Dexmedetomidine in OB Anesthesia Systemic application

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Disclosures

- I have never used dexmedetomidine in OB anesthesia
- Currently I am working in the ICU and I am not representing the views of the department of Anesthesia of the LUKS

Agenda

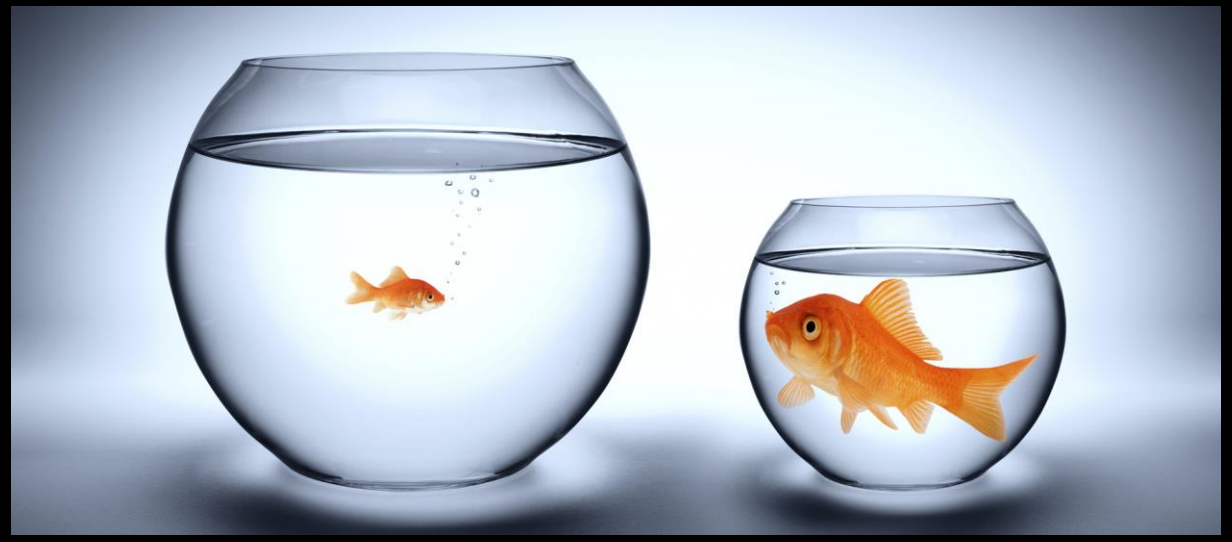
- Why Dexmedetomidine? Some general basics
- Safety first
- Dex in procedures related to general anesthesia
- Dex in procedures related to analgosedation
- Final considerations

Why dexmedetomidine ?

Some historical facts

- 1999: FDA-approval for sedo-analgesia < 24h
- 2011: EMA-approval first for sedo-analgesia in the ICU, secondarly also for procedural sedo-analgesia by anesthesiologists

My «history», approx. 2011:



Noxious Stimulation Response Index

A Novel Anesthetic State Index Based on Hypnotic–Opioid Interaction

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ABSTRACT

Background: The noxious stimulation response index (NSRI) is a novel anesthetic depth index ranging between 100 and 0, computed

0.85), and 0.70 (0.54–0.84), respectively. The P_k of effect-site propofol concentration, BIS, and AAI for observer assessment of alertness and sedation score and loss of eyelash reflex were be-

Anesthesia or sedation for gastroenterologic endoscopies

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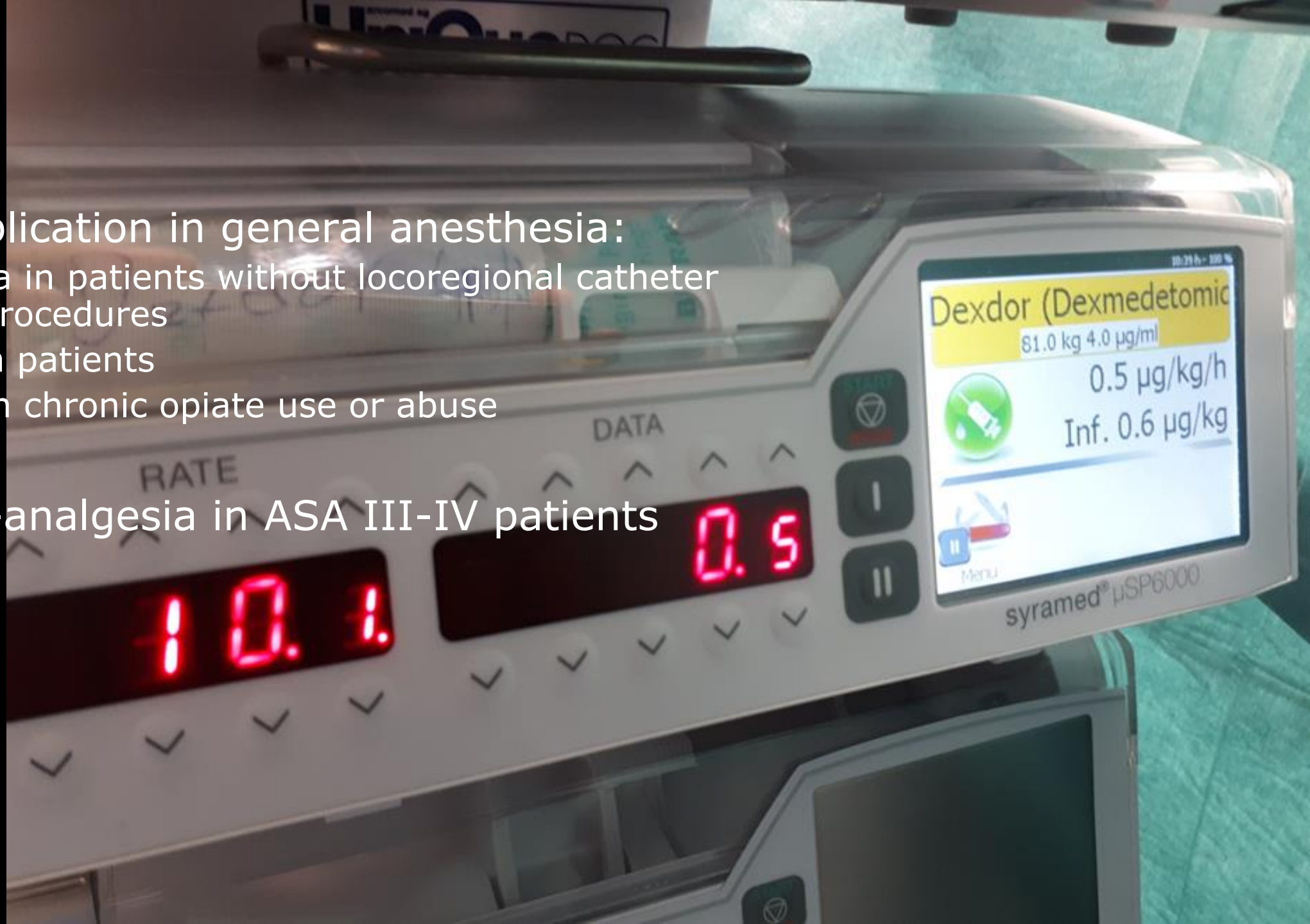
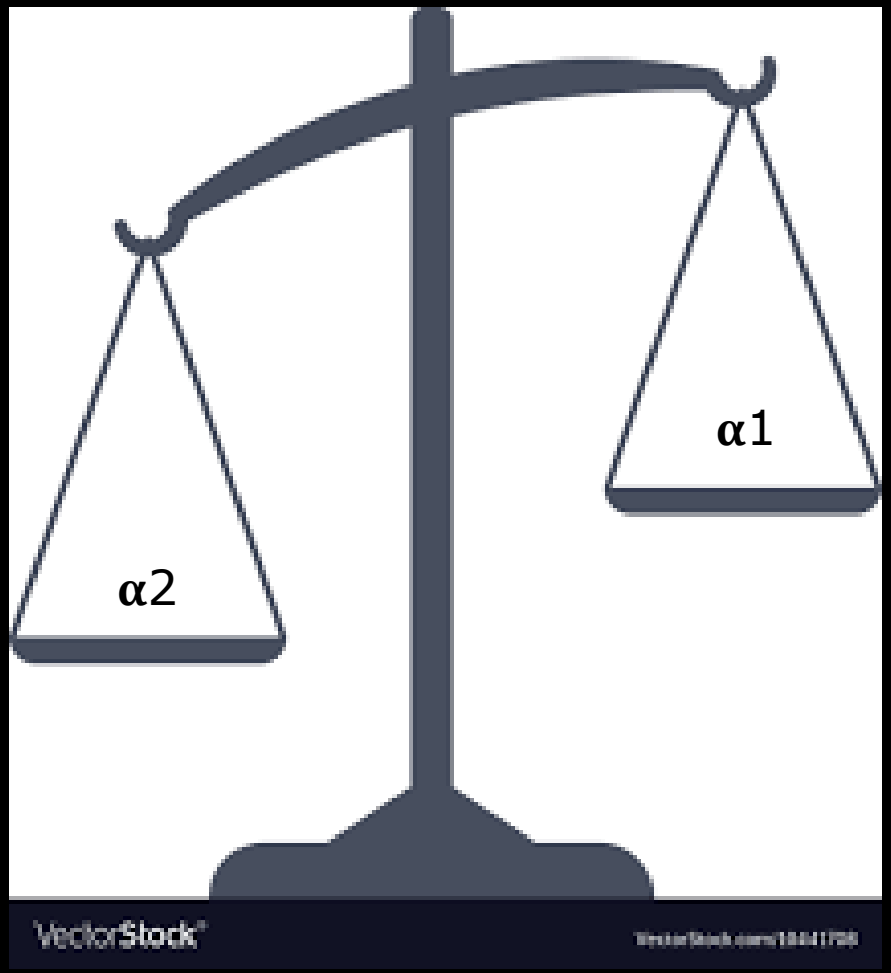
Purpose of review

