Spinal Anaesthesia

Newer Developments – Role of Adjuvants

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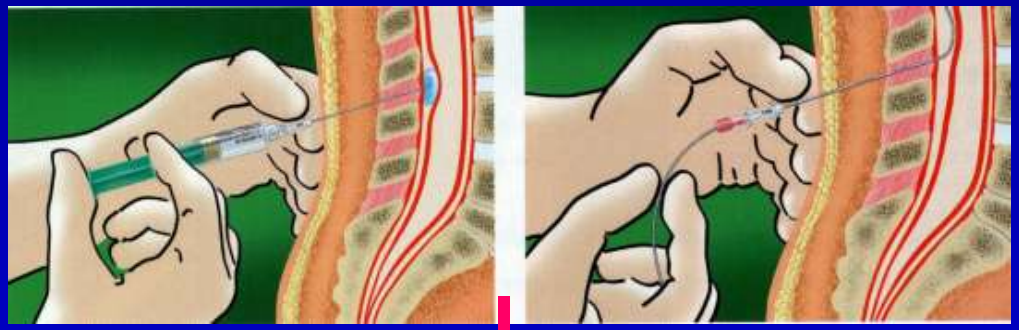
Adjuvant Drugs for RA

- Prolong local anaesthetics' analgesia and avoid their toxic doses
- Reduce the incidence of inadequate analgesia



Improvement of success of regional anaesthesia

Vadalouca A, 2002

Nerve Blockade

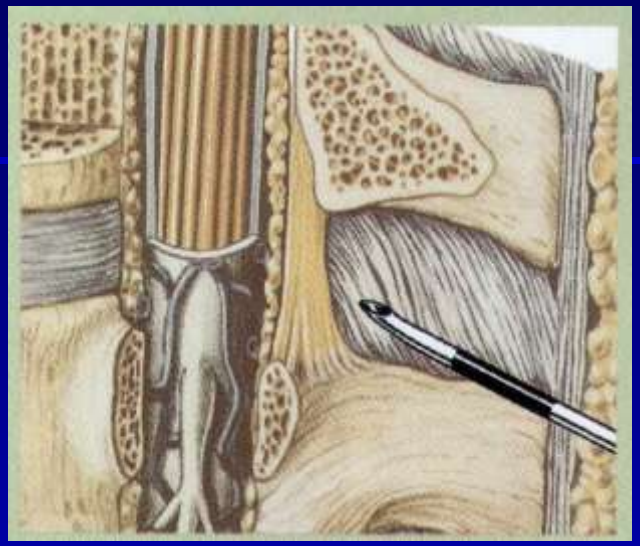
- Complete
- Reproducible
- With the desired duration of action

