating dogs, or in dogs intended for breeding.

6. Minimum age and weight: ANTISEDAN has not been evaluated in dogs less than four months of age or in dogs weighing less than 4.4 lbs (2 kg).

ADVERSE REACTIONS: Occasional vomiting may occur. At times, a period of excitement or apprehensiveness may be seen in dogs treated with atipamezole. Other effects of atipamezole include hypersalivation, diarrhea, and tremors.

CLINICAL PHARMACOLOGY: Atipamezole is a potent alpha$_2$-antagonist which selectively and competitively inhibits alpha$_2$-adrenergic receptors. The result of atipamezole administration in the dog is the rapid recovery from the sedative and analgesic effects produced by the alpha$_2$-adrenergic agonists dexmedetomidine or medetomidine. Atipamezole does not reverse the effects of other classes of sedatives, anesthetics, or analgesics.

Atipamezole is rapidly absorbed following intramuscular injection; maximum serum concentration is reached in approximately 10 minutes. Onset of arousal is usually apparent within 5 to 10 minutes of injection, depending on the depth and duration of dexmedetomidine- or medetomidine-induced sedation. Elimination half-life from serum is less than 3 hours. Atipamezole undergoes extensive hepatic biotransformation, with excretion of metabolites primarily in urine.

Dexmedetomidine or medetomidine activation of peripheral and central alpha$_2$-adrenergic receptors induces a pattern of pharmacological responses that include sedation, reduction of anxiety, analgesia, and bradycardia.

Blood pressure is initially increased due to peripheral vasoconstriction and thereafter drops to normal or slightly below normal levels.

A transient, decrease in systolic blood pressure occurs immediately after administration of atipamezole to dexmedetomidine- or medetomidine-sedated dogs, followed by a transient increase in arterial pressure within 10 minutes compared to pre-atipamezole levels. This is the opposite of the response to alpha$_2$-agonist treatment, and is probably due to atipamezole-induced peripheral vasodilation.

Atipamezole administration rapidly abolishes dexmedetomidine- or medetomidine-induced bradycardia, usually within 3 minutes. The magnitude of the effect of atipamezole on heart rate is greater when dexmedetomidine is administered intravenously compared to intramuscularly. Dogs receiving medetomidine or IM dexmedetomidine may not return to pre-sedative heart rates after atipamezole administration and some dogs briefly show heart rate elevations above baseline. Respiratory rate increases following atipamezole injection.

EFFECTIVENESS: One hundred and nine dogs received atipamezole in the field study (55 dogs received the reversal agent following dexmedetomidine; 54 following medetomidine). The mean age was 5.9 years and ranged between 17 weeks and 16 years. The mean weight was 45.5 lbs (20.7 kg), ranging from 4.8 lbs to 117 lbs (2.2 kg to 53.2 kg). Atipamezole was administered by the IM route of administration, within a range of 39-57 minutes after administration of either dexmedetomidine (IV and IM) or medetomidine (IV and IM).

Atipamezole reversed the effects of dexmedetomidine and medetomidine in all cases. In dexmedetomidine treated dogs, the onset of reversal was evident within 5 minutes after administration of atipamezole (57% could stand). Within 15 minutes, 96% of dexmedetomidine treated dogs were standing, 92% responded normally to sound, 86% had a normal muscle tone of jaw, and >90% had a normal pedal reflex response. Responses in dogs treated with medetomidine were similar or slightly later.

Following atipamezole, heart rate increased between 0 and 5 minutes following either alpha$_2$-agonist (IV dexmedetomidine dogs had heart rates from 60 to 85 bpm, and IV medetomidine dogs from 51 to 67 bpm; IM dexmedetomidine dogs had heart rates from 45 to 73 bpm, and IM medetomidine dogs from 52 to 79 bpm). Bradycardia resolved more slowly in the IM treatment groups. The body temperature remained at the same level during the 120 minutes of follow-up after atipamezole administration. Respiratory rates increased toward normal between 0 and 5 minutes after the administration of atipamezole in all treatment groups. Mucous membranes were described as normal after 5 minutes in 91% of dexmedetomidine dogs (IV or IM). By 120 minutes, 96% were normal (after IV dexmedetomidine)

- Premed

- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia

- Post Operative Cognitive Dysfunction (POCD) Reduction

- Blunting Surgical Stress inflammation

- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks

- Post Neuraxial Shivering

- ?PDPH treatment

- **Premed**

- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia

- Post Operative Cognitive Dysfunction (POCD) Reduction

- Blunting Surgical Stress inflammation

- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks

- Post Neuraxial Shivering

- ?PDPH treatment

- Premed
  - Anxiolytic
  - Sedative
  - Sympatholytic
  - Antisialagogue
  - Lack of respiratory depression

- Paediatric - Nasal
  - 30-60 min prior to induction or procedure
  - 3 – 4 mcg /kg (max 200 mcg) (IBW)

Intramuscular route

General anesthesia; Adjunct

1) Off-Label Dosage

a) Dosage: 0.5 to 1.5 mcg/kg IM 60 minutes prior to anesthesia induction [53][54]

b) Dosage (cataract surgery): 1 mcg/kg IM; providing lowering of intraocular pressure, yet without interfering with the patient's ability to cooperate (Virkkila et al, 1993). However, prolonged sedation has occurred and the IM route may not always be suitable for shorter surgical procedures [53][54].

- Premed

- **Opioid Sparing**
  - **ERAS**
  - **Bariatric**
  - **Neuroanaesthesia**

- Post Operative Cognitive Dysfunction (POCD) Reduction

- Blunting Surgical Stress inflammation

- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks

- Post Neuraxial Shivering

- ?PDPH treatment

Gynecologic Oncology 210 (2026) 153–173

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Enhanced recovery after surgery (ERAS®) society guidelines for gynecologic oncology: 2026 update☆

Gregg Nelson [a,b,*], Alon D. Altman [c], Amy Metcalfe [d], Christina Fotopoulou [e], Jolyn Taylor [f], Gretchen Glaser [g], Jamie Bakkum-Gamez [g], Amanika Kumar [g], Larissa A. Meyer [f], Rebecca Stone [h], Gabriel Mena [i], Kevin M. Elias [j], Steven P. Bisch [a], Oliver Zivanovic [k], Ester Miralpeix [l], Geetu Bhandoria [m], Ane Gerda Zahl Eriksson [n], Shannon M. Ruzycki [o], Pervez Sultan [p], Khara M. Sauro [q], Lindsay Blake [r], Mary E. Brindle [b,s], Pedro T. Ramirez [t,†], Sean C. Dowdy [g,†]

[a] Department of Obstetrics & Gynecology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[b] Ariadne Labs, Brigham and Women's Hospital, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[c] Department of Obstetrics, Gynecology and Reproductive Sciences, University of Manitoba, Winnipeg, Manitoba, Canada
[d] Departments of Obstetrics and Gynecology, Medicine, and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada
[e] Department of Surgery and Cancer, Faculty of Medicine, Imperial College London, London, UK
[f] Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
[g] Division of Gynecologic Oncology, Mayo Clinic College of Medicine, Rochester, MN, USA
[h] Department of Gynecology and Obstetrics, Johns Hopkins School of Medicine, Baltimore, MD, USA
[i] Department of Anesthesiology, Critical Care and Pain Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
[j] Section of Gynecologic Oncology, Obstetrics and Gynecology Institute, Cleveland Clinic Foundation, Cleveland, OH, USA
[k] Heidelberg University Hospital, Department of Obstetrics and Gynecology, Heidelberg, Germany
[l] Department of Obstetrics and Gynecology, Gynecological Cancer Multidisciplinary Unit, Hospital del Mar Research Institute, Barcelona, Spain
[m] Department of Gynecologic Oncology, Command Hospital, Kolkata, India
[n] Department of Gynaecological Oncology, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway
[o] Departments of Medicine, and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada
[p] Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, CA, USA
[q] Departments of Surgery, Community Health Sciences, Oncology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[r] UAMS Library, University of Arkansas for Medical Sciences, Little Rock, AR, USA
[s] Department of Surgery, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[t] Department of Obstetrics and Gynecology, Houston Methodist Hospital, Houston, TX, USA

HIGHLIGHTS

- The third updated review of the ERAS® Society gynecologic oncology guidelines is presented.
- This guideline will help integrate knowledge into practice and align perioperative care globally.
- ERAS teams are encouraged to adopt these recommendations and standardize perioperative pathways where possible.