Non-operating room anesthesia:
Ketofol: Propofol-Ketamine 10 ml/kg/h…..

WARNING
TO TOURISTS
DO NOT LAUGH
AT THE NATIVES

- Systemic application in general anesthesia:
  - Co-analgesia in patients without locoregional catheter for painful procedures
  - Chronic pain patients
  - Patients with chronic opiate use or abuse
- NORA: Sedo-analgesia in ASA III-IV patients
- TAVI’s





Adrenergic receptors

α1:(nor)adrenaline, phenylephrine..

α2: clonidine, dexmedetomidine

PK/PD

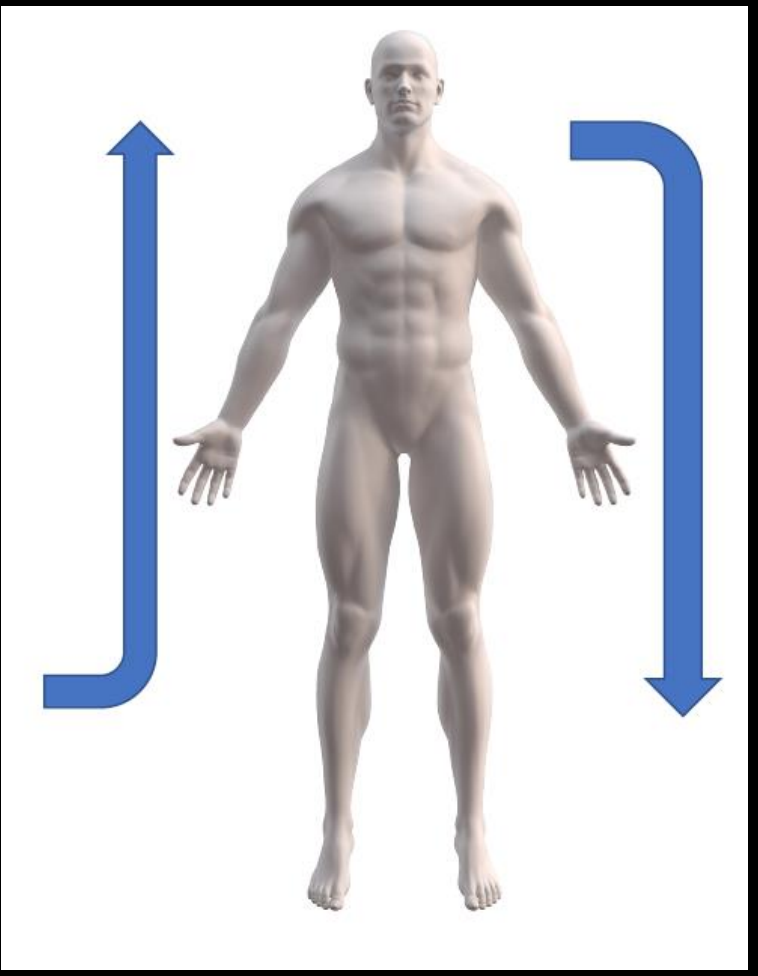
Clonidine is a α2-adrenergic receptor (α2-AR) agonist with a 220:1 ratio of α2: α1 receptor affinity

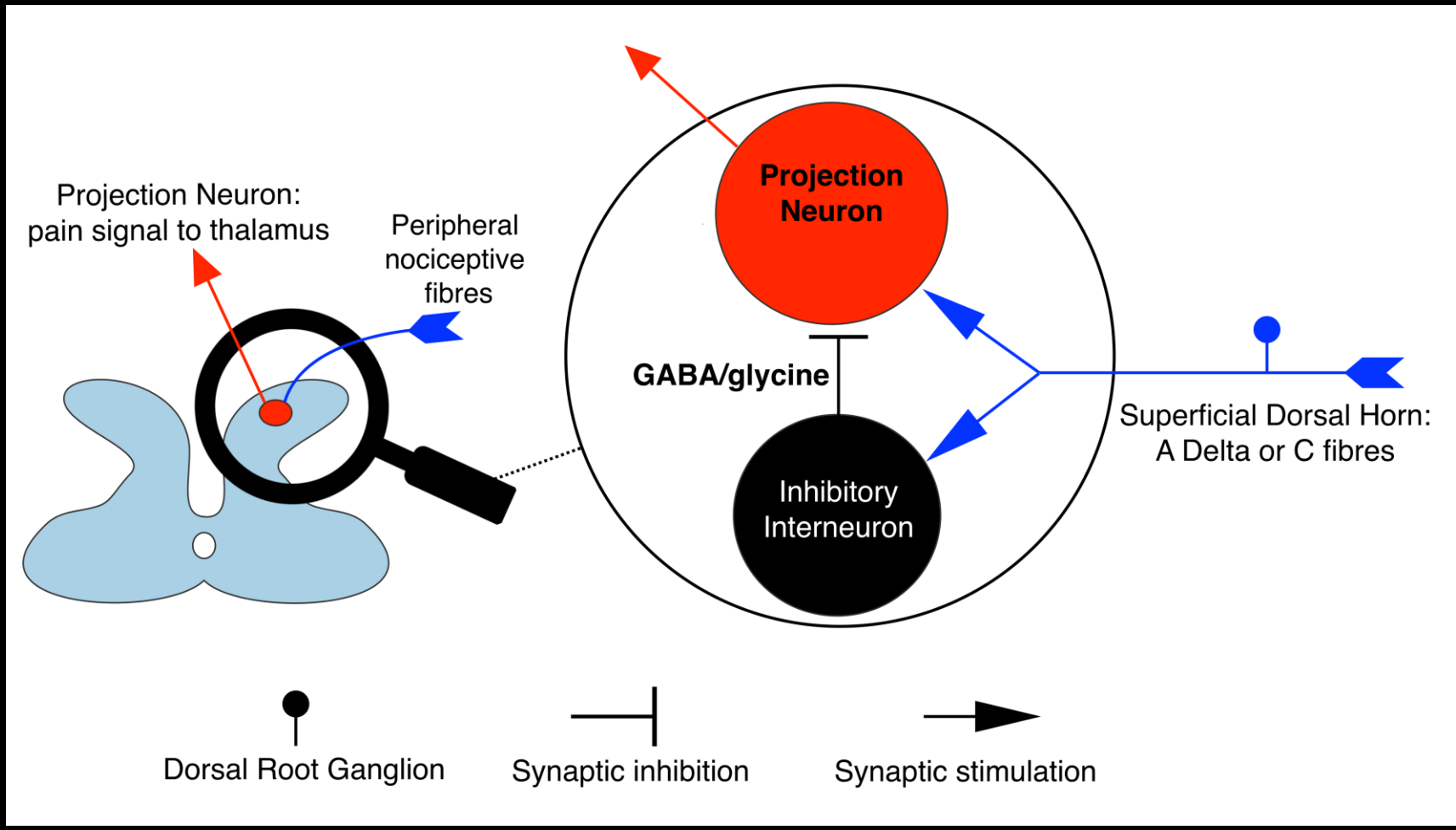
α1-AR activity is countersteered by the α2-AR. The higher the α2-AR affinity, the stronger the analgesic and sedative effect.