In the past

New local anaesthetics with

- Better spread
- Good separation of sensory and motor block

At present

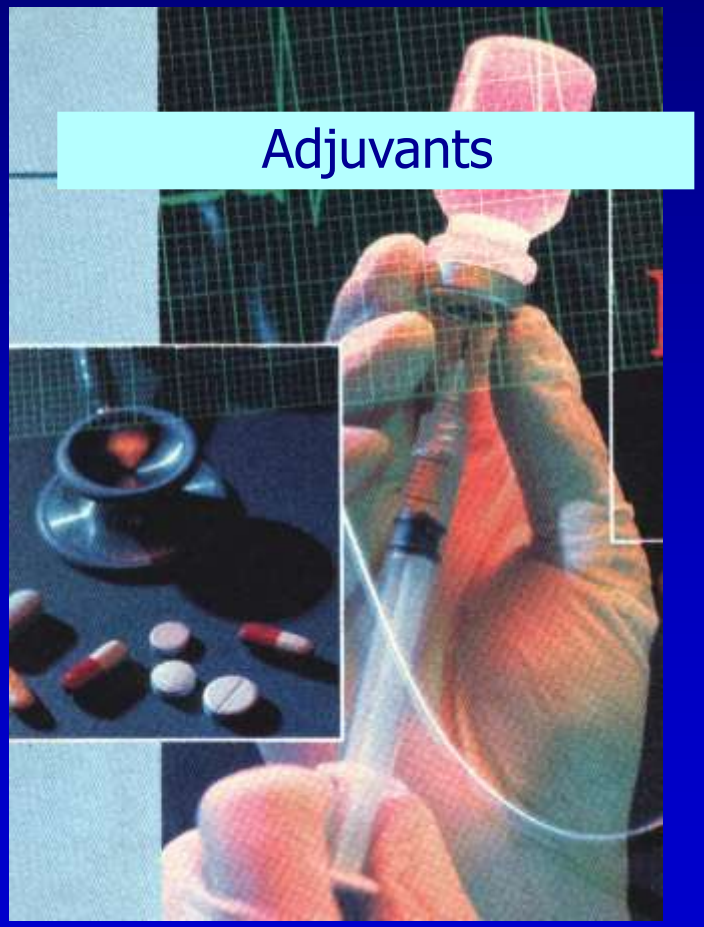


2nd drug added to local anaesthetic

adjuvant drug

- ↓ sensory input to CNS
- Improve the success of regional anaesthesia
- Action at secondary site different to LA

Adjuvant Drugs for Regional Anaesthesia that are in use



- Vasoconstrictors
- Opioids
- a2 – adrenergic agonists
- NMDA receptor antagonists
- Anticholinesterase drugs, cholinergic agonists

Vadalouca A, 2002

In the Future

Adjuvant Drugs

- Calcitonin
- Octreotide
- Adenosine
- Antioxidants
- Ziconotide

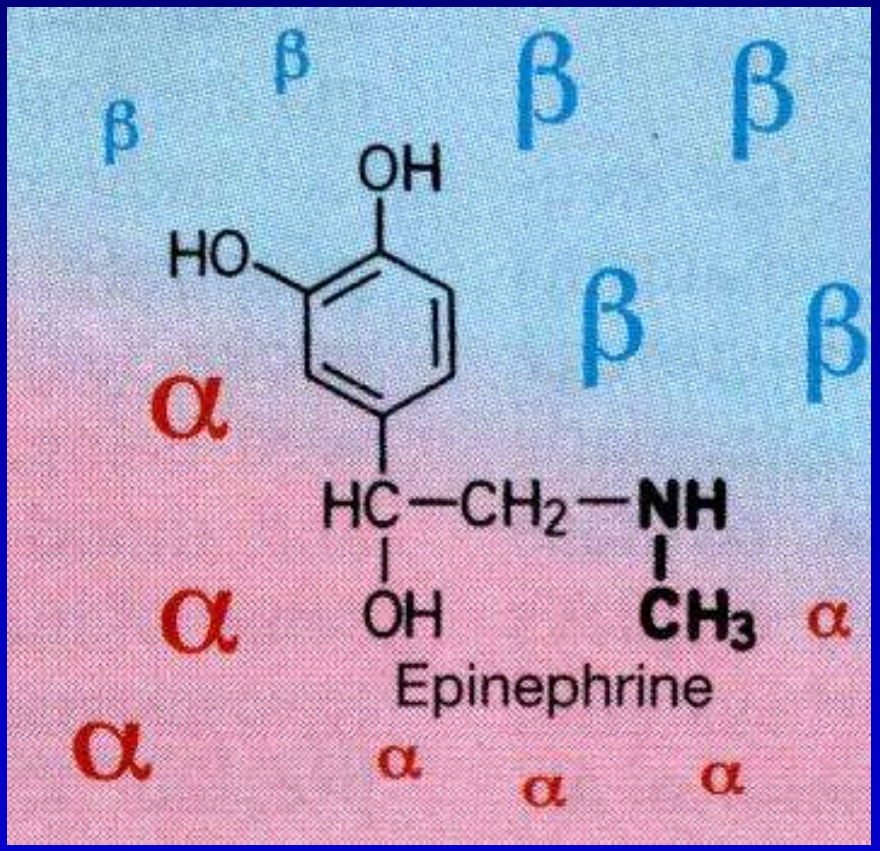
Ziconotide

- N – Type calcium channel blocker
- Intrathecal ziconotide in the treatment of *refractory pain* in patients with cancer or aids:
  randomized, controlled trial

Staats P et al, JAMA 2002

Vasoconstrictors

- For many years the only adjuvant drugs used in RA
- Even today they are commonly used

