Dexmedetomidine and labor analgesia

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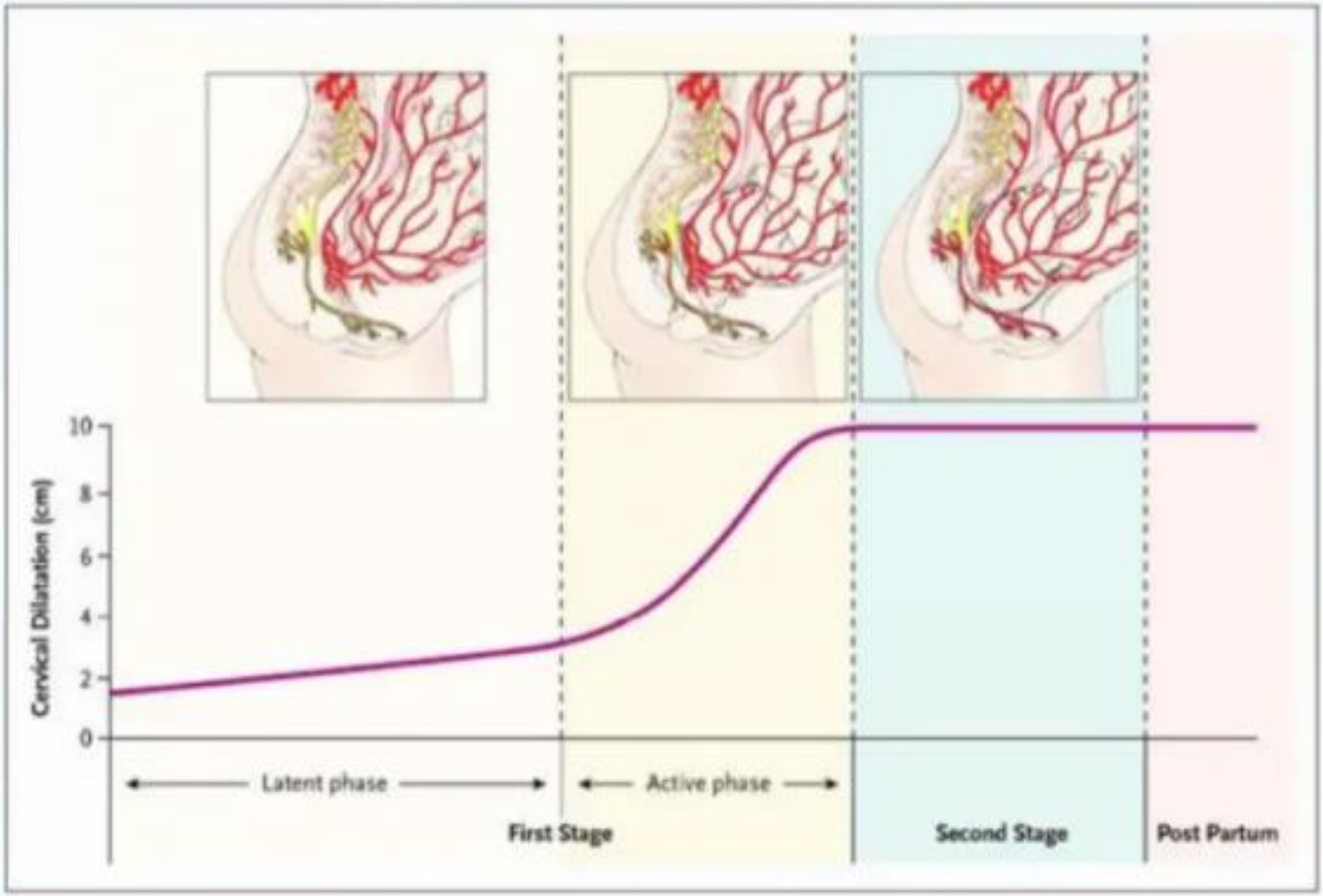
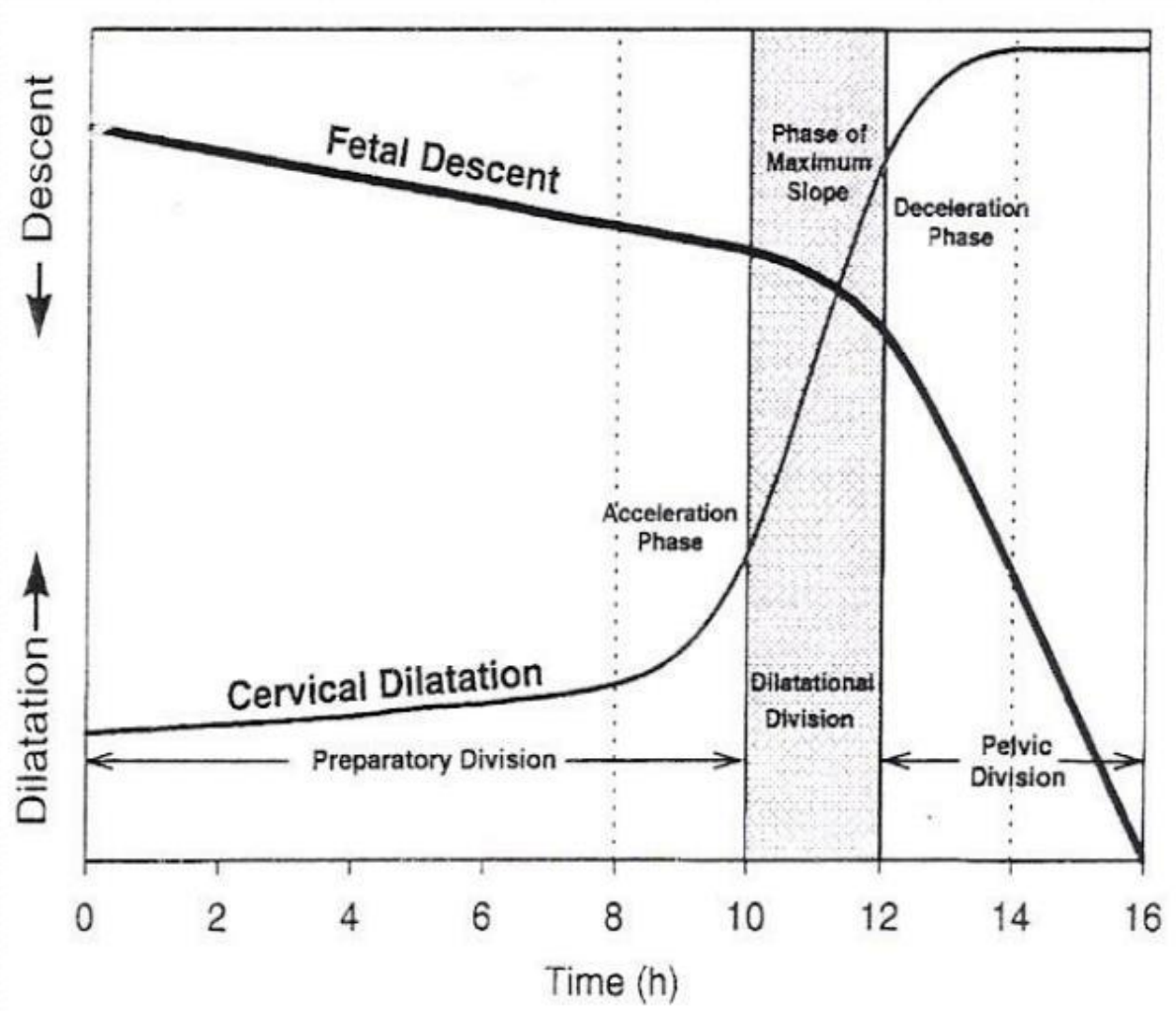
Board certificated