3.9. Standard anesthetic protocol

Anesthetic management in gynecologic oncologic surgery should be standardized to minimize physiological disturbances, mitigate the surgical stress response, incorporate multimodal opioid-sparing analgesia, promote functional recovery, and reduce length of stay [7]. Short-acting anesthetics, multimodal analgesia, opioid-sparing strategies such as regional anesthesia, lung-protective ventilation, maintenance of normothermia, and optimal fluid management aimed at a zero-balance or goal-directed fluid therapy using hemodynamic monitoring tools to track real-time dynamic indices and trends of flow and perfusion are recommended when feasible, especially for open or lengthy procedures in high-risk patients [172,173].

Intraoperative multimodal analgesia with acetaminophen and nonsteroidal anti-inflammatory drugs, gabapentinoids, and selective intravenous adjuncts such as low-dose ketamine, dexmedetomidine, or magnesium aims to minimize perioperative opioid consumption [174]. A recent meta-analysis of major abdominal cancer surgery showed that intravenous lidocaine infusion improved postoperative pain control, reduced opioid requirements, and enhanced gastrointestinal recovery [175].

Regional anesthesia remains a vital component of enhanced recovery after surgery (ERAS) pathways. Recent evidence suggests that the benefits of the transversus abdominis plane (TAP) block may be more limited than previously believed [176,177]. Disadvantages of the TAP block include its ineffectiveness for visceral pain and the need for a bilateral block for midline incisions [176]. A recent meta-analysis

BJA

British Journal of Anaesthesia, 133 (3): 615–627 (2024)

doi: 10.1016/j.bja.2024.06.007
Advance Access Publication Date: 16 July 2024
Review Article

QUALITY AND PATIENT SAFETY

Effectiveness of dexmedetomidine on patient-centred outcomes in surgical patients: a systematic review and Bayesian meta-analysis

Michael Verret[1,2,3,4,5,6,*], John B. P. Le[1,7], Manoj M. Lalu[1,2,5], Matthew S. Jeffers[1], Daniel I. McIsaac[1,2,5], Stuart G. Nicholls[1,5,8], Alexis F. Turgeon[3,4], Rashi Ramchandani[7,9], Hongda Li[10], Brian Hutton[1,5], Fiona Zivkovic[11], Megan Graham[11], Maxime Lê[11], Allison Geist[11], Mélanie Bérubé[3,6,12], Katie O'Hearn[13], Ian Gilron[14], Patricia Poulin[15], Helena Daudt[16], Guillaume Martel[1,17], Jason McVicar[1,18], Husein Moloo[1] and Dean A. Fergusson[1,5,7,17,19]

scale, the Quality of Recovery-15 (QoR-15) instrument was used (range 0–150 points, minimally important difference [MID] of 6 points).

Results: We identified 49,069 citations, from which 44 RCTs involving 5904 participants were eligible. Intraoperative dexmedetomidine administration was associated with improvement in postoperative QoR-15 (mean difference 9, 95% CrI 4–14, *n*=21 RCTs, moderate certainty of evidence). We found 99% probability of any benefit and 88% probability of achieving the MID. There was a reduction in chronic pain incidence (odds ratio [OR] 0.42, 95% CrI 0.19–0.79, *n*=7 RCTs, low certainty of evidence). There was also increased risk of clinically significant hypotension (OR 1.98, 95% CrI 0.84–3.92, posterior probability of harm 94%, *n*=8 RCTs) and clinically significant bradycardia (OR 1.74, 95% CrI 0.93–3.34, posterior probability of harm 95%, *n*=10 RCTs), with very low certainty of evidence for both. There was limited evidence to inform other secondary patient-centred outcomes.

Conclusions: Compared with placebo or standard of care, intraoperative dexmedetomidine likely results in meaningful improvement in the quality of recovery and chronic pain after surgery. However, it might increase clinically important bradycardia and hypotension.

Systematic Review Protocol: PROSPERO (CRD42023439896).

BMC Anesthesiology

RESEARCH Open Access

Application of opioid-free general anesthesia for gynecological laparoscopic surgery under ERAS protocol: a non-inferiority randomized controlled trial

Liang Chen[1,2], Wensheng He[2], Xue Liu[2], Fahui Lv[3] and Yuanhai Li[1*]

Abstract

Background Enhanced recovery after surgery (ERAS) is now widely used in various surgical fields including gynecological laparoscopic surgery, but the advantages of opioid-free anesthesia (OFA) in gynecological laparoscopic surgery under ERAS protocol are inexact.

Aims This study aims to assess the effectiveness and feasibility of OFA technique versus traditional opioid-based anesthesia (OA) technique in gynecological laparoscopic surgery under ERAS.

Methods Adult female patients aged 18 ~ 65 years old undergoing gynecological laparoscopic surgery were randomly divided into OFA group (Group OFA, $n = 39$) with esketamine and dexmedetomidine or OA group (Group OA, $n = 38$) with sufentanil and remifentanil. All patients adopted ERAS protocol. The primary outcome was the area under the curve (AUC) of Visual Analogue Scale (VAS) scores (AUC_{VAS}) postoperatively. Secondary outcomes included intraoperative hemodynamic variables, awakening and orientation recovery times, number of postoperative rescue analgesia required, incidence of postoperative nausea and vomiting (PONV) and Pittsburgh Sleep Quality Index (PSQI) perioperatively.

Results AUC_{VAS} was (Group OFA, 16.72 ± 2.50) vs (Group OA, 15.99 ± 2.72) ($p = 0.223$). No difference was found in the number of rescue analgesia required ($p = 0.352$). There were no between-group differences in mean arterial pressure (MAP) and heart rate (HR) ($p = 0.211$ and 0.659, respectively) except MAP at time of surgical incision immediately [(Group OFA, 84.38 ± 11.08) vs. (Group OA, 79.00 ± 8.92), $p = 0.022$]. Times of awakening and orientation recovery in group OFA (14.54 ± 4.22 and 20.69 ± 4.92, respectively) were both longer than which in group OA (12.63 ± 3.59 and 18.45 ± 4.08, respectively) ($p = 0.036$ and 0.033, respectively). The incidence of PONV in group OFA (10.1%) was lower than that in group OA (28.9%) significantly ($p = 0.027$). The postoperative PSQI was lower than the preoperative one in group OFA ($p = 0.013$).

Conclusion In gynecological laparoscopic surgery under ERAS protocol, OFA technique is non-inferior to OA technique in analgesic effect and intraoperative anesthesia stability. Although awakening and orientation recovery times were prolonged compared to OA, OFA had lower incidence of PONV and improved postoperative sleep quality.

Trial registration ChiCTR2100052761, 05/11/2021.

Contents lists available at ScienceDirect

Anaesthesia Critical Care & Pain Medicine

journal homepage: www.elsevier.com

Original Article

Opioid free *versus* opioid sparing strategies for multimodal antinociception during laparoscopic colectomy: a randomised controlled trial

Vincent Collange [a], Jean Baptiste Berruet [a], Frederic Aubrun [a], Marie Poiblanc [a], Eric Olagne [b], Nadège Golliet Mercier [c], Sebastien Parent [d], Philippe Noel [a], Simon Devillez [a], Maya Perrou [b], Joanna Ramadan [e], Sean Coeckelenbergh [e,f], Alexandre Joosten [g,*]

[a] Department of Anesthesiology, Medipole Villeurbanne Hospital, Villeurbanne, France
[b] Department of Anesthesiology, Hopital de la Croix Rousse, Lyon, France
[c] Department of Abdominal Surgery, Medipole Villeurbanne Hospital, Villeurbanne, France
[d] Department of Clinical Research, Medipole Villeurbanne Hospital, Villeurbanne, France
[e] Department of Anaesthesiology and Intensive Care, Paris-Saclay University, Paul Brousse Hospital, Assistance Publique Hôpitaux de Paris, Villejuif, France
[f] Outcomes Research Consortium, Cleveland, OH, United States
[g] Department of Anesthesiology and Perioperative Medicine, David Geffen School of Medicine, University of California Los Angeles, California, United States

ARTICLE INFO

Article history:
Available online 9 October 2024

Keywords:
ERAS
Hypoxemia
Nausea
Vomiting
Pain
Nociception
Sufentanil
Dexmedetomidine

ABSTRACT

Background: It remains unclear whether opioid-free anesthesia (OFA), when compared to opioid-sparing anesthesia (OSA), reduces postoperative opioid consumption while still providing adequate pain control. We thus tested the hypothesis that patients having an OFA strategy during laparoscopic colectomy would require less postoperative opioids when compared to an OSA strategy.