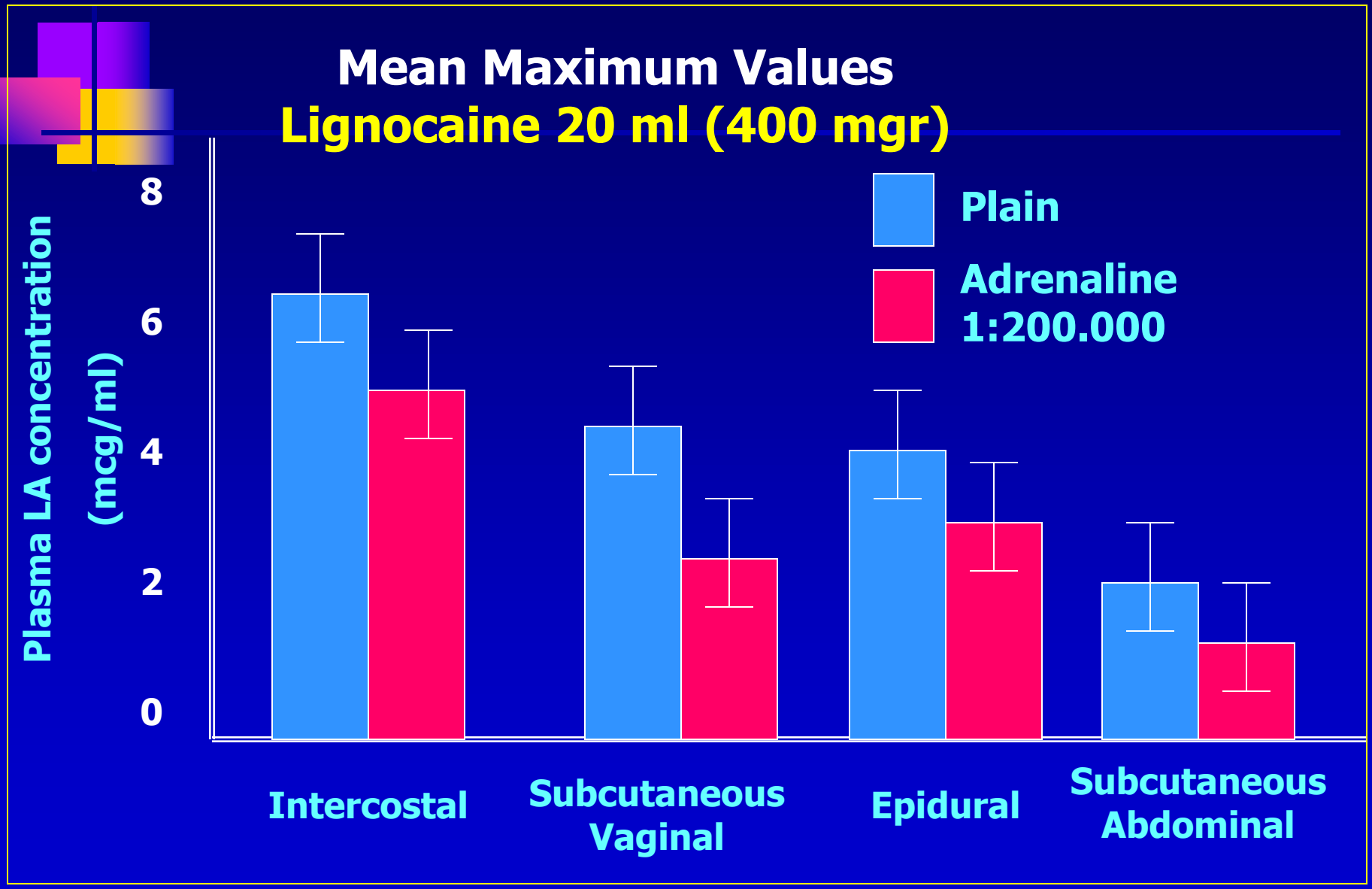


Vasoconstrictors

- **Prolongation of blockade** period by approximately **50%**
- **Decrease of the systemic absorption** of LA by approximately **one third**

Scott DB et al, 1972

Scott DB et al, 1972



Doses of epinephrine in LA solutions

- LA solutions + Epinephrine 1:200,000 (5mcg/ml) → Classic mixture
- Lignocaine +