Anesthesiologist, intensivist and pain medicine specialist

Stages of Labor



2nd STAGE OF LABOR: FETAL DESCENT



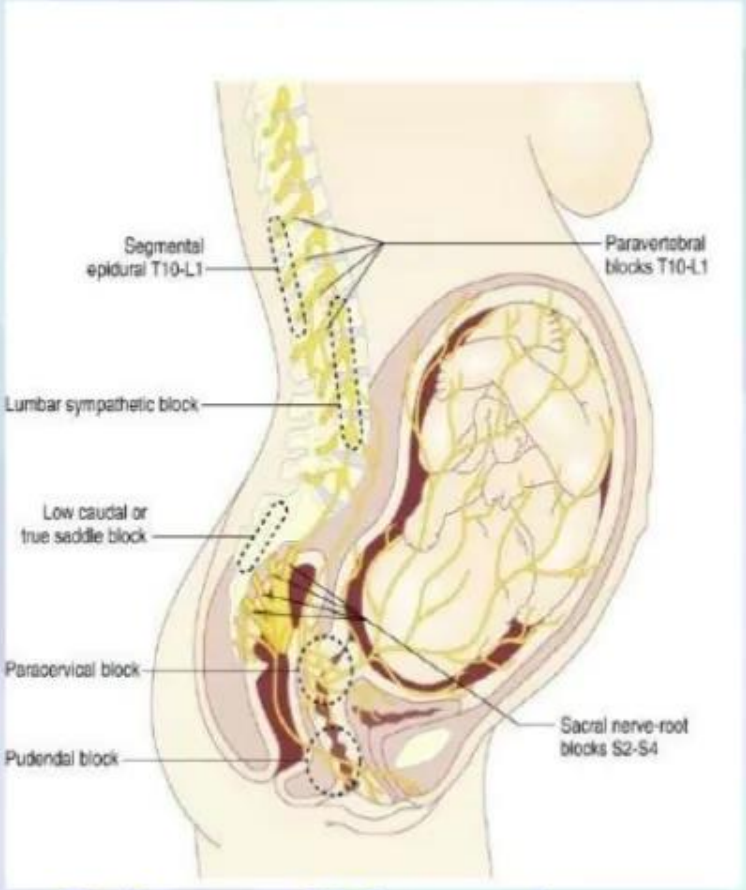
Pathophysiology of Labour pain

Visceral pain

- First stage
- T_{10} - L_1
- Distension and stretching of LUS

Somatic pain

- Second stage
- S_2-S_4
- Distension of pelvic and perinial structures and compression of LS plexus



Pathways of labour pain

Epidural infusion

- After loading dose start infusion
- Take 12ml of 0.5% Marcaine & dilute to 48ml to get 0.125% Marcaine. To this add 2ml (100mcg) Fentanyl to get total volume of 50ml. Start infusion at 8ml/hour using an infusion pump
- Measure and record maternal heart rate (HR), blood pressure (BP) and FHR at 5 minute intervals for first 15 min then half hourly
- Assess and record the sensory level of the block hourly
- The anaesthetist should be immediately available for review of women and management of initial complications for at least 20 minutes after initial dose

Maintenance epidural doses

- 50ml epidural mix dose can be repeated at intervals as required
- These can be given by appropriately trained nurses
- An appropriate position should be adopted
- Vital signs monitoring and block level assessment should continue as for initial dose