Dexmedetomidine's receptor affinity with a 1620:1 α2: α1 ratio (8~10 times stronger compared to clonidine)

Yu *et al*., 2016, Experimental and Therapeutic Medicine

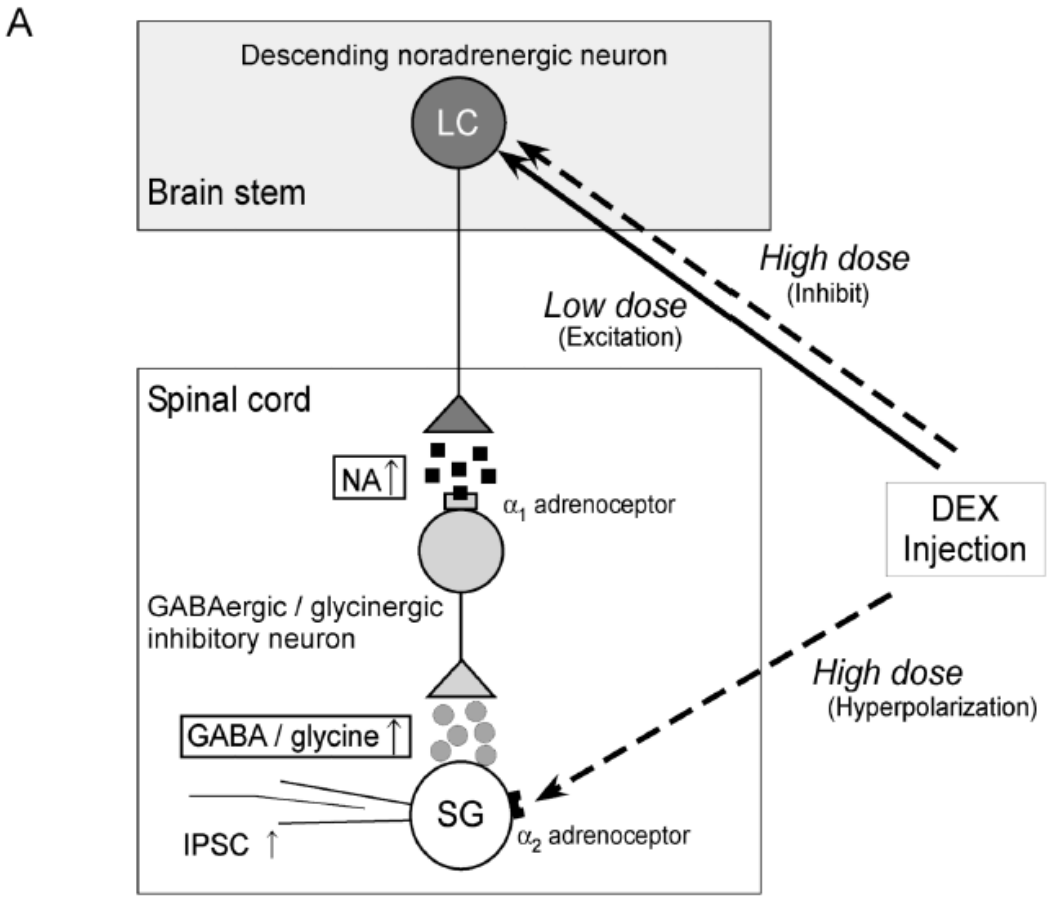
PK/PD

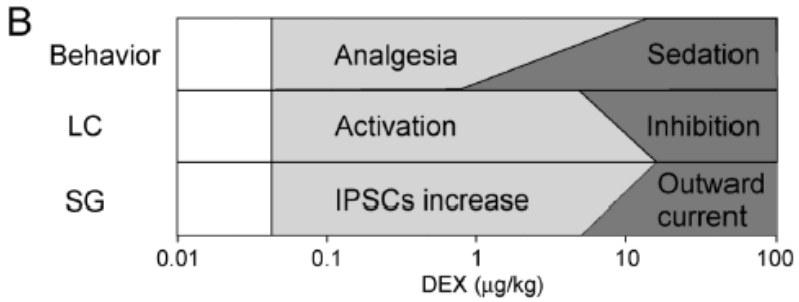




Vuilleumier *et al*., IASP, 2018

Vuilleumier *et al.*, Brain 2017





Funai *et al*., 2014, Pain

Obstetric use: Safety first

On Dec. 14, 2016, the US Food and Drug Administration issued a warning regarding impaired brain development in children following exposure to certain anesthetic agents used for general anesthesia, namely the inhalational anesthetics isoflurane, sevoflurane, and desflurane, and the intravenous agents propofol and midazolam, in the third trimester of pregnancy. Furthermore, this warning recommends that health care professionals should balance the benefits of appropriate anesthesia in young children and pregnant women against potential risks, especially for procedures that may last >3 hours or if multiple procedures are required in children <3 years old.

Olutoye *et al*., AJOG 2017

Dexmedethomidine ?

FDA category C medication:

Drug with little evidence for their safety in animals, humans or both

What is known about safety

- Degree of placental transfer 0,68-0,76 (maternal/fetal index): less than remifentanil and clonidine
- Dexmetedetomidine is fat soluble and retained in the placenta
- Increased uterine contractility in the gravid rat myometrium
- However reduced oxytocin-induced contractions in the rat myometrium
- However there is very limited in-vivo information

Chuanbao *et al*., BCPT 2015

Intravenous dexmedetomidine for obstetric anesthesia: Brainstorming possible benefits:

- Opiate sparing
- Minimal respiratory depression with sedation
- Blunting hemodynamic responses to stress and pain
- Anti-hypertensive
- Blunting opiate-induced hyperalgesia
- Better control of dose-response than clonidine
- Treatment of a shivering parturient