  Epinephrine 1:200,000

  Epinephrine 1:400,000

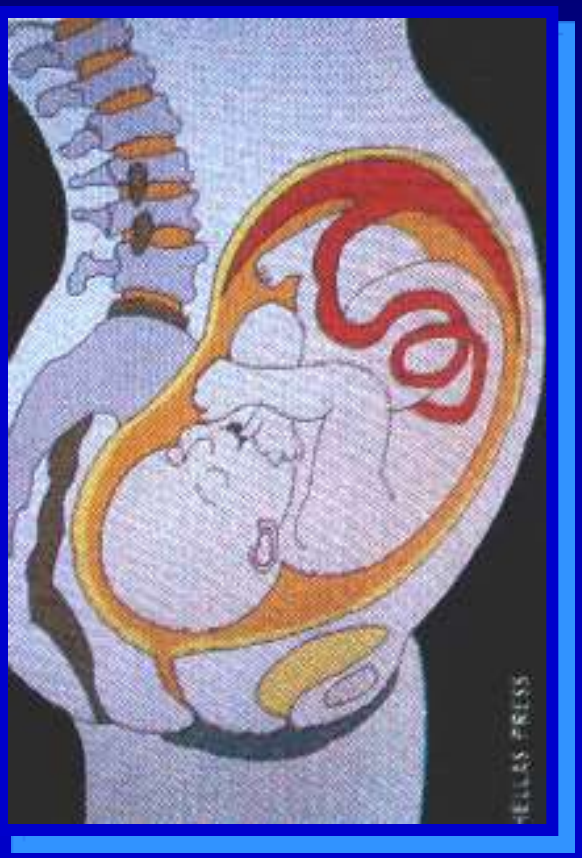
  Epinephrine 1:600,000

DiFazio CA et al, 1986

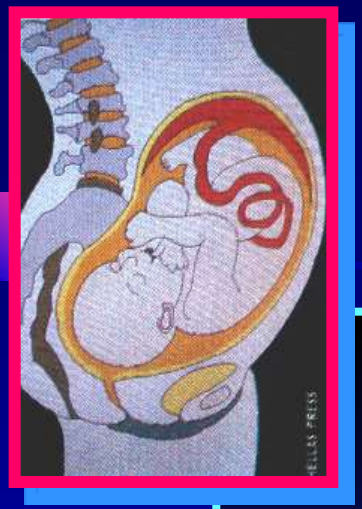
Doses of epinephrine in LA solutions in OBSTETRICS

- LA solutions + Epinephrine 1:200,000 (5mcg/ml) → Classic mixture
- Lignocaine + Epinephrine 1:600,000

Preferred especially in preeclamptic patients



Alahuhta S et al, 1991



Doses of epinephrine in LA solutions in OBSTETRICS

Labour Pain

- Bupivacaine 12.5 mgr (0.125%)

+

- Epinephrine 12.5 mcg (1:800,000)

A. Van Zundert, 1996

Epinephrine in LA solutions in the subarachnoid space

- Greater duration of sensory anaesthesia in the lower extremities
- Increased rate of success of spinal anaesthesia
- Significant prolongation with 0.6 mcg epinephrine added to 60 mgr hyperbaric lignocaine for spinal anaesthesia in thoracic dermatomes

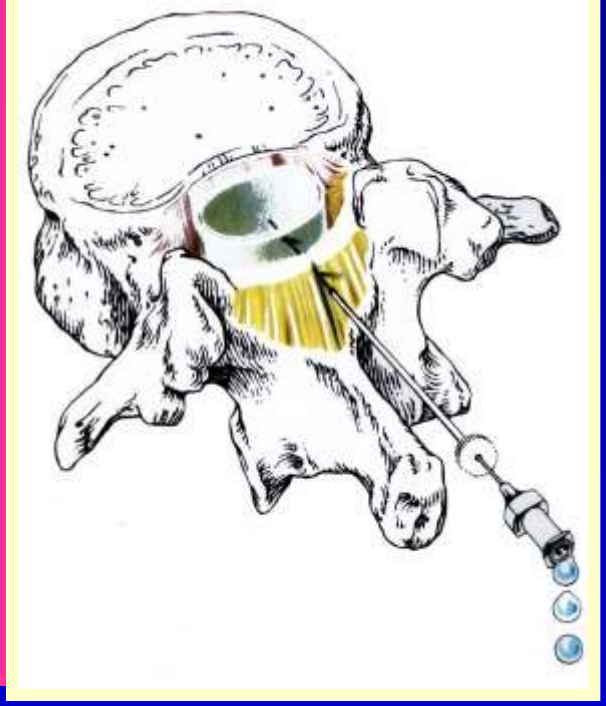
Carpenter RL, 1989
Kito K et al, 1998

Epinephrine in LA solutions in the subarachnoid space

Epinephrine + Procaine for spinal anaesthesia

- Prolongs sensory & motor blocks by 25%
- ↑ incidence of nausea
- ↓ possibility of systemic toxicity