Vital signs – Pulse, BP, Respn Rate – every 5 minutes for first 15min. If stable thereafter every hourly

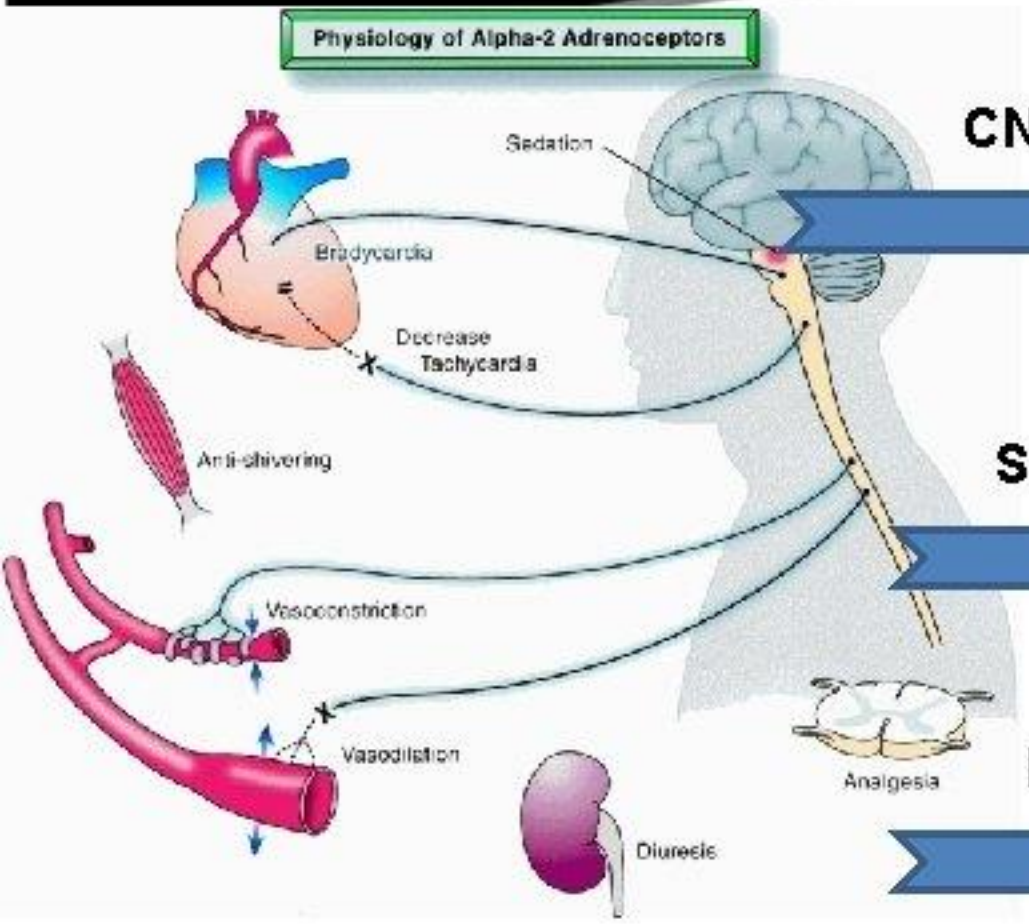
Modalities for systemic opioids

Meperidine	• Dose : 50-100 mg IM or 25-50 mg IV • onset: 45mins for IM , 5mins for IV • optimal time: Given early (>4hrs from expected labor) for IM and within 1 hour from labor for IV
Fentanyl	• 50-100µg/hr, peaks @ 3-5mins
Remifentanil	• ½life 6mins, 0.5mirogms/kg
Nalbuphine	• may also be used

Some centers advocate the use of **IV-PCA fentanyl pumps or accufusers** during labor with special considerations including :

- Loading dose of 50 – 100 ug
- No background infusion
- Carefully controlled bolus dose (around 10ug) and lockout periods (10mins) with a 4 hour limit of 300mg