Hemodynamics and stress, N=68,

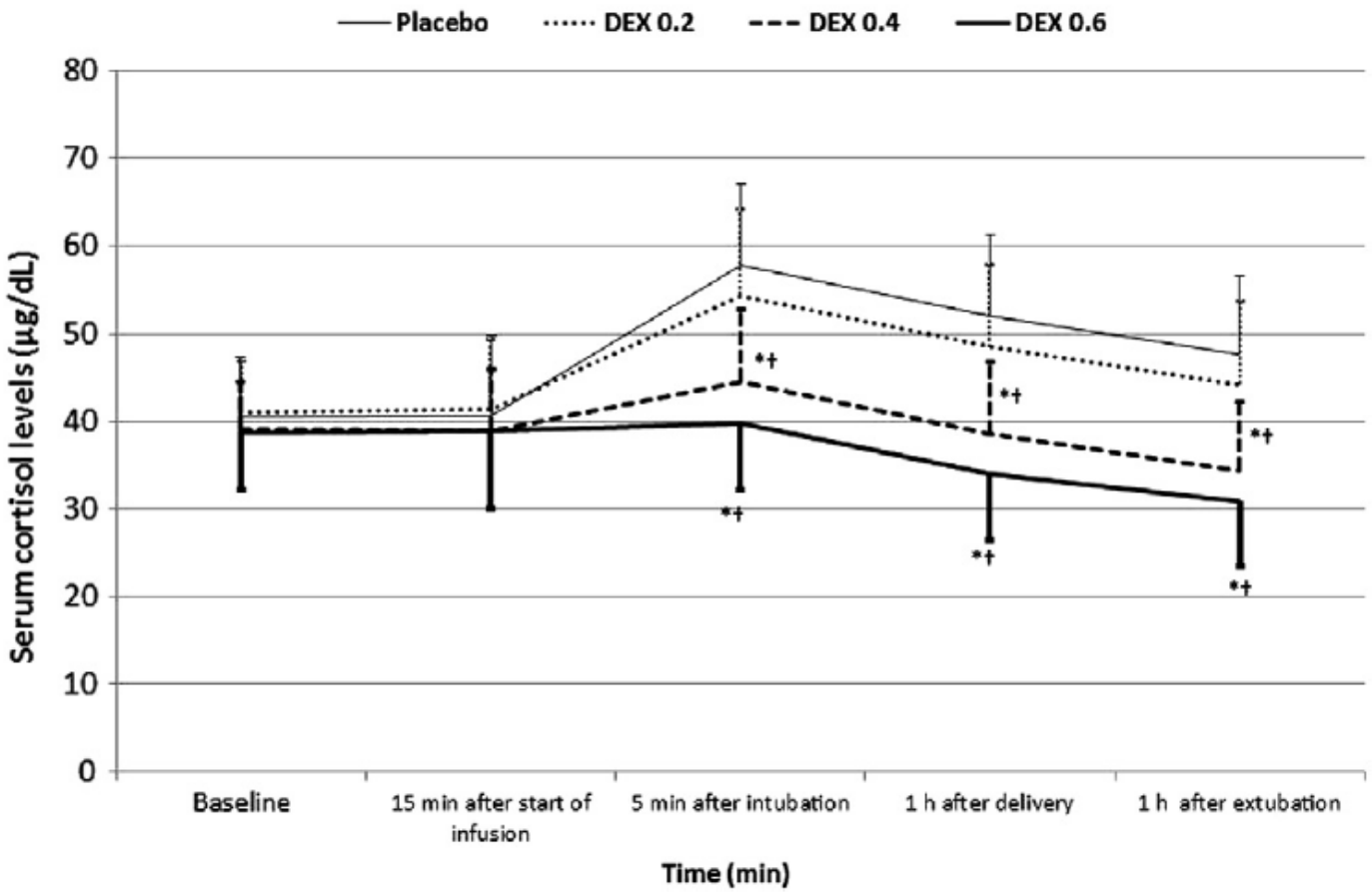


Fig. 3 Perioperative serum cortisol levels. Data are mean ± SD. $P < 0.008$ compared with the *placebo and †DEX 0.2 groups.

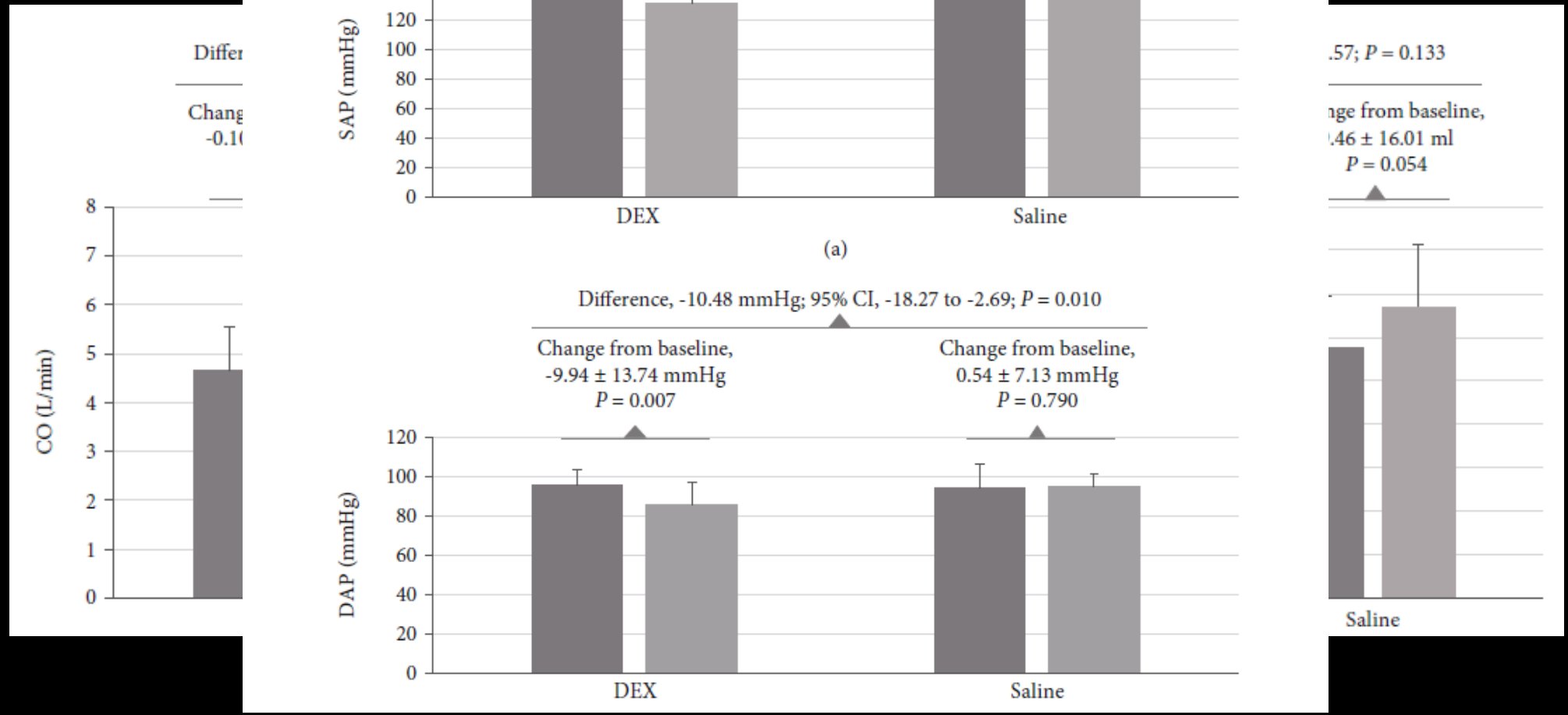
El-Tahan *et al*., IJOA 2012

	Placebo ($n = 17$)	DEX 0.2 ($n = 17$)	DEX 0.4 ($n = 17$)	DEX 0.6 ($n = 17$)
MAC-Sevo				
after intubation	0.72 ± 0.05	0.65 ± 0.16	$0.41 \pm 0.17^{*\dagger}$	$0.38 \pm 0.17^{*\dagger}$
15 min after delivery	0.64 ± 0.14	0.57 ± 0.14	$0.38 \pm 0.11^{*\dagger}$	$0.36 \pm 0.09^{*\dagger}$
30 min after delivery	0.66 ± 0.09	0.57 ± 0.13	$0.36 \pm 0.10^{*\dagger}$	$0.35 \pm 0.12^{*\dagger}$
VAS assessment of uterine relaxation	4 [2–4]	3 [2–3]	2 [1–3]*	1.5 [1–2]*†
Supplementary oxytocin (IU)	20 [10–30]	10 [10–15]*	10 [10–15]*	10 [10–10]*
Time to spontaneous ventilation (min)	4.94 ± 1.66	5.1 ± 1.25	4.8 ± 2.04	5.5 ± 2.24
Time to extubation (min)	8.3 ± 2.02	7.5 ± 1.59	7.4 ± 2.41	8.8 ± 2.62
Quality of tracheal extubation	4 [1–5]	2 [1–3]*	1 [1–3]*	1 [1–3]*
Sedation score				
5 min	1 [1–3]	1 [1–3]	1.5 [1–3]	2 [1–3]*†
15 min	1 [1–1]	1 [1–2]	1 [1–1]	2 [1–2]*†
30 min	1 [1–1]	1 [1–1]	1 [1–1]	1 [1–1]
60 min	1 [1–1]	1 [1–1]	1 [1–1]	1 [1–1]
Patients experiencing PONV	4 (23.5%)	1 (5.9%)	0*	0*

Data are mean ± SD, median [range] or number (%). VAS: visual analog scale; PONV: postoperative nausea and vomiting. $P < 0.05$ compared with *placebo and †DEX 0.2.; MAC-Sevo, minimum alveolar concentration of sevoflurane; VAS, visual analog scale; PONV, postoperative nausea and vomiting.