Methods: This single-center, prospective randomized controlled superiority trial, randomly allocated consecutive patients undergoing laparoscopic colectomy to receive either sevoflurane-dexmedetomidine anesthesia with a continuous infusion of lidocaine and ketamine (OFA group) or sevoflurane-sufentanil boluses anesthesia with a continuous infusion of lidocaine (OSA group). Both groups received multimodal antinociception with boluses of dexamethasone, lidocaine, and ketamine during anesthesia induction, as well as acetaminophen, ketoprofen, and nefopam before the end of the surgery. OFA patients also received a dose of magnesium sulfate during induction. The primary outcome was cumulative opioid consumption at 48 h after surgery, expressed in oral morphine equivalents (OME). Secondary exploratory outcomes were pain scores, opioid-related adverse events, and patient quality of life (WHODAS score).

Results: Of the 160 randomized patients, 155 were included in a modified intention-to-treat analysis. Median [Q1–Q3] OME consumption at 48 h after surgery did not differ between groups (9 [0–30] mg for OFA *vs.* 14 [0–30] mg for OSA; $p = 0.861$). Key secondary outcomes were not different between groups except a three time higher incidence of bradycardia in the OFA group.

Conclusions: In patients undergoing laparoscopic colectomy with a multimodal antinociception protocol, OFA, when compared to OSA, did not decrease postoperative opioid consumption.

Clinical trial registry and number: NCT05031234.

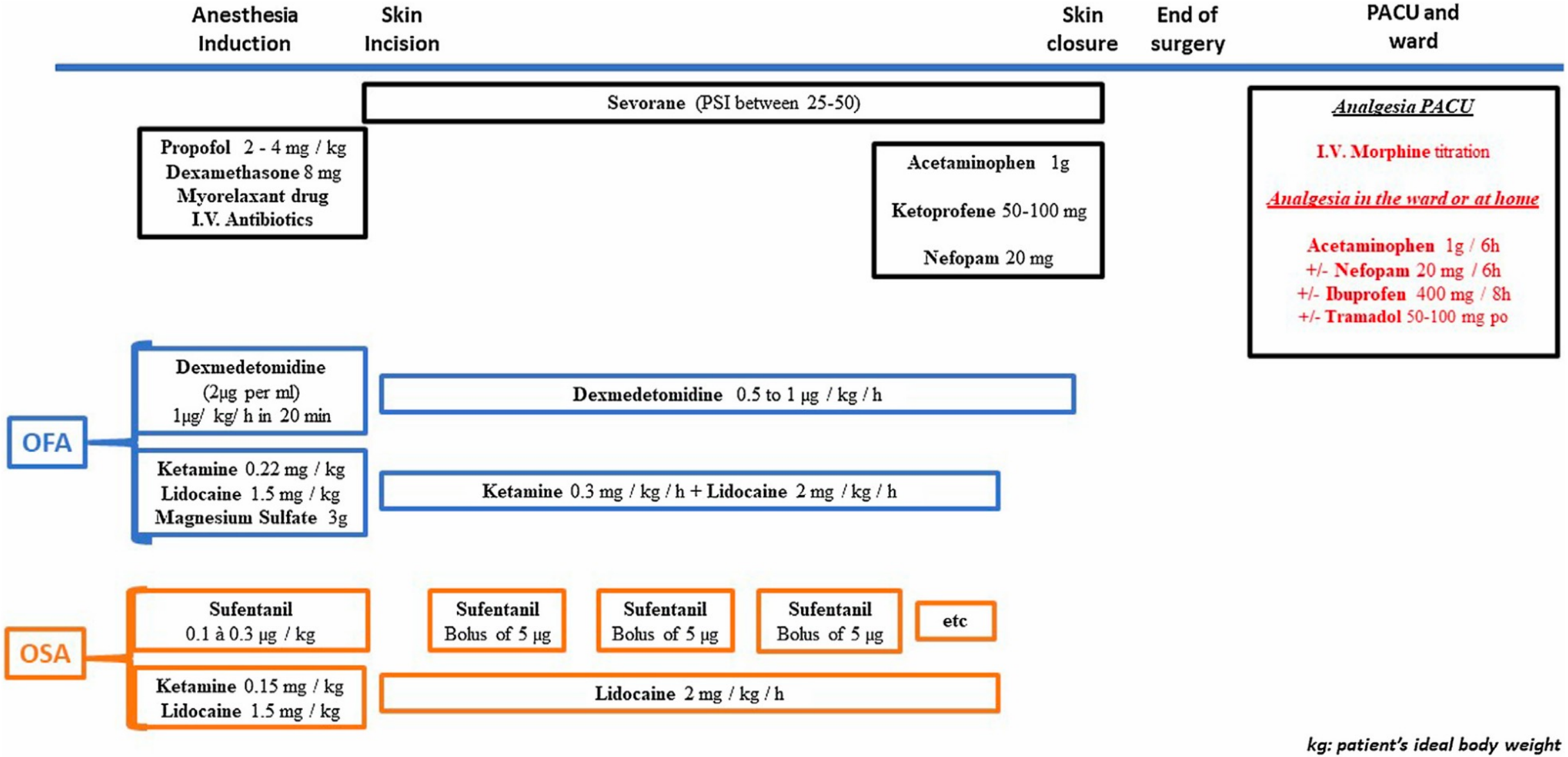


Fig. 1. Study design and drugs used in both groups.

Variables	OFA group (N = 78)	OSA group (N = 77)	*p*-value
Primary outcome			
Oral morphine equivalent consumption (mg)[a]	9.0 [0.0–30.0]	15 [0.0–30.0]	0.861
Secondary outcomes			
• Time to first bowel movement (days)	2 [1–4]	2 [1–3]	0.970
• Time to for first flatulence (hours)	31 ± 23	32 ± 26	0.829
• Hypoxemia, N (%) [b]	27 (37)	36 (46)	0.227
• PONV, N (%) [b]	10 (13)	17 (23)	0.102
• Intraoperative bradycardia, N (%)	12 (15)	4 (5)	0.037
• WHODAS 2.0 at 30 days post-surgery	4 [0–11]	4 [1–9]	0.755
• WHODAS 2.0 at 90 days post-surgery	1 [0–7]	3 [0–5]	0.657
Length of stay			
• In the post-anesthesia care unit (hours)	2.1 [1.4–2.4]	1.5 [1.3–2.2]	0.010
• In the hospital (days)	2 [1–5]	2 [1–4]	0.859

Data are expressed as number and (%), or median and [quartiles].
OFA: opioid-free anesthesia; OSA: opioid-sparing anesthesia; PONV postoperative nausea and vomiting; WHODAS 2.0: The World Health Organization Disability Assessment Schedule.

[a] From PACU arrival to 48 h post-surgery: include IV morphine titration at PACU and oral morphine derivates, expressed in oral morphine equivalents.

[b] Between arrival in the PACU to 48 h postop; # at 30 days post-surgery.

Journal of Cardiothoracic and Vascular Anesthesia 36 (2022) 1064–1072

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Original Article

Intraoperative Dexmedetomidine and Ketamine Infusions in an Enhanced Recovery After Thoracic Surgery Program: A Propensity Score Matched Analysis

Gabriel E. Mena, MD[*], Andres Zorrilla-Vaca, MD[*,†,‡,1], Ara Vaporciyan, MD[†], Reza Mehran, MD[†], Javier D. Lasala, MD[*], Wendell Williams, MD[*], Carla Patel, APRN[†], TaCharra Woodward, APRN[†], Brittany Kruse, DBH[*], Girish Joshi, MD[§], David Rice, MD[†]

[*]*Department of Anesthesiology and Perioperative Medicine, University of Texas MD Anderson Cancer Center, Houston, TX*

[†]*Department of Thoracic and Cardiovascular Surgery, University of Texas MD Anderson Cancer Center, Houston, TX*

[‡]*Department of Anesthesiology, Perioperative, and Pain Medicine, Brigham and Women's Hospital, Boston, MA*

[§]*Department of Anesthesiology, University of Texas Southwestern Medical Center, Dallas, TX*

Objectives: To assess the impact of intraoperative dexmedetomidine and ketamine on postoperative pain and opioid consumption within an ERAS program in thoracic pulmonary oncologic surgery.

Design: Retrospective, propensity-score matched analysis

Setting: Enhanced Recovery After Surgery (ERAS) program.

Participants: Patients undergoing thoracic pulmonary oncologic surgery between March 2016 and April 2020.

Interventions: Continuous infusion of dexmedetomidine and ketamine.