Action of Dexmedetomidine

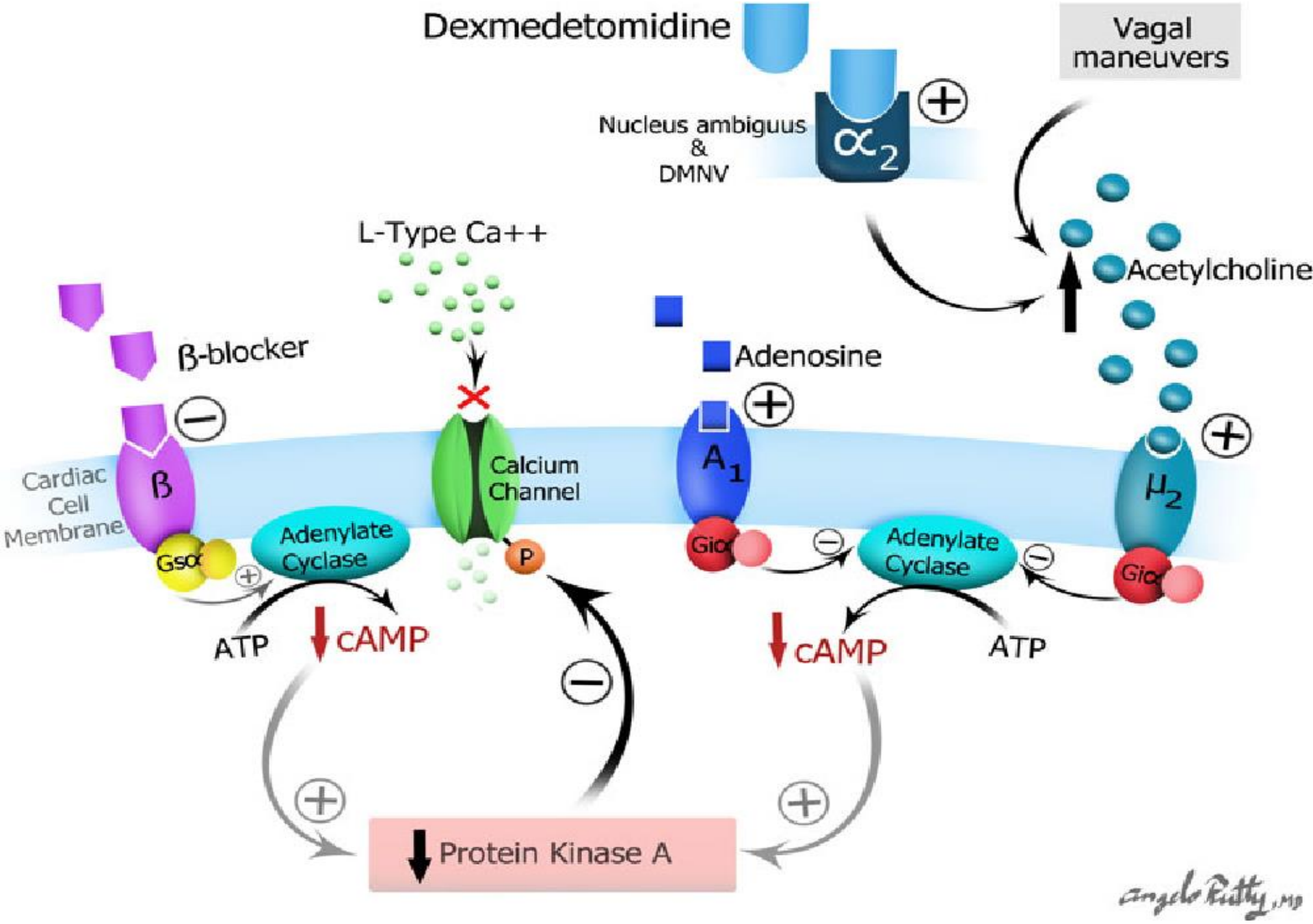


CNS → **SEDATION, SYMPATHOLYSIS**

SC → **ANALGESIA**

PNS → **ANALGESIA**

- Dexmedetomidine is a highly selective, nonsubtype-specific alpha-2 adrenergic agonist that is approved for clinical use for its sedative properties.Alpha-2 adrenergic agonists mediate haemodynamic effects by several different mechanisms. They mediate sympatholytic effects through activation of centrally and peripherally located alpha-2 adrenoceptors. They also activate vascular smooth muscle alpha-2 adrenoceptors, which are responsible for direct peripheral vasoconstrictive effects.
- Arachidonic acid may play an important role in the enhancement of myometrial contraction induced by dexmedetomidine by increasing myofilament calcium sensitivity. Dexmedetomidine may be used as a sedative agent to promote uterine muscle contraction and suppress bleeding after fetal delivery.


Dexmedetomidine
Vagal maneuvers
Nucleus ambiguus & DMNV
α2
L-Type Ca++
Acetylcholine
β-blocker
Adenosine
Cardiac Cell Membrane
β
Calcium Channel
A1
M2
Gsα
Adenylate Cyclase
Gio
Adenylate Cyclase
Gio
P
ATP
cAMP
cAMP
ATP
Protein Kinase A

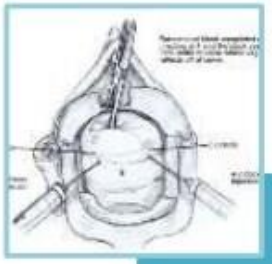
Dexmedetomidine

Recently , intravenous infusion of Dexmedetomidine is being used in combination with remifentanil infusion for labor analgesia.

Advantages

- Opioid sparing effect
- Adequate level of sedation
- Minimal haemodynamic side effects.
- Very low incidence of nausea and vomiting