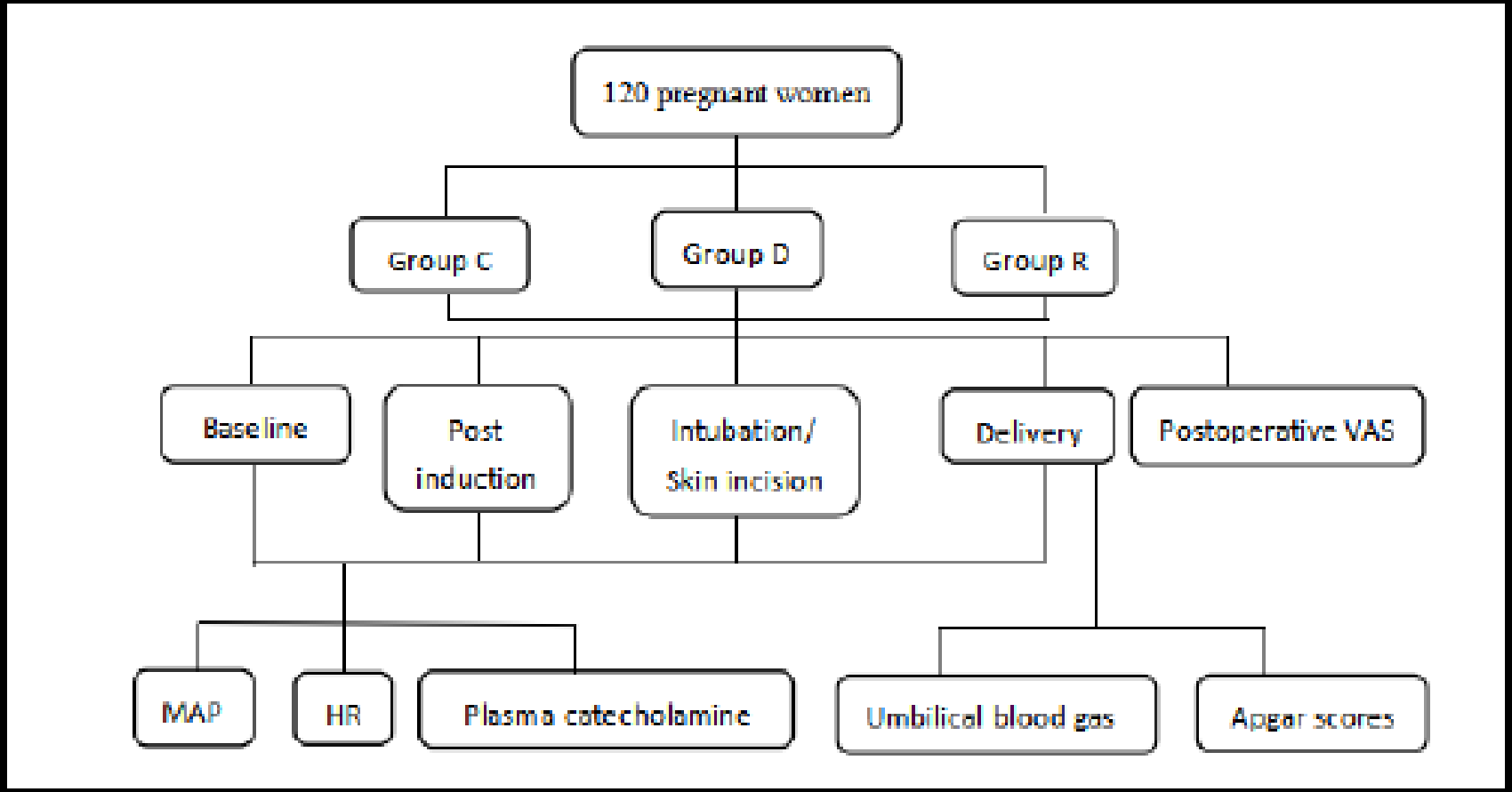
El-Tahan *et al.*, IJOA 2012

Preeclampsia and CS in GA N=36
Measur er CS

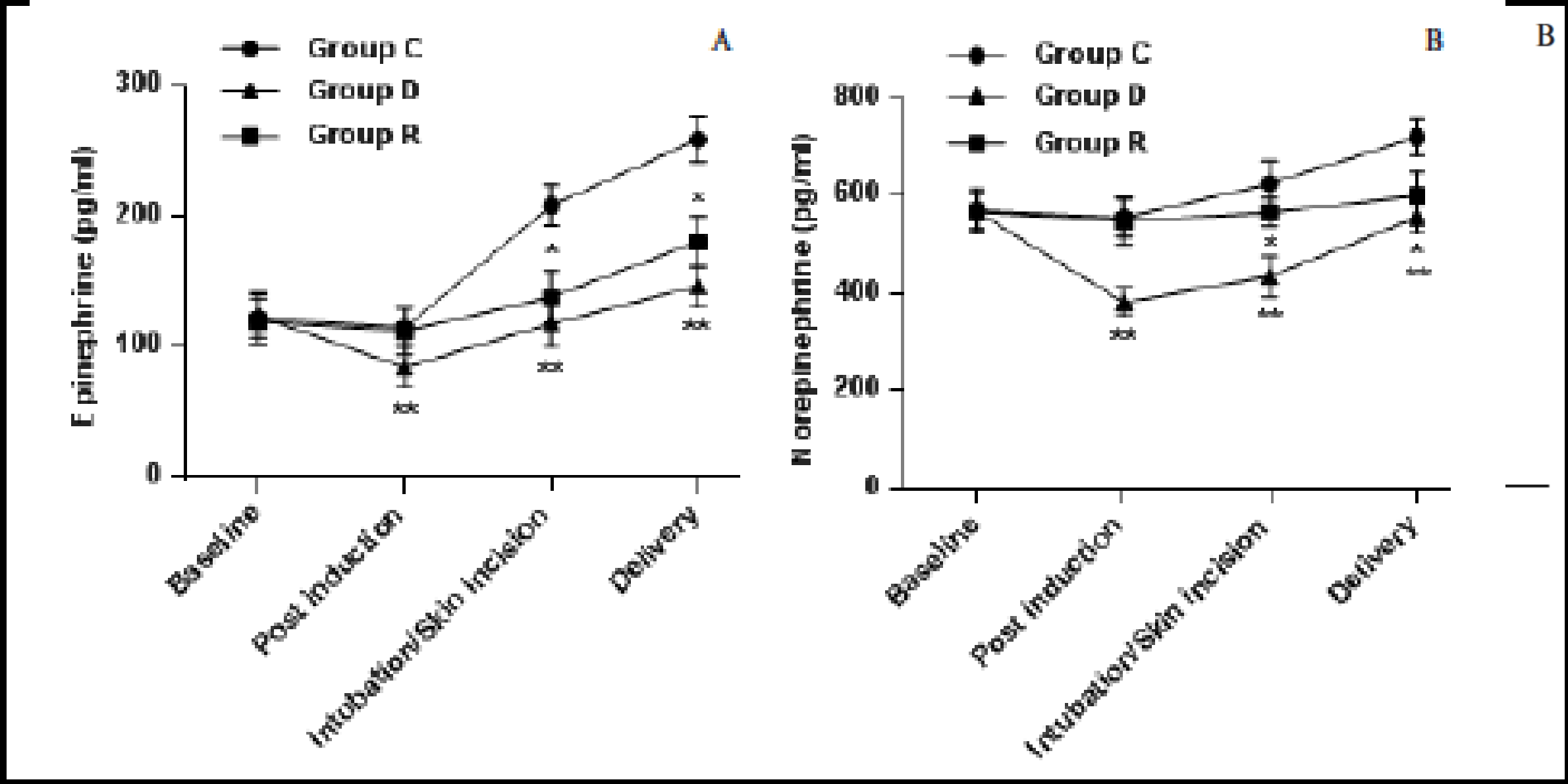


Lv *et al.*, Computational and Mathematical Methods in Medicine 2022

Dexmedetomidine vs. Remifentanil in GA
N=120



Yu *et al*., Biomed Pap Med Fac Univ Palacky Olomouc 2020



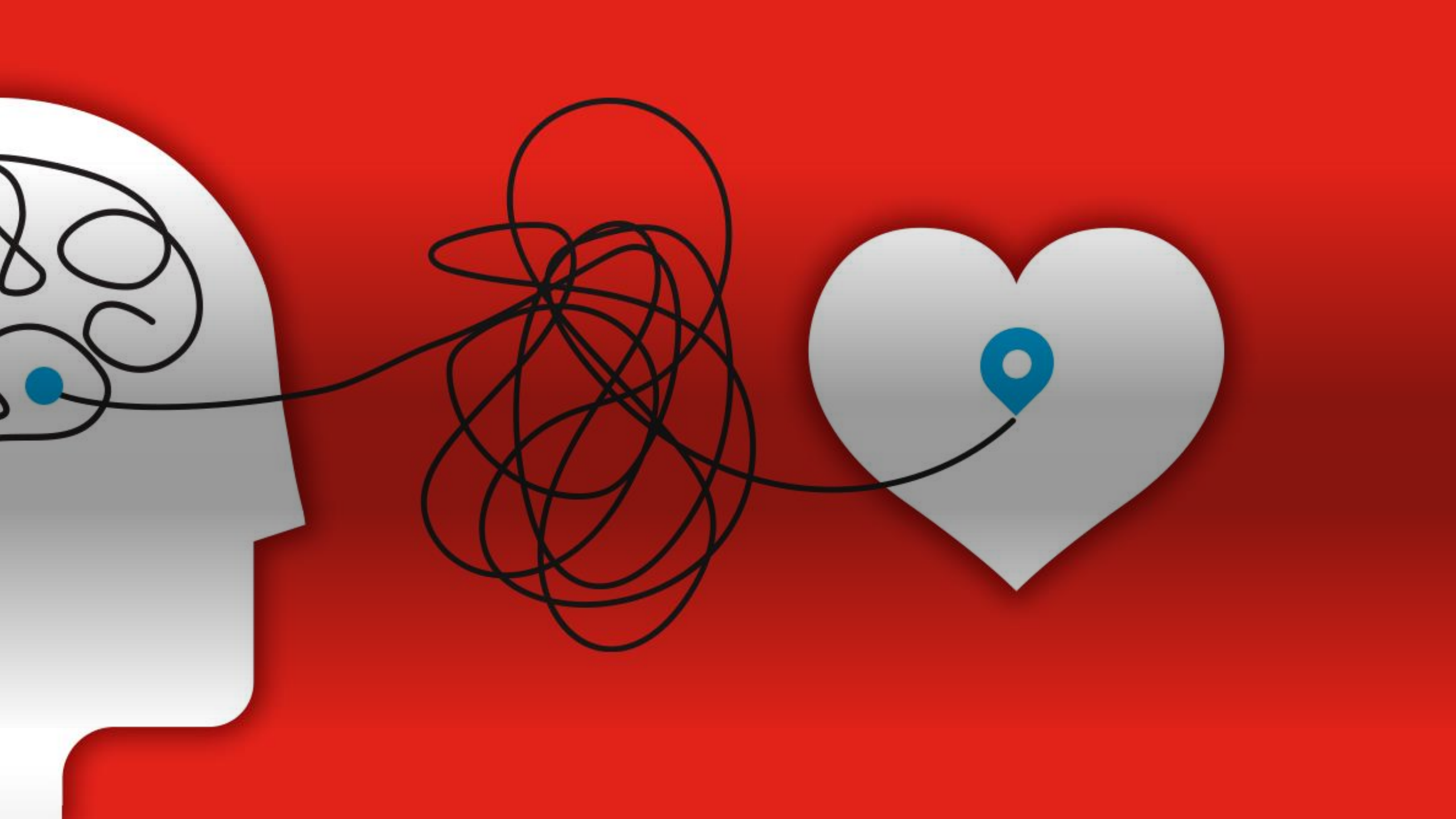
Yu *et al*., Biomed Pap Med Fac Univ Palacky Olomouc 2020

Table 2. Maternal postoperative VAS and total tramadol consumption.

	Group C (n = 40)	Group R (n = 40)	Group D (n = 40)	*P*
Postoperative VAS				
1h	5.2±1.13	4.9±1.07	1.9±0.89*	<0.001
2h	4.4±1.10	4.3±1.05	3.2±1.06*	<0.001
3h	3.6±1.08	3.4±1.12	3.3±1.23	0.493
Total tramadol consumption (mg)	152±18.0	146±21.0	80±22.0*	<0.001

*$P<0.05$ compared with the control and remifentanil groups.Values are presented as the mean ± standard deviation.

Yu *et al*., Biomed Pap Med Fac Univ Palacky Olomouc 2020



Other uses in Obstetric Anesthesia/Analgesia?

- Remifentanil PCA – Antihyperalgesic effect
- IVF – Analgesia and sedation for oocyte retrieval
- Analgosedation for intrauterine procedures (Laser for FFTS, placement of drains)

A case report first..from Brigham Women's Hospital

- 31 yo parturient with a spina bifida for induction of labor
- @ 3 cm dilatation start of a "standard" Fentanyl iv PCA, bolus 13 mcg/lockout 3 minutes
- Over a period of 12 h uncontrollable pain, refuses more opiates and refuses a CS
- Bolus dose of 0.5 mcg/kg followed by 0.2 mcg/kg/h with a VAS reduction from 9 to 2/10, however gradually increased to 0.6 mcg/kg/h
- 16 hours later -> chorioamnionitis -> CS
- Dexmedetomidine continued during the CS

A. Palanisamy *et al*., IJOA 2009

- Hemodynamics stable
- Healthy baby, APGAR 7/8/10
- Uneventful maternal outcome, normal postoperative analgesic needs
- Mother happy and desires the same “drugs” for the next baby

Double blind combination of remifentanil and dexmetedomidine N=60

- Group I: Remifentanil 0.25 mcg/kg, lockout 2 min,
  with Bolus Dexmetedomidine 1 mcg/kg followed by 0.5 mcg/kg/h
- Group II: Remifentanil 0.25 mcg/kg, lockout 2 min