Measurements & Main Results: The authors initially analyzed data of 1,630 patients undergoing thoracic pulmonary oncologic surgery within their ERAS program. In total, 117 matched pairs were included in this analysis. Patients in the intraoperative dexmedetomidine + ketamine group were more likely to be opioid-free (76.6% vs 60.9%, P<0.01). Raw analysis showed lower pain scores at PACU admission (2.8±2.0 vs 3.4±2.0, P=0.03) and less opioid consumption at PACU admission (5 MED [0-10] vs 7.5 MED [0-15], P=0.03) in the dexmedetomidine + ketamine group; however, these differences were not present after adjusting for multiplicity. There were no significant differences in the length of PACU stay (1.9 hours [1.5-2.8] vs 2.0 hours [1.4-2.9], P=0.48) or hospital stay (three days [two-five] vs three days [two-five], P=0.08). Both groups had similar rates of pulmonary complications (5.9% vs 9.4%, P=0.326), ileus (0.9% vs 0.9%, P=1.00), and 30-day readmission (2.6% vs 4.3%, P=0.722).

Conclusions: There were no differences in postoperative pain scores and opioid consumption throughout their hospital stay between patients receiving concomitant dexmedetomidine and ketamine infusions versus patients who did not receive these infusions during thoracic surgery.

Key Words: Thoracic surgery; Multimodal analgesia; Opioid-free anesthesia; Postoperative Pain; Postoperative outcomes

Table 2
Outcome comparisons between the matched groups.

Outcome	Standard analgesia (n=117)	Dexmedetomidine + Ketamine(n=117)	P value	Adjusted P value*
PACU time (h)	1.9 [1.5-2.8]	2.0 [1.4-2.9]	0.481	
Length of hospital stay (days)	3 [2-5]	3 [2-4]	0.082	
Opioid consumption (MED)				
PACU	5 [0-15]	5 [0-10]	0.024	1.000
POD 1	0 [0-5]	0 [0-5]	0.386	0.386
POD 2	0 [0-10]	0 [0-5.6]	0.567	1.000
POD 3	0 [0-21]	0 [0-20]	0.581	0.762
POD 4	0 [0-15]	0 [0-20]	0.249	0.980
POD 5	0 [0-10]	0 [0-10]	0.805	0.901
Total	15 [5-47.5]	10 [5-40]	0.141	
Average pain scores				
PACU	3.34 ± 2.18	2.75 ± 2.04	0.033	0.168
POD 1	2.34 ± 1.68	1.97 ± 1.59	0.094	0.307
POD 2	2.17 ± 1.55	2.25 ± 1.59	0.698	0.970
POD 3	2.35 ± 1.59	2.29 ± 1.45	0.739	0.990
POD 4	2.00 ± 1.51	1.95 ± 1.63	0.710	0.990
POD 5	1.86 ± 1.42	1.92 ± 1.62	0.956	0.990
Maximum pain scores				
PACU	3.70 ± 2.55	3.59 ± 2.64	0.777	0.941
POD 1	5.15 ± 2.83	4.79 ± 2.69	0.341	0.861
POD 2	4.82 ± 2.61	5.01 ± 2.71	0.537	0.941
POD 3	5.11 ± 2.96	5.09 ± 2.38	0.894	0.951
POD 4	4.57 ± 2.54	4.36 ± 2.48	0.625	0.941
POD 5	4.91 ± 3.01	4.21 ± 2.41	0.422	0.861
Postoperative opioid-free, n (%)	19 (16.2%)	27 (23.1%)	0.188	
Discharge opioids prescribed, MED	124 ± 238	145 ± 286	0.732	
Ileus, n (%)	1 (0.9%)	1 (0.9%)	1.000	
Pneumonia, n (%)	1 (0.9%)	3 (2.6%)	0.622	
Pulmonary complications, n (%)	7 (5.9%)	11 (9.4%)	0.326	
Postoperative transfusion, n (%)	5 (4.3%)	4 (3.4%)	0.734	
Reoperation due to bleeding	2 (1.7%)	1 (0.8%)	0.561	
30-day readmission, n (%)	3 (2.6%)	5 (4.3%)	0.722	

BMC Anesthesiology

SYSTEMATIC REVIEW Open Access

Dexmedetomidine for opioid-sparing postoperative analgesia: a systematic review and meta-analysis

Yanli Sun[1], Yu Yao[1], Ying Li[1] and Wei Deng[2*]

Abstract

Introduction Postoperative opioid use is associated with adverse effects and increased risk of long-term dependence. Dexmedetomidine (Dex), a selective alpha-2 adrenergic agonist, has analgesic and sedative properties and may reduce opioid requirements when used perioperatively. This systematic review assessed its efficacy in reducing postoperative opioid consumption and improving recovery outcomes in adult surgical patients.

Methods A systematic search of PubMed, Embase, and the Cochrane Library (to 1 May 2025) identified randomised controlled trials comparing intravenous Dex with placebo or standard opioid-based analgesia in adults undergoing surgery. The primary outcome was cumulative opioid consumption in the first 24 h postoperatively. Secondary outcomes included pain intensity, postoperative nausea and vomiting, sedation, haemodynamic events, and indicators of recovery. Data were synthesised using a random-effects model. Risk of bias and certainty of evidence were assessed using the Cochrane Risk of Bias 2 tool and GRADE approach, respectively. This review was prospectively registered in PROSPERO (CRD420251126259).

Results Twenty studies involving 1,793 patients met inclusion criteria. Dex was administered intraoperatively (bolus 0.5–1 µg per kilogram; infusion 0.2–0.7 µg per kilogram per hour) or via patient-controlled analgesia (PCA). Compared with control, Dex significantly reduced 24-hour opioid consumption (mean difference −7.7 milligrams morphine equivalents; 95% confidence interval −9.5 to −6.0; $P < 0.001$; $I^2 = 46\%$). Pain scores were lower, and incidence of postoperative nausea and vomiting was reduced. Bradycardia and hypotension were more frequent but typically transient and manageable.

Discussion Dex is an opioid sparing adjunct that modestly reduces postoperative opioid requirements and is associated with lower pain scores and less postoperative nausea and vomiting. Haemodynamic monitoring is advised during administration, and Dex should be integrated into wider multimodal analgesia pathways rather than used as a stand alone solution to opioid reduction.

Prospero registration CRD420251126259.

Keywords Dexmedetomidine, Opioid-sparing, Postoperative analgesia, Multimodal analgesia, Enhanced recovery

Table 2 Summary of findings (Dexmedetomidine vs. Control) for key outcomes in postoperative analgesia

Outcome (Units)	No. of Studies (Patients)	Effect Estimate (95% CI)	Certainty of Evidence (GRADE)	Comments
24 h Opioid Consumption (mg morphine)	18 RCTs (≈1,300 patients)	MD −7.7 mg (−9.5 to −6.0) favoring Dex	Moderate ⊕⊕⊕◯	Dex reduces opioid requirements by ~30%. Downgraded 1 level for heterogeneity (I2 46%) but consistent direction of effect.
Pain intensity (VAS 0–10) at 24 h	~15 RCTs (1,200 patients)	Dex group ~1 point lower pain scores (range 0.5–1.5 lower across studies)	Moderate ⊕⊕⊕◯	Most trials show lower pain with Dex. Some variability in timing; downgraded 1 for indirectness (varied pain measures).
Post-op Nausea or Vomiting (PONV) (incidence)	12 RCTs (800 patients)	RR 0.69 (0.55–0.85) favoring Dex (e.g. 15% vs. 22%)	High ⊕⊕⊕⊕	Significant reduction in PONV with Dex. Consistent and precise effect; no serious limitations.
Sedation level (early post-op)	10 RCTs (700 patients)	Dex increases sedation (e.g. Ramsey + 1); no respiratory depression	High ⊕⊕⊕⊕	All studies: more sedated but arousable patients with Dex. Considered a pharmacologic effect; not an adverse outcome per se.
Bradycardia (HR < 50 requiring intervention)	12 RCTs (including meta [24])	RR ~3.0 (Dex ~12% vs. Ctrl ~4%) – increased with Dex	High ⊕⊕⊕⊕	High certainty: reproducible across studies. Dex causes more bradycardia; usually transient and treatable (atropine).
Hypotension (requiring treatment)	12 RCTs (2,000 + patients)	RR ~1.2 (Dex ~20% vs. Ctrl ~16%)	High ⊕⊕⊕⊕	Slight increase in hypotension events with Dex, mainly intra-op. Well-documented effect.
Delirium (post-op incidence)	1 meta [24] + 1 RCT (≈4,000)	RR ~0.68 (0.50–0.90) favoring Dex	Moderate ⊕⊕⊕◯	Dex likely reduces delirium; evidence mainly from cardiac ICU patients. Downgraded 1 for indirectness (not all populations).
Length of hospital stay (days)	5 RCTs (various surgeries)	No significant difference (mean ~0 to 0.5 day reduction with Dex)	Low ⊕⊕◯◯	Inconsistent findings; not powered for LOS. Most show no change. Low certainty.
Chronic postoperative pain (3–6 mo)	1 RCT (Bielka 2018)	Dex 0% vs. Ctrl 13% chronic pain at 3 mo	Low ⊕⊕◯◯	Single small trial suggests possible benefit. Insufficient evidence overall.