Bergeron L et al, 1999



- **Combined use of** epinephrine with hyperbaric tetracaine in the supine position can **enhance** the cephalad spread of sensory block levels compared with hyperbaric tetracaine alone in the lithotomy position

Inoue S et al, 2004

Acta Anaesth Scand

Hyperbaric spinal 2 – chloroprocaine:

- Effective
- Anaesthetic profile appropriate for case in the surgical outpatient
- Over the dose range 30 – 60 mgr

Addition of epinephrine

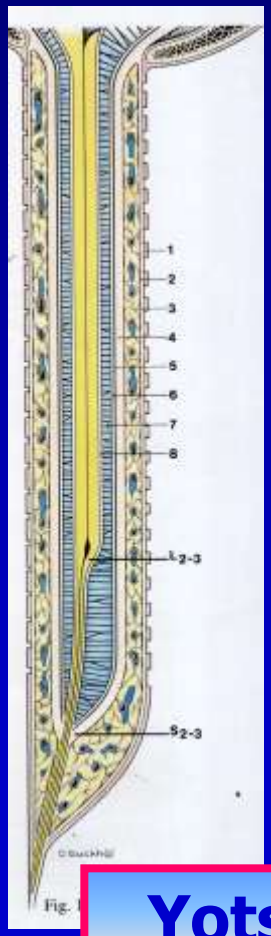
- Not recommended
- Frequent incidence of side effects

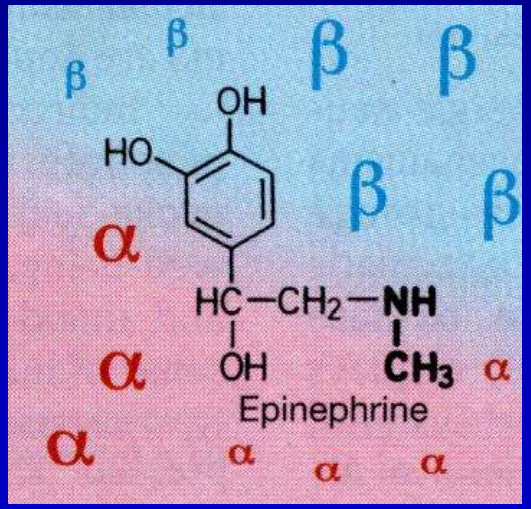
Smith KN et al, 2004

Anaesth Analg

Intrathecal Epinephrine

- Augments the *sedative effect* of propofol during spinal anaesthesia
- Augments the *depression of BIS* during intraoperative propofol sedation