Abdalla *et al*., Saudi Journal of Anesthesia 2015

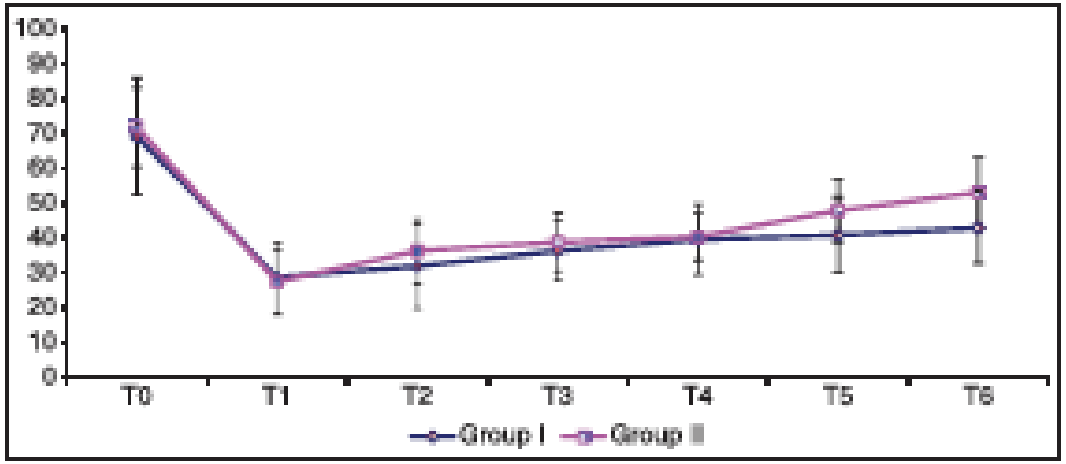


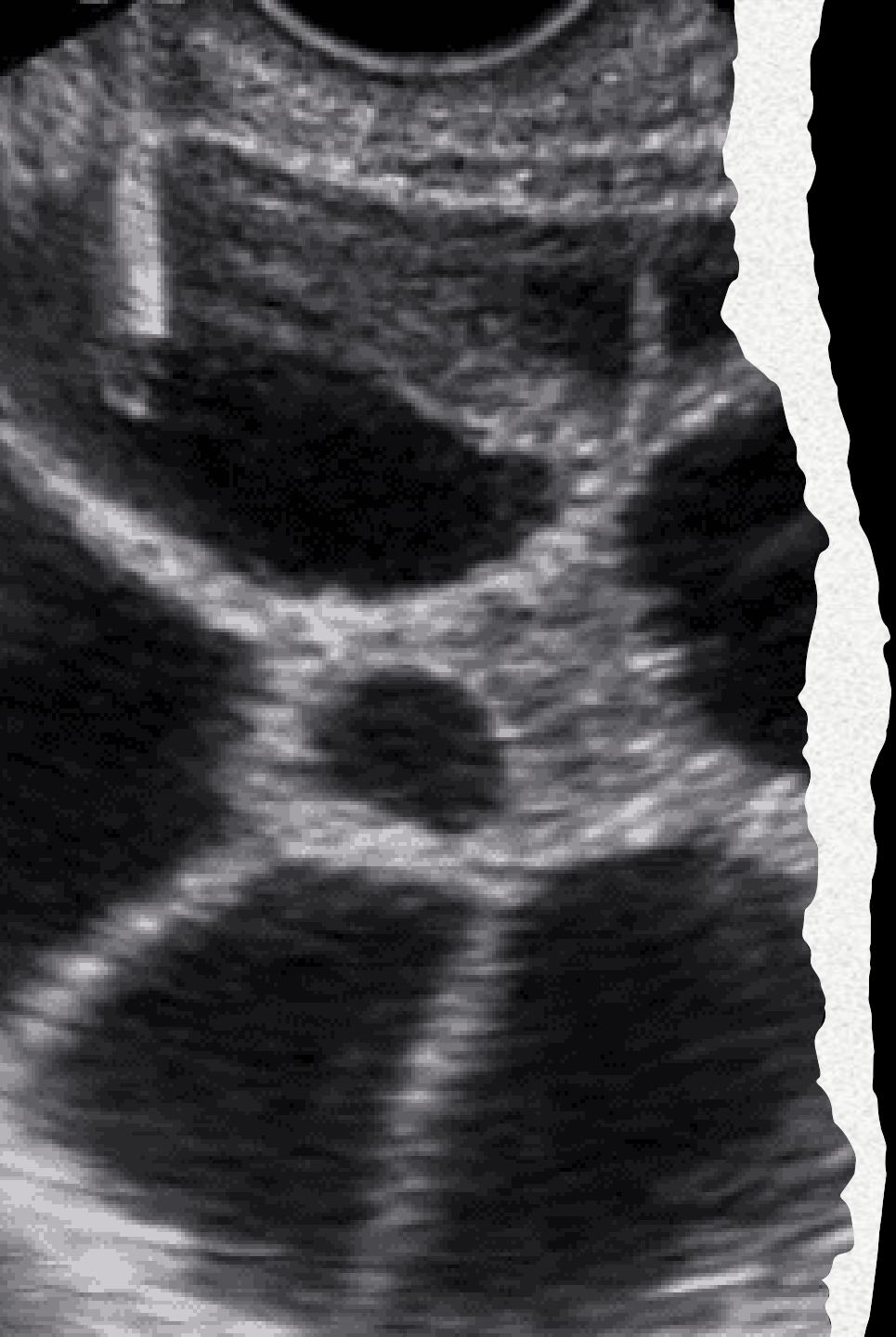
Figure 1: Visual analog scale pain score; data are expressed as mean ± standard deviation

- More desaturations in the remi mono group
- More nausea and vomitting in the remi mono group
- Less remifentanil consumption in the combined group
- Higher maternal satisfaction in the combined group
- Not significant: Hemodynamics, CS conversion rate, foetal outcomes, nonreassuring FHR

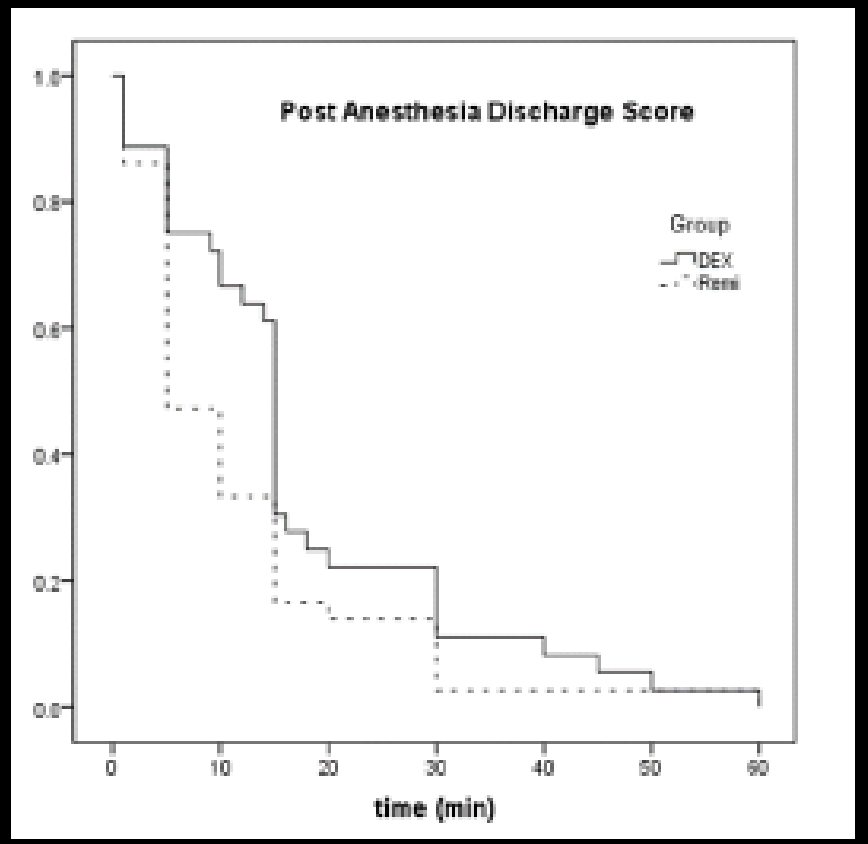
RCT, N=60, Dexmetedomidine vs Midazolam

Variable	Group (D) (n=26)	Group (M) (n=26)	P
VAS			
At 0 time	43.68±13.18	47.84±13.77	0.14 NS
At 5 min	40.32±12.38	47.68±14.8	0.03*
At 10 min	39.92±12.88	49±14.15	0.01*
At 15 min	43.08±12.49	47.44±13.39	0.11 NS
At 20 min	42.04±11.51	46.88±12.95	0.08 NS
At 25 min	35.24±10.99	39.88±12.43	0.08 NS
Amount of rescue propofol (mg) Median (range)	55 (20-100)	130 (100-230)	<0.01†