CI confidence interval, *RR* risk ratio, *MD* mean difference. High certainty: very confident in effect estimate; Moderate: further research could change estimate; Low: limited confidence (evidence sparse or inconsistent). GRADE downgrading factors: risk of bias, inconsistency, indirectness, imprecision, publication bias. We found overall robust evidence for opioid-sparing, pain, PONV, and known side effects. Evidence for delirium and longer-term outcomes is less certain

- Premed
- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia
- **Post Operative Cognitive Dysfunction (POCD) Reduction**
- Blunting Surgical Stress inflammation
- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks
- Post Neuraxial Shivering
- ?PDPH treatment

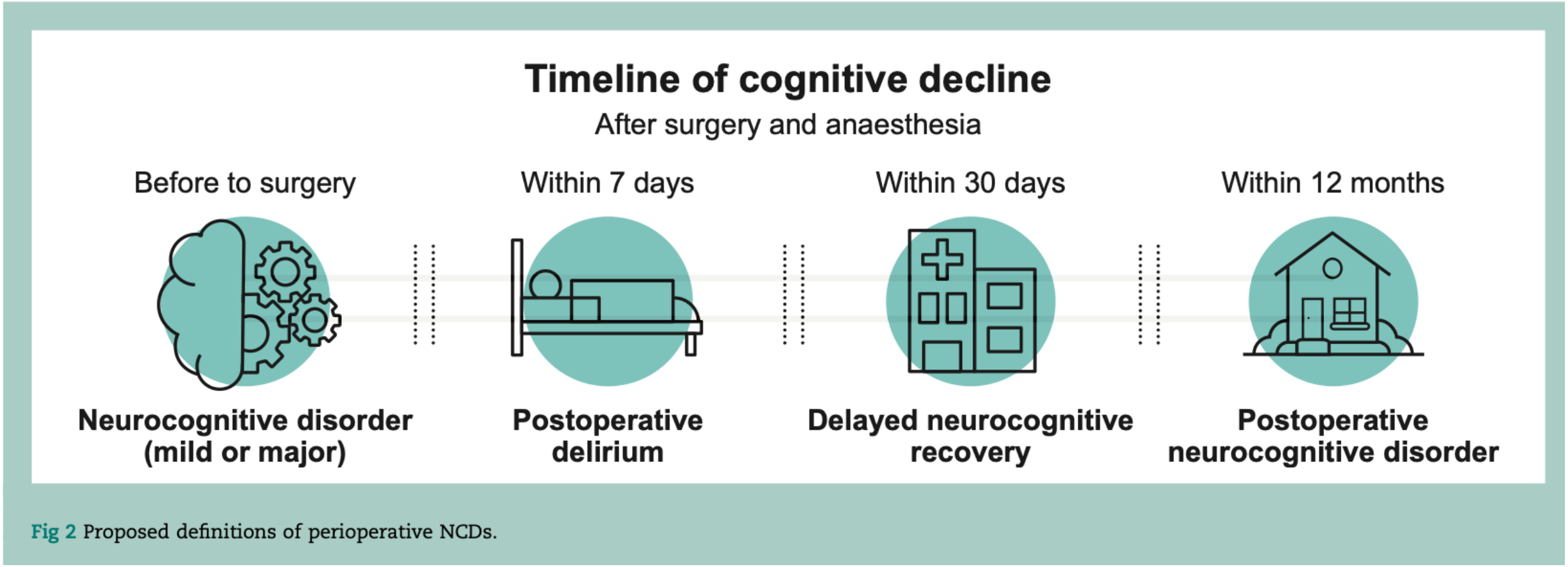


Fig 2 Proposed definitions of perioperative NCDs.

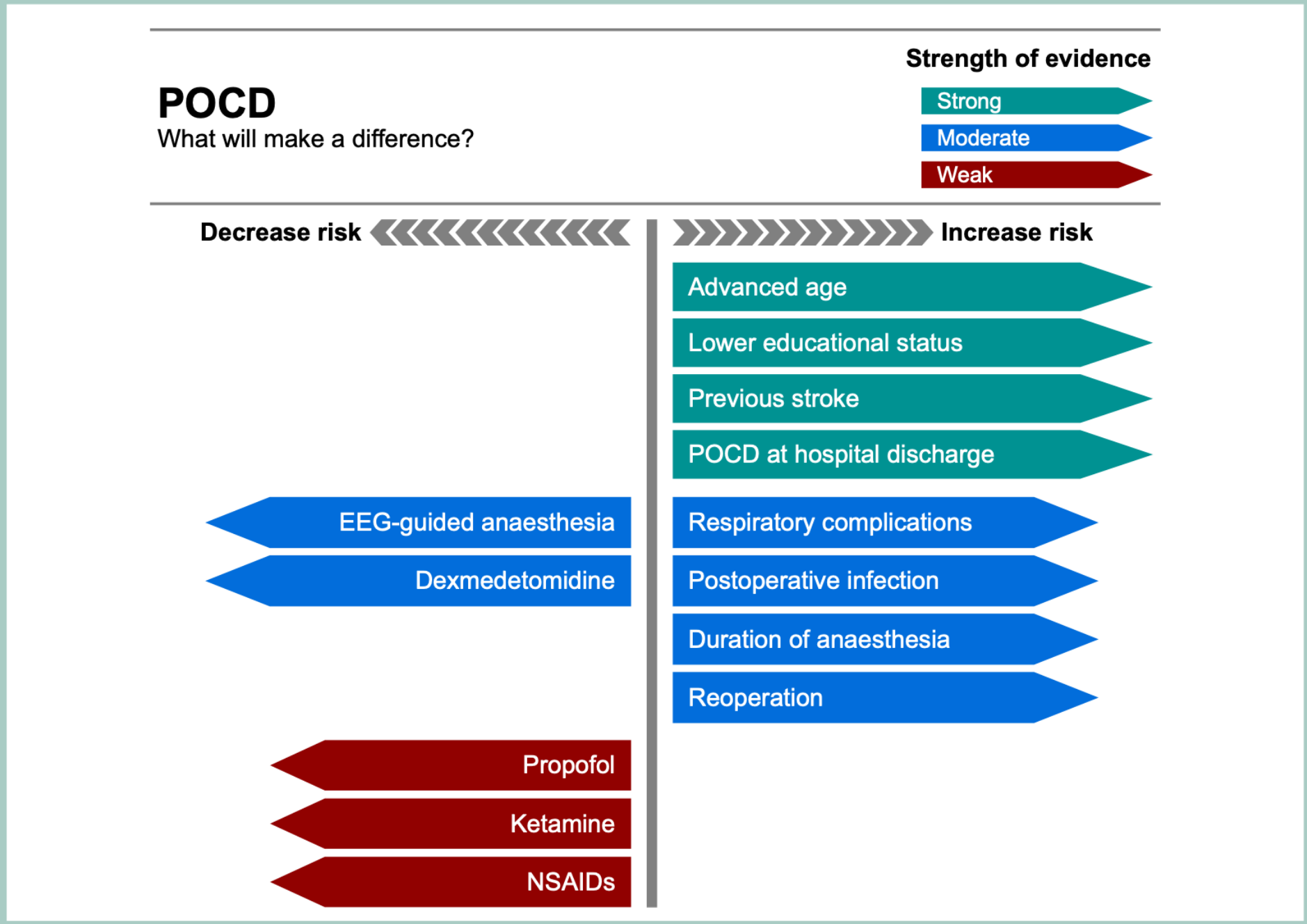


Fig 3 Infographic detailing strength of evidence for factors that increase and decrease the risk of POCD.