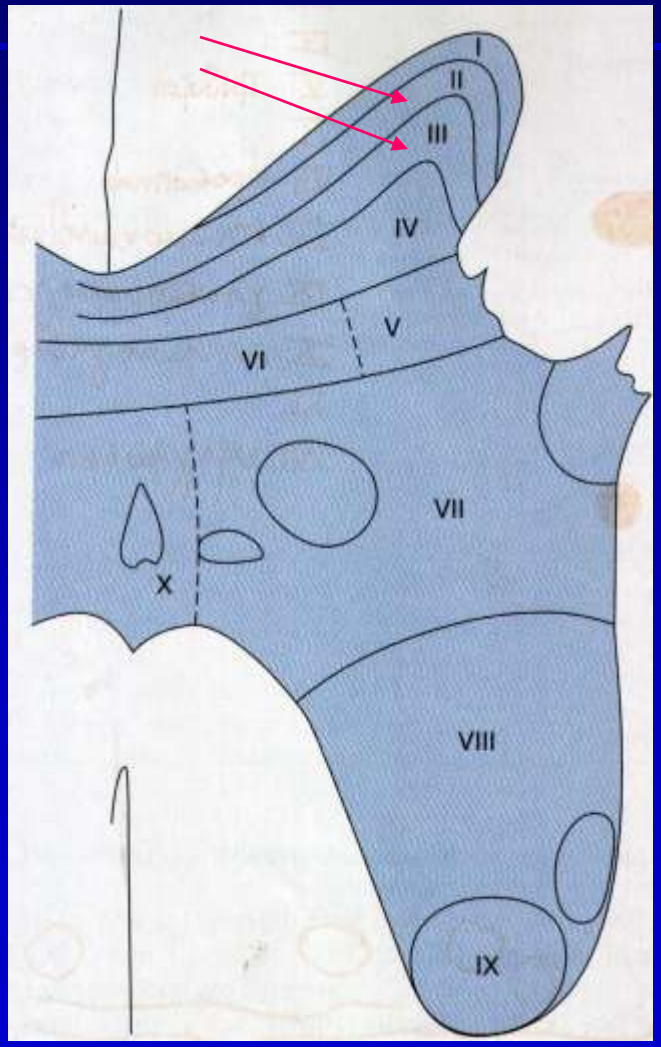




Yotsui T et al, 2004

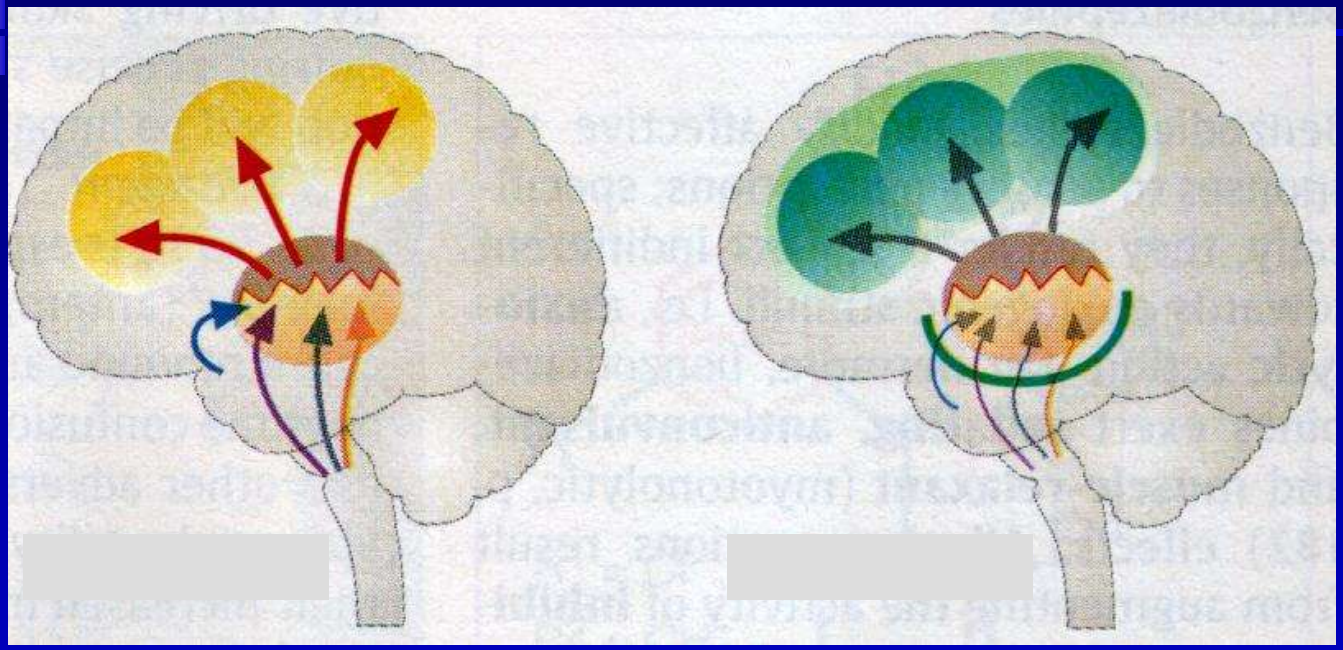
Opioids as Adjuvant Drugs in RA

- Opioids in epidural – subarachnoid anaesthesia
- Opioid receptors in substantia gelatinosa of the spinal cord Rexed Lamina II - III