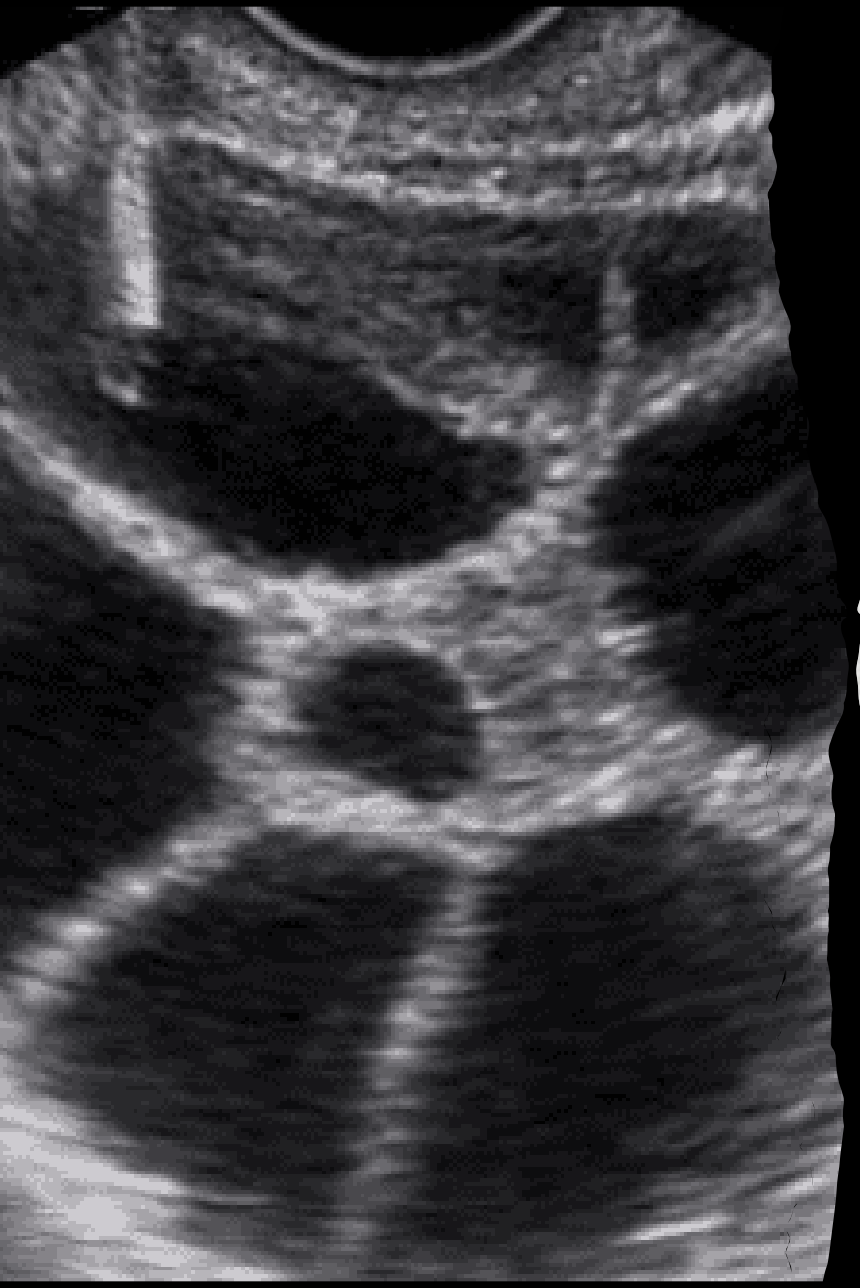
Enabtiti *et al*., Anesth Essays Res. 2017



Comparison of dexmetedomidine and fentanyl vs midazolam and remifentanil
Endpoint: Propofol rescue and IVF success
N=72



Matsota *et al*., Journal of Clinical Medicine 2021



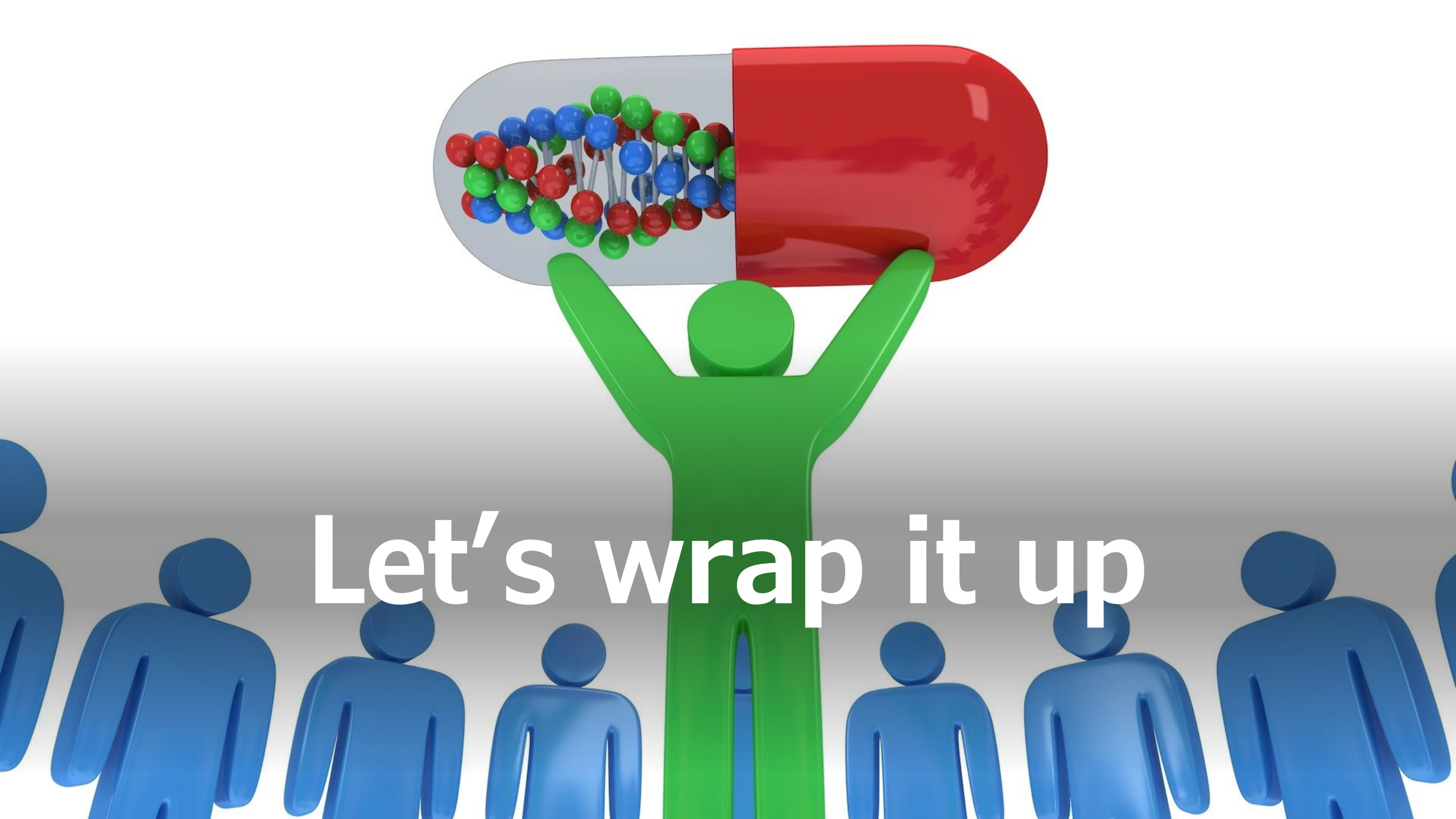
Physician satisfaction (Gynecolologist): NS

Dexmetedomidine: More propofol rescue needed

Dexmetedomidine: 10 more minutes to discharge

Oocytes: Better quality @ day 3 in the Dex group

IVF outcome parameters similar in both groups



Let’s wrap it up

Pro's

Con's

✓ General Anesthesia:
- Antihypertensive
- Sedative
- Uterine contraction maintained
- Postoperative analgesia

✓ Obstetric Analgesia:
- Opiate sparing
- Maternal satisfaction
- PONV-rates lower

✓ Oocyte retrieval
- No effect on oocytes or fertilization rate
- Equivocal propofol recue needed (depending on comparator)

X
- Off label
- Unknown effect on foetus
- Maternal hypotension/bradycardia

X
- Unknown effect on foetus

X
- Data very limited concerning fertilization rate
- Data very limited on effect on oocytes

Until further notice
Off-label use
Studies performed up to date somewhat..
Large studies needed for safety

Questions?
Thank you