- Premed

- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia

- Post Operative Cognitive Dysfunction (POCD) Reduction

- **Blunting Surgical Stress inflammation**

- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks

- Post Neuraxial Shivering

- ?PDPH treatment

Attenuation of Stress Response to Surgery

- Perioperative dexmedetomidine - reduced levels of adrenaline, noradrenaline and cortisol
- Effect immune cells / inflammatory cytokine levels
- Major abdo surgery
  - Dexmedetomidine + GA blunt stress response similarly to Epidural + GA

- Premed
- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia
- Post Operative Cognitive Dysfunction (POCD) Reduction
- Blunting Surgical Stress inflammation
- **Regional anesthesia**
  - **Intrathecal**
  - **Epidural**
  - **Peripheral nerve blocks**
- Post Neuraxial Shivering
- ?PDPH treatment

Product Description

Generic :	Dexmedetomidine
Brand:	Ever Pharma
Strength:	200microgram/2mL
Form:	Ampoule

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dexmedetomidine hydrochloride is a white or almost white powder, freely soluble in water and its pKa is 7.1. The partition coefficient in octanol: water at pH 7.84 is 2.89.

DEXMEDETOMIDINE EVER PHARMA is a clear, colourless, sterile and isotonic concentrated solution with a pH of 4.5 to 7.0. DEXMEDETOMIDINE EVER PHARMA is a concentrated sterile, non-pyrogenic solution suitable for intravenous infusion after dilution. Each 1 mL of DEXMEDETOMIDINE EVER PHARMA contains 118 microgram of dexmedetomidine hydrochloride (equivalent to 100 microgram dexmedetomidine base). The solution is preservative-free and contains no additives or chemical stabilisers.

For the full list of excipients, see Section 6.1 List of excipients.

dexmedeTOMIDine hydrochloride

Epidural route

Postoperative pain

1) Off-Label Dosage

a) Dosage range: 0.5 to 1 mcg/kg epidurally with background anesthesia; up to 1.5 mcg/kg has been used [43]

Intramuscular route

General anesthesia; Adjunct

1) Off-Label Dosage

a) Dosage: 0.5 to 1.5 mcg/kg IM 60 minutes prior to anesthesia induction [53][54]

b) Dosage (cataract surgery): 1 mcg/kg IM; providing lowering of intraocular pressure, yet without interfering with the patient's ability to cooperate (Virkkila et al, 1993). However, prolonged sedation has occurred and the IM route may not always be suitable for shorter surgical procedures [53][54].

Intrathecal route

General anesthesia; Adjunct

1) Off-Label Dosage

a) Cesarean section: 5 mcg in 1 mL NS intrathecally given with 9 mg (1.2 mL) of bupivacaine 0.75% [55]

Procedural sedation, Nonintubated patients

1) Off-Label Dosage

a) Dosage, sensory and motor block for lower abdominal and lower limb surgery: 10 mcg intrathecally with bupivacaine 0.5% 3 mL (diluted in preservative-free NS to a total volume of 3.5 mL) [18]

Contents lists available at ScienceDirect

International Journal of Obstetric Anesthesia

journal homepage: www.elsevier.com/locate/ijoa

Maternal hemodynamic effects associated with intravenous and neuraxial dexmedetomidine during labor and cesarean delivery: a single center retrospective study (2021–2024)

S.L. Armstrong [1], A.A. Berger [1], S. Zec, M. Douek, K. Li, M.C. Borrelli, Y. Li, P.E. Hess [*]

Department of Anesthesia, Critical Care, and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, United States

A B S T R A C T

Background: Dexmedetomidine is a highly selective alpha$_2$-adrenoceptor agonist with anxiolytic, sedative, and analgesic properties. The use of this medication in obstetric anesthesia has increased with publications describing intravenous (IV) use for shivering, and epidural and intrathecal use for anesthesia and analgesia. Limited data exists on the frequency of adverse events during clinical use. We reviewed our use of dexmedetomidine in the peripartum period to identify specific indications and maternal adverse events

Methods: We performed a retrospective review of dexmedetomidine administration during labor and delivery over three years (2022–2024). The route of administration, indication and doses were collected and all identifiable adverse events related to dexmedetomidine administration were recorded.

Results: There were 1,177 records available for review and 1,100 were analyzed. Dexmedetomidine was administered most often for augmentation of cesarean anesthesia, treatment of breakthrough pain during labor, and for shivering. Maternal heart rate abnormalities were noted in 47 cases (6.1%; 95% CI 4.5-8.0), bradycardia in 16 cases (2.1%; 95% CI 1.2-3.4), hypotension in 57 cases (7.2%; 95% CI 5.5-9.3), and sedation in 9 cases (1.2% 95% CI 0.6-2.3). Maternal adverse events were less common after neuraxial administration compared with IV.

Conclusions: Our clinical experience demonstrated maternal adverse events that might be traced to the administration of either IV or neuraxial dexmedetomidine, which were more common after IV administration. As adverse events are likely to be dose-related, we would recommend starting with the lowest appropriate dose and titrating to the desired effect.

- Epidural Dexmedetomidine most common (561/574 or 97.7%)
  - Single or repeated bolus
  - Also added to the epidural infusion in 13 (2.2%) cases. Clinician-made solutions containing bupivacaine + fentanyl + dexmedetomidine [0.5 mcg/mL for 2.5–7.5 mcg/hr]

  - Epidural dose as low as 4 mcg (mean 16.0 ±6.5 mcg)
  - Cumulative epidural-only dose ranged 8 - 75 mcg (Mean 20.5 ±9.5 mcg)

- Intrathecal Dexmedetomidine (n =15)
  - Dose range: 5 mcg - 20 mcg (Mean 10 mcg)

- Premed
- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia
- Post Operative Cognitive Dysfunction (POCD) Reduction
- Blunting Surgical Stress inflammation
- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks
- **Post Neuraxial Shivering**
- ?PDPH treatment

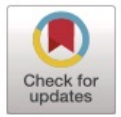
International Journal of Obstetric Anesthesia 62 (2025) 104345

Contents lists available at ScienceDirect

International Journal of Obstetric Anesthesia

journal homepage: www.elsevier.com/locate/ijoa

Review Article



Intravenous dexmedetomidine use in obstetric anesthesia: a focused review

M.S. Douglas [a,b], L.J. Soloniuk [a,b,c,d,*], J. Jones [a], R. Derderian [a], C. Baker [a], G. Stier [a,b]

[a] Department of Anesthesiology and Perioperative Medicine, Riverside University Health System, Moreno Valley, CA, USA
[b] Department of Anesthesiology, Loma Linda University, Loma Linda, CA, USA
[c] Department of Gynecology and Obstetrics, Loma Linda University, Loma Linda, CA, USA
[d] Department of Internal Medicine, University of California Riverside, Riverside, CA, USA

ARTICLE INFO

Keywords:
Alpha-$_2$ adrenergic receptor agonist
Anxiolysis
Cesarean delivery
Dexmedetomidine
Light sedation
Obstetric anesthesia
Post-traumatic stress disorder
Postoperative nausea and vomiting
Postoperative shivering
Postpartum depression

ABSTRACT

Dexmedetomidine is an alpha-$_2$ adrenergic receptor agonist with analgesic properties. Dexmedetomidine is currently U.S. Food and Drug Administration (FDA) approved for intravenous (IV) administration in non-pregnant patients. However, it has shown promise for various off-label indications in obstetric anesthesia. This review focuses on reported uses for IV dexmedetomidine in obstetric anesthesia. Intravenous dexmedetomidine has reported efficacy for producing light sedation, analgesia, and anxiolysis in the parturient. In addition, the use of IV dexmedetomidine during cesarean delivery has been reported to alleviate symptoms of postpartum depression and reduce the incidence of shivering and postoperative nausea and vomiting. In the setting of trauma, IV dexmedetomidine may reduce the risk of post-traumatic stress disorder. Further understanding of IV dexmedetomidine's benefits and the recent advances in its clinical use allows clinicians to leverage its versatility to improve patient outcomes.

Table 1
Summary of indications and studies reporting on peripartum intravenous dexmedetomidine.