Local Techniques



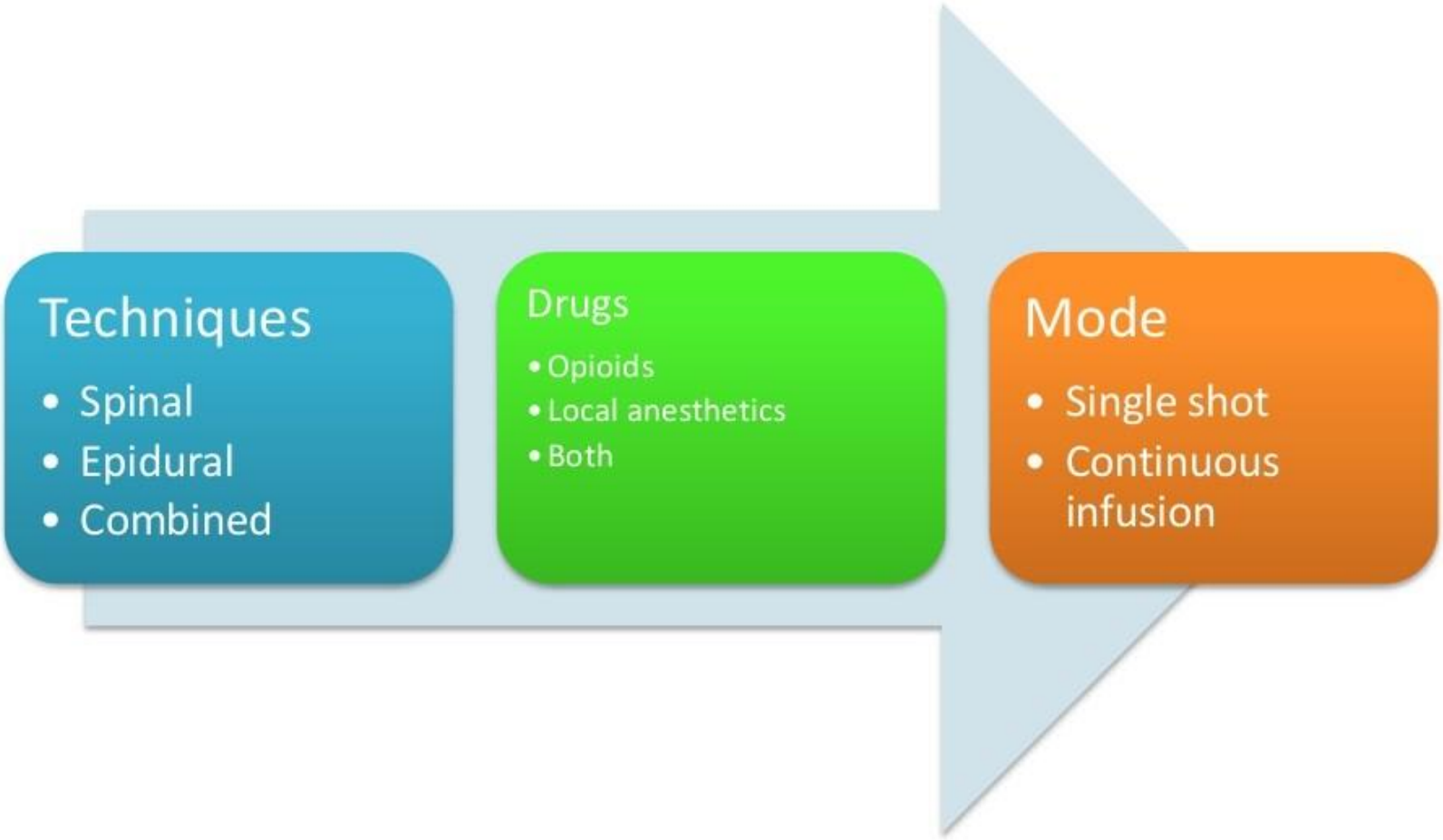
Paracervical block

- Local bilateral injection near the cervix
- Given during 1st stage of labor
- Disadvantage
  - fetal bradycardia
  - Lidocaine toxicity

Pudendal Block

- Causes perineal anesthesia
- Useful in 2nd stage of labor

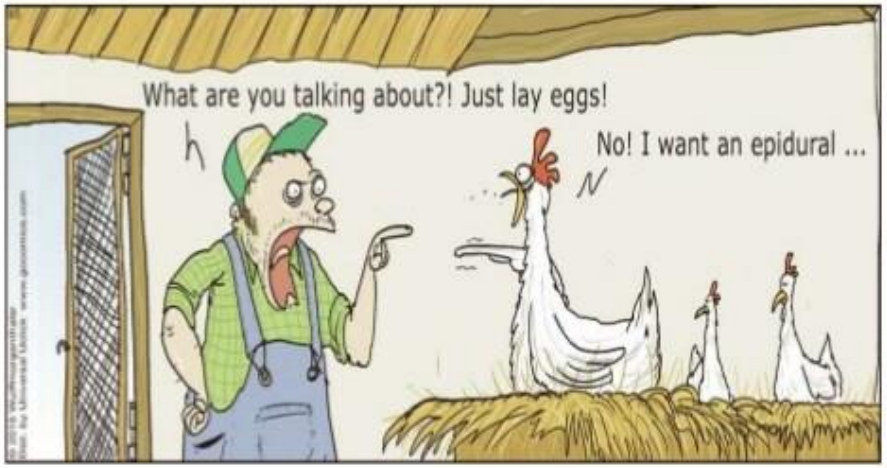
Neuraxial Blocks



Neuraxial Blocks

Advantages

- Most effective & Least depressant
- Great versatility in strength & Duration
- Reduces maternal Catecholamines
- Improved Uteroplacental perfusion
  - Low dose LA – *NO Effect on Uterine activity*
  - Low dose opioids – *NO neonatal depression*



Neuraxial Blocks

Specific Fetal Advantages

- Uterine perfusion maintained
- Doesn't affect Apgar scores, acid-base status
- Neurobehavioral effects absent
- LA toxicity - *extremely* rare

Specific Maternal Advantages

- <u>Blunts Haemodynamic response in :</u>
  - Hypertensive disorders
  - Cardiac disease
  - Asthma
  - Diabetics
- <u>Avoids depressant effects of opioids in :</u>
  - Prolonged labor
  - Prematurity
  - Multiple gestation
  - Breach delivery

Contraindications to neuroaxial blocks

ABSOLUTE

- Patients refusal
- Inability to cooperate
- Increased intracranial pressure
- Infection at the site
- Frank coagulopathy
- Hypovolemic shock

RELATIVE

- Systemic infection
- Preexisting neurological deficiency
- Mild coagulation abnormalities
- Relative hypovolemia
- Poor communication