Cousins MJ, 1984

Action of opioids



- Brain Stem
- Spinal Cord
- Peripheral Sites

Stein C, 1993

Opioid Receptors

- μ – receptors (μ1 & μ2)
- δ – receptors
- κ – receptors

Atcheson R et al, 1994

Bupivacaine

\+

Fentanyl

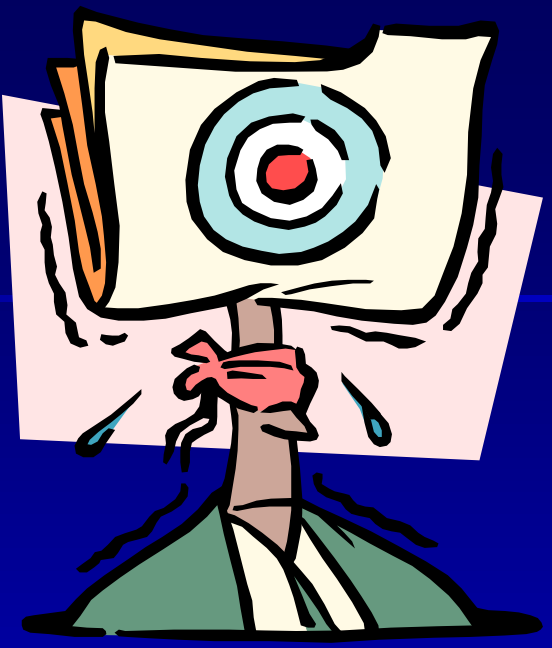
10 – 30 mcg/h

Sufentanil

1 – 3 mcg/h

↓ 30% the dose of LA

Atcheson R et al, 1994



Side Effect Profiles are similar although sufentanil > fentanyl for respiratory depression

Norris M et al, 1994

Hermann N et al, 1999

Spinal Anaesthesia

Bupivacaine 0.5% (12.5 mgr)

+

Morphine 0.2 mgr

→ Good Analgesia

→ Fewer Side Effects

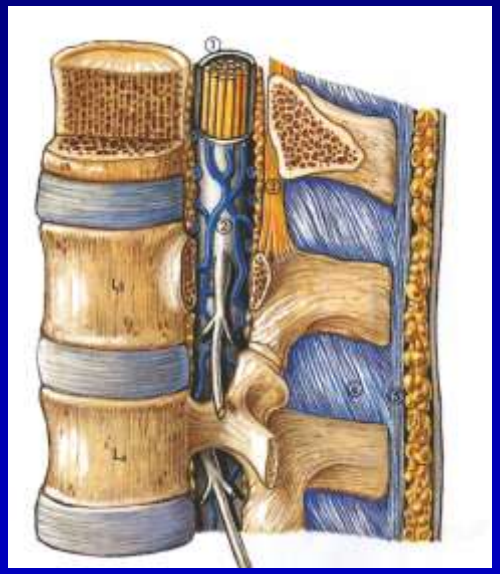
Rodanant O et al, 2003

Spinal in the elderly

4 mgr Bupivacaine

+

25 mcg fentanyl

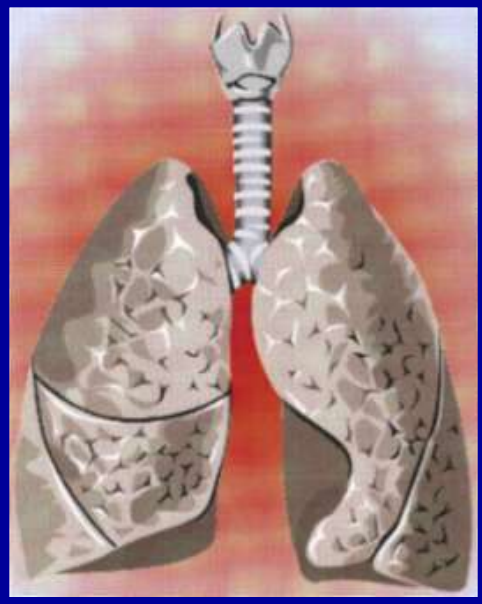


- Adequate Analgesia
- Fewer Side Effects
- Prostatectomy

Kararmaz A et al, 2003

The addition of fentanyl (25 mcg) to hyperbaric bupivacaine (10 mgr) & limiting the spread of the block ***does not improve*** either haemodynamic or pulmonary function compared with bupivacaine 15 mgr in transurethral prostatectomy

Walsh KH et al, 2003



Outpatient Surgery

- Attention to technique
- Reduction of dose
- Addition of fentanyl to lignocaine

- Effective spinal anaesthesia
- Rapid recovery
- Few side effects - complications

Urmey WF et al, 2003

Labour Analgesia

- ***Spinal:*** Bupivacaine 2 mgr
  +
  12.5 mcg Fentanyl

Labour Analgesia for 85 min

- ***Epidural:*** Morphine 125 mcg ⟶ improves pain control

Hess PT et al, 2003

CS

Sufentanil 5 & 7.5 mcg

+

Hyperbaric Bupivacaine 0.5% (12.5 mgr)