Study	Design	Number of participants	Clinical question	Conclusion
Dexmedetomidine and lactation				
Wang et al. (2020)[37]	Single-center, prospective, randomized, double-blinded, parallel, controlled trial	n=160	To assess if IV dexmedetomidine plus sufentanil, immediately after delivery, and in PCIA can be beneficial for breastfeeding as compared to sufentanil alone.	Dexmedetomidine groups progressed to exclusive breastfeeding earlier, the first lactation time was sooner, and the amount of breast milk on the second day after delivery increased. Additionally, patients in the dexmedetomidine group had improved recovery quality and comfort with reduced VAS and anxiety scores and a lower incidence of nausea.
Anxiolysis and analgesia during cesarean delivery under neuraxial anesthesia				
Davis et al. (2021)[14]	Single center, retrospective cohort study	n=107	To assess dexmedetomidine use for rescue analgesia under neuraxial anesthesia.	With dexmedetomidine, there was no significant difference in conversion to general anesthesia compared to other adjuvants. Maternal bradycardia was significantly more frequent after dexmedetomidine though use of vasopressor and inotropic support was similar.
Kang et al. (2023)[2]	Single center, prospective, randomized controlled trial	n=60	To compare the efficacy of IV dexmedetomidine 0.7 μg/kg with midazolam 0.3 mg/kg for anxiolysis during cesarean delivery.	Similar satisfaction scores for maternal sleep, feeling comfortable, and reducing anxiety. No difference in adverse effects, hemodynamic parameters, or temperature
Nie et al. (2018)[15]	Multicenter, prospective, randomized controlled trial	n=208	To assess the efficacy of dexmedetomidine plus sufentanil in IV patient-controlled analgesia after cesarean delivery compared to sufentanil alone.	In the study group, there was significantly less sufentanil consumption, lower pain scores, higher analgesic satisfaction, and lower use of rescue analgesia compared to the control group.

Perioperative shivering

Mohammed et al. (2024)[4]	Meta-analysis	n=926 from 10 randomized controlled trials	To assess the effect of dexmedetomidine in the management of shivering.	Dexmedetomidine for both prophylaxis and treatment is superior to normal saline in the management of perioperative shivering during cesarean delivery but is comparable to other commonly used anti-shivering agents.
*Sween et al. (2021)[3]	Prospective, randomized, double blinded, controlled trial	n=85	To assess the degree of postoperative shivering in women who underwent cesarean delivery with neuraxial anesthesia who received either IV normal saline or dexmedetomidine 10 μg immediately after delivery.	Prophylactic administration of IV dexmedetomidine 10 μg after delivery reduced postoperative shivering without notable side effects at 30 min and 60 min upon arrival at PACU.
*Yang et al. (2024)[17]	Prospective, randomized dose–response study	n=75	To assess the dose dependence of dexmedetomidine for treating postoperative shivering.	The ED50 and ED95 of IV dexmedetomidine to treat severe shivering is 0.23 μg/kg and 0.39 μg/kg, respectively. There were no significant differences in hemodynamic parameters, temperature, respiratory depression, or nausea and vomiting between the groups.
*Lamontagne et al. (2019)[16]	single-center randomized double-blind controlled trial	n=80	To assess whether dexmedetomidine 30 μg after delivery reduces the duration of postoperative shivering associated with neuraxial anesthesia during cesarean delivery compared with the control group receiving saline.	A single bolus of IVdexmedetomidine 30 μg decreased the duration of shivering for up to 15 min after cesarean delivery compared to normal saline.

Postoperative nausea and vomiting				
Hu et al. (2020)[5]	Single center, randomized controlled trial	n=105	To compare dexmedetomidine, midazolam, and saline to prevent nausea and vomiting after carboprost tromethamine injection in postpartum hemorrhage during cesarean delivery	Significantly lower incidence of postoperative nausea and vomiting after dexmedetomidine or midazolam versus saline (6%, 17%, and 71%, respectively)
Postpartum depression				
*Yu et al. (2019)[7]	Randomized, placebo-controlled study	n=600	To evaluate prophylactic dexmedetomidine and postpartum depressive symptoms measured by EPDS	Administration of IV dexmedetomidine in the early postpartum period was associated with lower EPDS scores
Xu et al. (2024)[8]	Meta-analysis of randomized controlled trials	n=1711, from 13 randomized controlled trials	To review available literature on the efficacy of dexmedetomidine in preventing postpartum depression.	Patients who received IV dexmedetomidine had significantly lower EPDS scores compared to the control group.
Gastrointestinal function after cesarean delivery				
Sun et al. (2024)[24]	Randomized, double blind, placebo-controlled, clinical trial	n=220	To assess if dexmedetomidine administered postoperatively following a cesarean delivery improves the time to first flatus as compared to normal saline.	Patients who received dexmedetomidine had significantly shorter times to first flatus and first bowel movement.
Hypertensive disorders of pregnancy and control of hemodynamic responses				
El-Tahan et al. (2012)[25]	Randomized dose–response study	n=68	To determine if dexmedetomidine reduces the maternal hemodynamic and hormonal responses to elective cesarean delivery	The use of dexmedetomidine infusions at 0.4 μg/kg/h and 0.6 μg/kg/h attenuated maternal hemodynamic and hormonal responses to tracheal intubation, extubation, and surgical stimulation during cesarean delivery without neonatal adverse effects.
Hariharan (2014)[27]	Case report	n=1	Dexmedetomidine was used to control refractory hypertension and uterine tone during emergency cesarean delivery under general anesthesia.	Dexmedetomidine improved blood pressure in a case of refractory pregnancy-induced hypertension.
Eskandr et al. (2018)[28]	Randomized double-blind controlled trial	n=60	To assess the effect of dexmedetomidine on mean arterial blood pressure in patients with preeclampsia receiving general anesthesia for cesarean delivery.	Patients who received an initial dexmedetomidine 1 μg/kg infusion over 10 min prior to intubation and either a 0.4 μg/kg/h or 0.6 μg/kg/h of dexmedetomidine had significantly lower mean arterial blood pressures and heart rates compared to patients who received normal saline alone.

Key: Post-anesthesia care unit (PACU); patient-controlled intravenous analgesia (PCIA); Visual analog scale (VAS); Edinburgh Postnatal Depression Scale (EPDS).
*Studies are included in the meta-analysis of their respective sections.

- Premed

- Opioid Sparing
  - ERAS
  - Bariatric
  - Neuroanaesthesia

- Post Operative Cognitive Dysfunction (POCD) Reduction

- Blunting Surgical Stress inflammation

- Regional anesthesia
  - Intrathecal
  - Epidural
  - Peripheral nerve blocks

- Post Neuraxial Shivering

- **<u>?PDPH treatment</u>**

BMC Anesthesiology

SYSTEMATIC REVIEW Open Access

Nebulized dexmedetomidine for post-dural puncture headache after cesarean delivery: a systematic review and meta-analysis

Yanyan Yang[1†], Hong Tang[1†] and Fuhai Bai[1*]

Abstract

Background There are limited effective non-invasive treatment options for post-dural puncture headache (PDPH) following cesarean delivery. This meta-analysis aimed to investigate the efficacy and safety of nebulized dexmedetomidine in treating PDPH after cesarean delivery.

Methods Electronic databases were systematically searched from the inception to March 2025. Primary outcomes included pain scores based on the numerical rating scale (NRS) and the visual analogue scale (VAS) at 6, 12, 24, 48, and 72 h after the intervention. Secondary outcomes included the need for epidural blood patch (EBP) and adverse events, such as bradycardia and dry mouth. The Cochrane Risk of Bias 2 (RoB 2) tool was employed to assess the quality of the included studies, and the certainty of evidence was evaluated using the grading of recommendations assessment, development, and evaluation (GRADE) approach.

Results Four randomized controlled trials with 228 patients were included in this meta-analysis. Compared to participants in the control group who received saline or fentanyl, patients with PDPH who received nebulized dexmedetomidine following cesarean delivery exhibited lower pain scores at 6, 12, 24, 48, and 72 hours after the intervention. The quality of evidence ranged from 'very low' to 'moderate'. The nebulized dexmedetomidine group less frequently needed EBP compared to the control group, while there were no significant differences between the two groups in terms of adverse effects.

Conclusion Nebulized dexmedetomidine is a promising non-invasive option for managing PDPH in patients undergoing cesarean delivery. It effectively reduces pain intensity and decreases the need for invasive procedures, such as epidural blood patches, with an acceptable safety profile. This nebulized delivery method may offer practical advantages over traditional systemic approaches, particularly in the postpartum setting.

Trial registration We registered this network meta-analysis with PROSPERO (registration no. CRD420251016279).

Keywords Post-dural puncture headache, Nebulized dexmedetomidine, Meta-analysis, Cesarean delivery

BMJ Neurology Open

Efficacy of nebulised dexmedetomidine versus aminophylline for treatment of postdural puncture headache in patients undergoing subarachnoid block posted for caesarean section: a double-blind, randomised controlled study

R K V Kavya [1], Neeraj Kumar [2], Abhyuday Kumar [2], Monika Anant [3], Alok Ranjan [4]

To cite: Kavya RKV, Kumar N, Kumar A, *et al*. Efficacy of nebulised dexmedetomidine versus aminophylline for treatment of postdural puncture headache in patients undergoing subarachnoid block posted for caesarean section: a double-blind, randomised controlled study. *BMJ Neurology Open* 2026;**8**:e001530. doi:10.1136/bmjno-2025-001530

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjno-2025-001530).