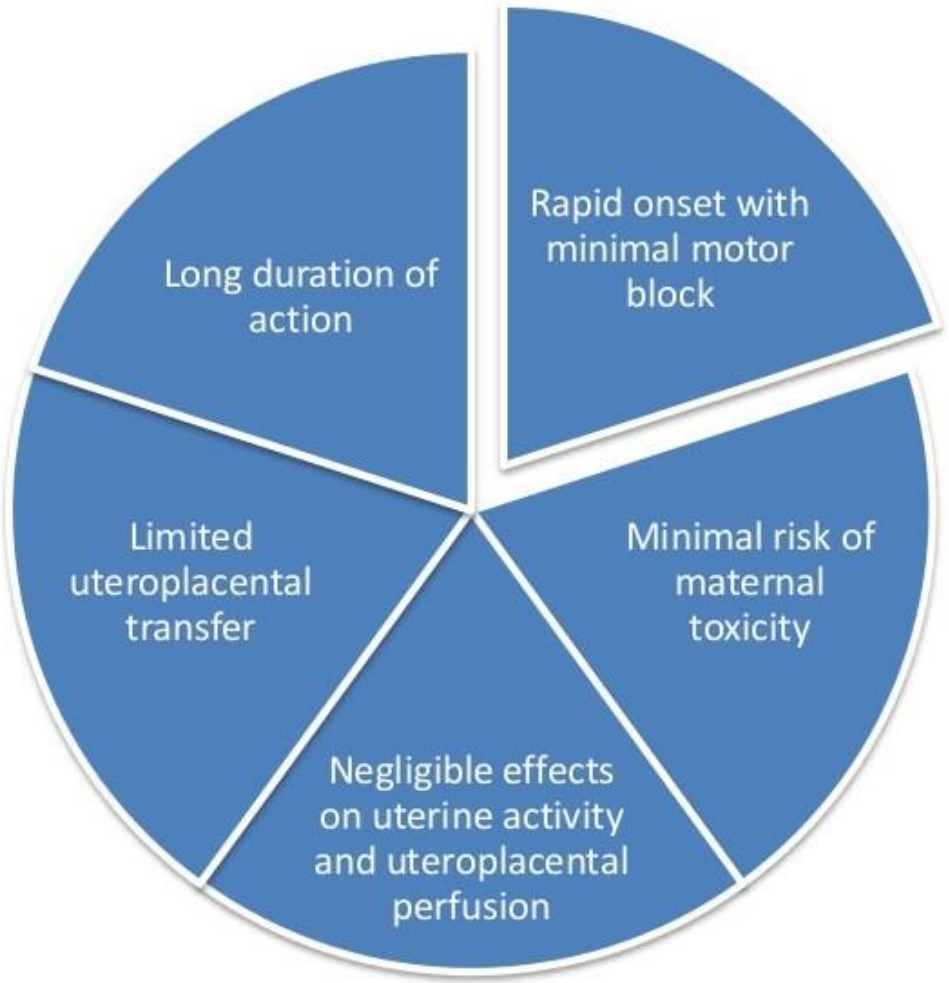
Spinal Anelgesia

Involves intrathecal injection of opiods, Local anesthetics or more commonly a mixture of both.

Has the benefit of having the most rapid onset of analgesia.

The most commonly used modality for labor, the “saddle block” provides profound perineal analgesia with minimal hemodynamic side effects.

Choice Of Local Anesthetic



Local Anesthetic agents

Lignocaine	• Rapid onset • Dense motor block • Risk for cumulative toxicity
Bupivacaine (0.0625%)	• Good sensory block • Minimal motor block • No adverse effects on labor
Ropivacaine	• Lower toxicity • Less motor block • Less potent
Levobupivacaine	• Lower toxicity than Bupivacaine

Intrathecal opioids

- Inadequate analgesics if used alone
- Synergize with local anesthetics
- Speed onset of analgesia
- Improve quality of analgesia
- Permit use of very dilute LA solutions
- Help relieve persistent perineal pain and unblocked segments

Side effects of Intrathecal opioids

Nausea, Vomiting

Pruritis

Sedation

At very high doses can cause respiratory depression and fetal bradycardia

These side effects can be controlled via

- Using the least effective doses
- Mixing opioids with local anesthetics

Continuous Spinal Analgesia

Used by some centers in Europe, however it is restricted by FDA regulations in the US.

Uses 28 or 32-G catheters for 22 or 26-G spinal needles.

Risks include development of cauda Equina Syndrome, hypotension and nerve injury.

Complications of Epidural analgesia

- Hypotension
- Inadequate analgesia
- Extensive motor blockade
- Respiratory depression
- Faulty placement
- Back pain

Dexmedetomidine is a highly selective α-2 adrenergic receptor agonist with several diverse actions like sedation, anxiolysis, sympatholysis, analgesia, and decreased intraoperative anesthetic requirements (narcotic, inhalational), cardiovascular stability, smooth recovery when used as an adjunct to general anesthesia, and above all, preserves respiratory function. It was approved by United States Food and Drug Administration (US FDA) in 1999 for use in humans for short term sedation and analgesia in Intensive Care Unit (ICU) for less than 24 hours..

There are several off label uses of dexmedetomidine like sedation for FOB (fiberoptic bronchoscopy) and intubation, sedation for Magnetic Resonance Imaging (MRI), endoscopies and ophthalmic surgeries, as an anti-shivering agent post operatively, for alcohol and opioid withdrawal.

Though not approved for use in pediatric patients, especially infants, there is a lot of literature available in the form of case reports and review articles that describes successful use of dexmedetomidine in this group of patients as well.

It is been rigorously explored as an adjunct to local anesthetic in spinal and epidural anesthesia. [But there is some reluctance in using dexmedetomidine by anesthesiologists in parturients; the reason being possible uteroplacental transfer and untoward effects on the baby.

There are several case reports describing successful use of dexmedetomidine in labor analgesia if regional was contraindicated, if patient not willing for labor epidural or as an adjunct to labor epidural if pain relief was not satisfactory, without any adverse fetal outcomes in the recommended doses (1 ug/kg loading dose over 10-15 minutes followed by an infusion at 0.2-0.7 ug/kg/hour). Remifentanil is now considered safe for use in labor analgesia as it gets metabolized by esterases and thus has negligible uteroplacental transfer.

Similarly, literature describes that as dexmedetomidine has a high placental retention, it doesn't cross the placenta to reach the fetus.

Epidural analgesia remains the gold standard for labor. But in parturients with cardiac ailments who cannot tolerate hemodynamic disturbance during labor, parturients in whom epidural is contraindicated (coagulopathy, spinal cord diseases, etc) or epidural is not effective, dexmedetomidine can be used by experienced clinicians.

- Dexmedetomidine may be used as a sedative agent to promote uterine muscle contraction and suppress bleeding after fetal delivery.

- Dexmedetomidine might differently alter the spontaneous contraction-forces and contraction-frequencies of uterine rings in all pregnancy terms of rats in Krebs and Ca2+-free solutions.

- Using a clinically-relevant dosing regimen, intravenous infusion of dexmedetomidine produced significant maternal sedation without altering fetal physiologic status

Maternal and preterm fetal sheep responses to dexmedetomidine

K. Uemura, K. Shimazutsu, R. J. McClaine, D. J. McClaine, R. J. Manson, W. D. White, P. B. Benni, J. D. Reynolds

Int J Obstet Anesth. Author manuscript; available in PMC 2013 Oct 1.

Published in final edited form as: Int J Obstet Anesth. 2012 Oct; 21(4): 339–347. Published online 2012 Aug 28. doi: 10.1016/j.ijoa.2012.06.010

PMCID: PMC3462238

- bupivacaine-dexmedetomidine epidural analgesia showed better maternal satisfaction for labor pains control compared with bupivacaine – fentanyl without deleterious effect on utroplacental circulation and newborns outcome.

Comparative evaluation of epidural bupivacaine – dexmedetomidine and bupivacaine –fentanyl on Doppler velocimetry of uterine and umbilical arteries during labor

Mohamed Fouad Selim, Ali Mohamed Ali Elnabtity, Ali Mohamed Ali Hasan

J Prenat Med. 2012 Jul-Sep; 6(3): 47–54.

PMCID: PMC3503522

- Dexmedetomidine-induced vasoconstriction is mediated by vascular smooth muscle alpha-2B receptors 3. This vasoconstrictive effect is rapid (t½ for equilibration 2.16 min). Most other alpha-2 agonist-mediated effects, such as sedation and sympatholytic effects, may take 10–15 min to approach their maximum 20, 21.

Pharmacokinetics and pharmacodynamics of dexmedetomidine-induced vasoconstriction in healthy volunteers

Pekka Talke, Brian J. Anderson

Br J Clin Pharmacol. 2018 Jun; 84(6): 1364–1372. Published online 2018 Apr 2. doi: 10.1111/bcp.13571

PMCID: PMC5980451

- Dexmedetomidine significantly improved the analgesic quality; increased sedation was observed, but the patient was easily rousable to verbal stimuli. No episodes of maternal hypotension or bradycardia, or fetal heart rate irregularities occurred. Cesarean delivery was required for prolonged first stage of labor and presumed chorioamnionitis; it was conducted under general anesthesia during which the dexmedetomidine infusion was continued. A healthy baby boy was delivered with normal Apgar scores and no discernible neurobehavioral or other deficits.

- received 0.5 µg/mL dexmedetomidine with 0.1% ropivacaine for epidural labor analgesia
- Dexmedetomidine is superior to sufentanil in analgesic effect and duration in first-stage labor during epidural analgesia when combined with 0.1% ropivacaine

Comparison of dexmedetomidine and sufentanil as adjuvants to local anesthetic for epidural labor analgesia: a randomized controlled trial

Tao Zhang, Yulong Yu, Wang Zhang, Jin Zhu

Drug Des Devel Ther. 2019; 13: 1171–1175. Published online 2019 Apr 11. doi: 10.2147/DDDT.S197431

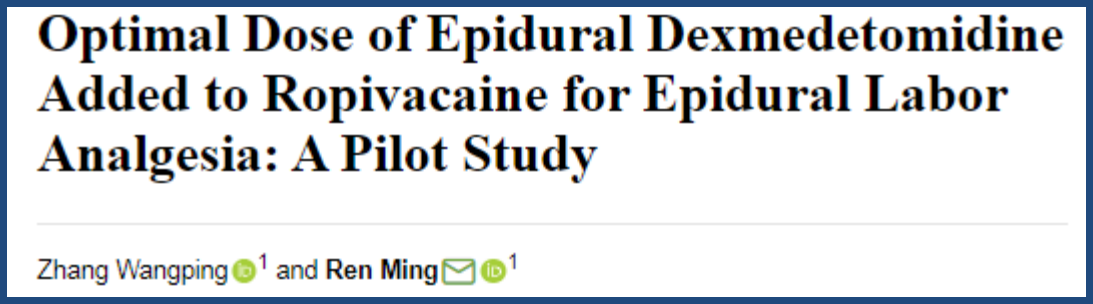
- Low concentration of epidural ropivacaine (0.125%) combined with dexmedetomidine (0.5 μg/kg) reduces the feeling of pain, and does not show the problems of motor blockage, hemodynamic instability, extension of production process, and complications such as nausea and vomiting.