Received 22 December 2025
Accepted 02 May 2026

For numbered affiliations see end of article.

Correspondence to
Dr Neeraj Kumar;
neeraj.jlnmc@gmail.com

ABSTRACT

Background Postdural puncture headache (PDPH) following spinal anaesthesia significantly affects postpartum recovery. We evaluated the efficacy of nebulised dexmedetomidine and aminophylline in women with moderate to severe PDPH after caesarean delivery.

Methods In this single-centre, double-blind, randomised controlled trial, 96 postpartum women, with American Society of Anesthesiologists physical status II, Visual Analogue Scale (VAS), with PDPH (VAS>4; Lybecker>2) after subarachnoid block were allocated to receive nebulised dexmedetomidine (1 µg/kg), aminophylline (1.5 mg/kg) or saline placebo. All participants received standardised conservative treatment and remained supine for 72 hours. Nebulisation was administered two times per day for ≤72 hours. The primary endpoint was change in VAS pain score at 24 hours. Secondary endpoints included VAS and Lybecker scores at 48 hours and 72 hours, Patient Global Impression of Change (PGIC) and adverse events.

Results Baseline characteristics were comparable between groups. At 24 hours, median VAS was significantly lower with dexmedetomidine (3 (3–4)) and aminophylline (4 (3–6)) compared with control (6 (5.5–6)) ($p<0.001$). Pain reduction persisted at 48 hours and 72 hours, with dexmedetomidine producing the fastest resolution. Lybecker scores improved earlier in the treatment groups ($p<0.001$). PGIC showed 'very much improved' in 100% (dexmedetomidine), 53.1% (aminophylline) and 0% (control) ($p<0.001$). Adverse events were mild and infrequent, with cough and nausea occurring only in the aminophylline group.

Conclusions Nebulised dexmedetomidine and aminophylline provided effective, well-tolerated, non-invasive treatment for PDPH. Dexmedetomidine produced the greatest and earliest improvement. These therapies may represent practical alternatives for PDPH management in postpartum patients; larger multicentre trials allowing early mobilisation are warranted.

Trial registration number Clinical Trials Registry-India (CTRI/2024/01/061322; date of prospective trial registration: 10 January 2024, date of first patient enrolment: 15 January 2024, https://ctri.nic.in/Clinicaltrials/login.php).

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Postdural puncture headache (PDPH) is a common complication following neuraxial anaesthesia in obstetric patients. Conservative treatments often provide incomplete relief, and epidural blood patch, although effective, is invasive.

WHAT THIS STUDY ADDS

⇒ In this double-blind randomised trial, nebulised dexmedetomidine and aminophylline significantly reduced PDPH severity compared with conservative therapy alone, with dexmedetomidine showing earlier and greater improvement in pain and functional recovery.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings suggest that nebulised pharmacological therapies may offer a non-invasive treatment option for PDPH, supporting further research to confirm their effectiveness and establish optimal dosing strategies.

INTRODUCTION

Postdural puncture headache (PDPH) is one of the most common and distressing complications following spinal or epidural anaesthesia, particularly in obstetric patients undergoing caesarean delivery. Despite advances in needle design and the use of smaller-gauge pencil-point spinal needles, PDPH continues to affect 0.5–2% of parturients worldwide following neuraxial anaesthesia.[1] However, the incidence of PDPH after spinal anaesthesia performed with a Quincke

Conclusion

- Evolved for many roles outside of co-operative sedation in ICU
- More evidence emerging of its benefits but with conflicting information
- Many potential uses but with caveats of haemodynamic compromise / prolonged sedation
  - Premed
  - Opioid Sparing Anaesthesia
  - Chronic Pain Reduction
  - PONV Reduction
  - POCD Reduction
  - Attentuation of Surgical stress / Inflammatory Response
  - Regional Anaesthesia
  - Obstetrics – Post Operative Shivering
  - ?PDPH Treatment

Magic, myth… or Missing from your practice


Thanks for listening

References

- Scott-Warren V, Sebastian J. Dexmedetomidine: its use in intensive care medicine and anaesthesia. BJA Education, 16, 242-246
- Verret M, Le J, Lalu M. Effectiveness of dexmedetomidine on patient-centred outcomes in surgical patients: a systematic review and Bayesian meta-analysis. British Journal of Anaesthesia, 2024; 133, 615-627
- Uptodate. Dexmedetomidine: Drug information
- Crowe. G, et al Perioperative Applications of Dexmedetomidine. ATOTW 469 — Perioperative Applications of Dexmedetomidine (5 April 2022)
- Brodier E, Cibelli M, Postoperative cognitive dysfunction in clinical practice. BJA Education, 2020; 21, 75-82
- Douglas M, et al. Intravenous dexmedetomidine use in obstetric anesthesia: a focused review. International Journal of Obstetric Anesthesia, 2025; 62
- Douglas MS, Soloniuk LJ, Jones J, Derderian R, Baker C, Stier G. Intravenous dexmedetomidine use in obstetric anesthesia: a focused review. Int J Obstet Anesth. 2025 May;62:104345. doi: 10.1016/j.ijoa.2025.104345. Epub 2025 Feb 13. PMID: 40090158
- Dexmedetomidine EVER PHARMA. Product information
- dexmedeTOMIDine. DRUGDEX Evaluations
- Nelson G, Bakkum-Gamez J, Kalogera E, Glaser G, Altman A, Meyer LA, Taylor JS, Iniesta M, Lasala J, Mena G, Scott M, Gillis C, Elias K, Wijk L, Huang J, Nygren J, Ljungqvist O, Ramirez PT, Dowdy SC. Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations-2019 update. Int J Gynecol Cancer. 2019 May;29(4):651-668. doi: 10.1136/ijgc-2019-000356. Epub 2019 Mar 15. PMID: 30877144.

- Yang Y, Tang H, Bai F. Nebulized dexmedetomidine for post-dural puncture headache after cesarean delivery: a systematic review and meta-analysis. BMC Anesthesiol. 2025 Oct 21;25(1):513. doi: 10.1186/s12871-025-03339-w. PMID: 41120897; PMCID: PMC12542067.
- Kavya RKV, Kumar N, Kumar A, Anant M, Ranjan A. Efficacy of nebulised dexmedetomidine versus aminophylline for treatment of postdural puncture headache in patients undergoing subarachnoid block posted for caesarean section: a double-blind, randomised controlled study. BMJ Neurol Open. 2026 May 18;8(1):e001530. doi: 10.1136/bmjno-2025-001530. PMID: 42164173; PMCID: PMC13185029
- Nelson G, Altman AD, Metcalfe A, Fotopoulou C, Taylor J, Glaser G, Bakkum-Gamez J, Kumar A, Meyer LA, Stone R, Mena G, Elias KM, Bisch SP, Zivanovic O, Miralpeix E, Bhandoria G, Eriksson AGZ, Ruzycki SM, Sultan P, Sauro KM, Blake L, Brindle ME, Ramirez PT, Dowdy SC. Enhanced recovery after surgery (ERAS®) society guidelines for gynecologic oncology: 2026 update. Gynecol Oncol. 2026 Jun 5;210:153-173. doi: 10.1016/j.ygyno.2026.05.022. Epub ahead of print. PMID: 42247726.
- Chen L, He W, Liu X, Lv F, Li Y. Application of opioid-free general anesthesia for gynecological laparoscopic surgery under ERAS protocol: a non-inferiority randomized controlled trial. BMC Anesthesiol. 2023 Jan 27;23(1):34. doi: 10.1186/s12871-023-01994-5. PMID: 36707777; PMCID: PMC9881250.
- Sun Y, Yao Y, Li Y, Deng W. Dexmedetomidine for opioid-sparing postoperative analgesia: a systematic review and meta-analysis. BMC Anesthesiol. 2026 Jan 13;26(1):103. doi: 10.1186/s12871-025-03606-w. PMID: 41527017; PMCID: PMC12888162.
- Mena GE, Zorrilla-Vaca A, Vaporciyan A, Mehran R, Lasala JD, Williams W, Patel C, Woodward T, Kruse B, Joshi G, Rice D. Intraoperative Dexmedetomidine and Ketamine Infusions in an Enhanced Recovery After Thoracic Surgery Program: A Propensity Score Matched Analysis. J Cardiothorac Vasc Anesth. 2022 Apr;36(4):1064-1072. doi: 10.1053/j.jvca.2021.09.038. Epub 2021 Sep 27. PMID: 34690059.