Effect of Epidural Dexmedetomidine Combined With Ropivacaine in Labor Analgesia

A Randomized Double-Blinded Controlled Study

Zhao, Yang MD*; Xin, Yan MD†; Liu, Yongbo MD‡; Yi, Xuanlong MD*; Liu, Yingzhi MD*

- The addition of 0.25, 0.5, and 0.75 µg/ml of dexmedetomidine to 0.1% ropivacaine provided safe and effective analgesia, but 1 µg/ml of dexmedetomidine resulted in increasing incidence of motor block. The hemodynamic parameters were similar between groups.
- When dexmedetomidine is combined with 0.1% ropivacaine, the optimal concentration of dexmedetomidine is 0.5 µg/ml for epidural labor analgesia



Optimal Dose of Epidural Dexmedetomidine Added to Ropivacaine for Epidural Labor Analgesia: A Pilot Study

Zhang Wangping[1] and **Ren Ming**[1]

- Intrathecal administration of 5 μg Dex could improve epidural labor analgesia effects.

Intrathecal dexmedetomidine improves epidural labor analgesia effects: a randomized controlled trial

Gehui Li, Hao Wang, Xiaofei Qi, more... Show all authors

- The present study showed that dexmedetomidine could reduce the incidence of intrapartum fever and relieve pain during labor without increasing adverse events.....received 0.1% ropivacaine with 0.5 μg/mL dexmedetomidine for epidural analgesia during labor.....

Epidural Dexmedetomidine for Prevention of Intrapartum Fever During Labor Analgesia: A Randomized Controlled Trial

Li Li, Zeyong Yang & Wangping Zhang

- This article summarizes two cases where dexmedetomidine was used successfully as an analgesic adjunct to intravenous remifentanil during labor.

Colombian Journal of Anestesiology
Print version ISSN 0120-3347

Rev. colomb. anestesiol. vol.40 no.1 Bogotá Jan./Mar. 2012

- Using sedatives and narcotics in a parturient have always been controversial as these drugs tend to cross the uteroplacental barrier and can have deleterious effects on the baby. But newer drugs like remifentanil and dexmedetomidine due to their different and unique pharmacokinetics do not cross placenta significantly. Dexmedetomidine has a high placental retention (0.77 maternal/fetal index). Also, it is highly lipophilic as a result of which it is retained in placental tissue.
- Because of these properties, it doesn't cross the uteroplacental barrier, and even if it does cross, it is negligible. Also, it increases the frequency and amplitude of uterine contraction directly. But one must be able to justify the use of dexmedetomidine in a parturient, as it is still an off-label use, if used for labor analgesia or as an adjunct to general anesthesia for cesarean section. However, in maternal conditions like Pulmonary Hypertension (primary/acquired), PIH Rheumatic Heart Disease (especially mitral Stenosis), Thyrotoxicosis, and Coronary artery disease were hemodynamic fluctuations during labor or cesarean section can be disastrous, dexmedetomidine can be used in recommended doses due to its desirable properties of analgesia, sedation, sympatholysis, and ability to reduce anesthetic requirement. But dexmedetomidine must be used by an experienced Anesthesiologist in a well-equipped set up with meticulous hemodynamic monitoring. Most of the case reports that described the use of dexmedetomidine in parturients have mentioned that babies delivered were with normal Apgar scores which proves that even if there is any uteroplacental transfer, it doesn't affect the fetal well-being. However caution has to be taken while using dexmedetomidine in presence of bradyarrhythmias, severe left ventricular or biventricular dysfunction and in volume depleted patients. Also, use of dexmedetomidine requires dose adjustment in presence of hepatic or renal dysfunction.

- Dexmedetomidine also has no adverse effects on newborns. Dexmedetomidine can pass through the placenta under epidural anaesthesia with a transfer rate of 0.68.

J Int Med Res. 2017 Jun; 45(3): 964–972. PMCID: PMC5536431
Published online 2017 Apr 28. doi: 10.1177/0300060517698330 PMID: 28449631

Effect and placental transfer of dexmedetomidine during caesarean section under epidural anaesthesia

Changsheng Wang,* Shijiang Liu,* Chuanbao Han, Min Yu, Youli Hu, and Cunming Liu

- Intrathecal DEX is safe for the fetus during cesarean section and can improve the blockade effects of spinal anesthesia on puerperae.
- This meta-analysis shows that dexmedetomidine is safe for neonates who are delivered by caesarean section. Moreover, dexmedetomidine used in neuraxial anaesthesia can improve the characteristics of motor and sensory block and prolong the maternal pain-free period. Dexmedetomidine can also reduce the maternal incidence of postoperative adverse effects.

Med Sci Monit. 2020; 26: e918523-1–e918523-13.
Published online 2020 Jan 29. doi: 10.12659/MSM.918523
PMCID: PMC7001518
PMID: 31995551

Fetal and Maternal Responses to Dexmedetomidine Intrathecal Application During Cesarean Section: A Meta-Analysis

ShuJun Sun,[1,A,D,E] JiaMei Wang,[2,B,C] JingXu Wang,[1,B] FuQuan Wang,[1,C] HaiFa Xia,[✉1,A,B] and ShangLong Yao[✉1,A]

- Epidural dexmedetomidine is comparable to epinephrine as an adjuvant to epidural lidocaine in fastening the onset of surgical anesthesia and resulted in better intraoperative analgesia and in longer duration of sensory and motor block in the settings of converting labor epidural analgesia for emergency CS.

Egyptian Journal of Anaesthesia
Volume 32, Issue 3, July 2016, Pages 351-356

Research Article

Extending labor epidural analgesia using lidocaine plus either dexmedetomidine or epinephrine for emergency cesarean section

Riham Hasanein [a, b], Sahar Elshal [a]


Thank
You