- Adequate analgesia for CS
- Good post-operative analgesia
- 7.5 mcg ⟶ pruritus

Brage AF et al, 2003

CSE

- Bupivacaine 0.25 mgr
- Adrenaline 25 mcg
- Sufentanil 2.5 mcg

Spinally

VAS< 2 ⟶ ± 140 min

- Bupivacaine 1.25 mgr
- Adrenaline 12.5 mcg
- Sufentanil 10 mcg

Epidural Top-up

VAS< 2 ⟶ ± 120 min

Albert Van Steenberge, 1998

Spinal anaesthesia *for appendicectomy*

Hyperbaric bupivacaine 0.5% (4 ml)
+
fentanyl (20 mcg)

significantly

- Improved quality of anaesthesia
- Prolonged duration of analgesia
- Delayed analgesic requirement in the early postoperative period
- Less shivering in the fentanyl group

Techanirate A et al, 2004

Spinal 2 – chloroprocaine (40 mgr)

Rapid onset
Reliable anaesthesia
No signs of transient neurological symptoms

Addition of fentanyl

- Lengthening of the regression to L1 dermatome
- Lengthening of tourniquet time
- Minimally increased duration of block

Vath JS et al, 2004

a_2 – adrenergic agonists as adjuvants in RA

- Mostly a_2 – adrenergic agonists: clonidine, dexmetomidine, tizanidine
- Reduction of sympathetic nervous system output from CNS
- Also antihypertensive drugs
- 1984: first time clonidine was used epidurally (Torsten Gordth)
- Analgesia, no adverse effects of opioids
- But: hypotension & dry mouth

Eisenach JC et al, 1996

Clonidine in the epidural / subarachnoid space

- ***Dose-dependent Analgesia***
- ***Does not produce***
  1. Ventilatory Depression
  2. Pruritus
  3. Nausea
  4. Vomiting

Filos K et al, 1994
Eisenach J, 1996
Asai et al, 1997

Clonidine as an adjuvant in RA in children

- The use of clonidine as an adjuvant drug in the field of regional anaesthesia in children seems to be very effective and safer than opioids and adrenaline

Ivani G et al, 1998

..... *Clonidine 1 mcg/kg,* added to spinal isobaric bupivacaine doubles the duration of the block in the neonates without significant deleterious haemodynamic or respiratory effects

Rocchette A et al, Anesth Analg 2004

Clonidine administration through various routes

- There is clear evidence that a fixed dose of clonidine im, epidurally or intrathecally has a clear order of duration:
- **Intrathecal > epidural > im**
- Thus supporting intrathecal administration

Bernard JM et al, 1995

Eisenach JC, 1998

Clonidine

Spinal ***(Inguinal Herniorapy)***

Hyperbaric Bupivacaine (6 mgr)

+ clonidine 15 mcg

- ↑ Spread of analgesia
- Prolongs time to 1st analgesic request
- ↓ post-op pain

Dobrydnjov I et al, 2003

Clonidine

Intravenous: 3 mcg/kg

1h after spinal block

- Prolongs bupivacaine spinal anaesthesia for 1h approximately
- Without adverse effects

Rhee K et al, Acta Anaesth Scand 2003

Clonidine

Spinal
(Total Knee Arthroplasty)

Hyperbaric Bupivacaine (15 mgr)
+ clonidine 25 or 75 mcg
+ morphine 250 mcg

- Post-operative analgesia improvement compared with intrathecal morphine alone

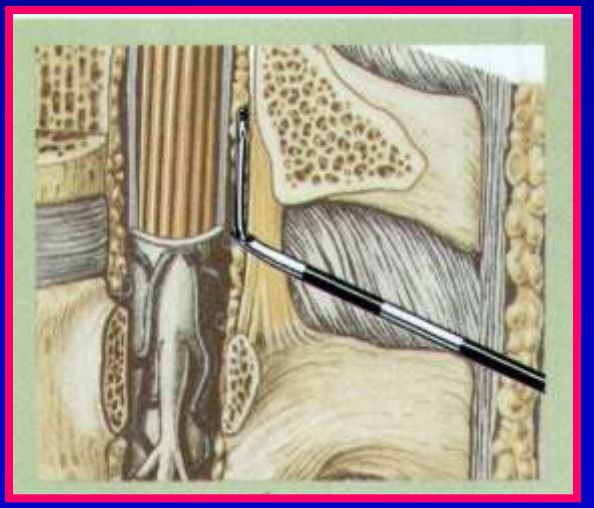
Sites BD et al, 2003

Clonidine
Lower Spine Procedures

Epidural administration: 150 mcg

Supplement to spinal anaesthesia

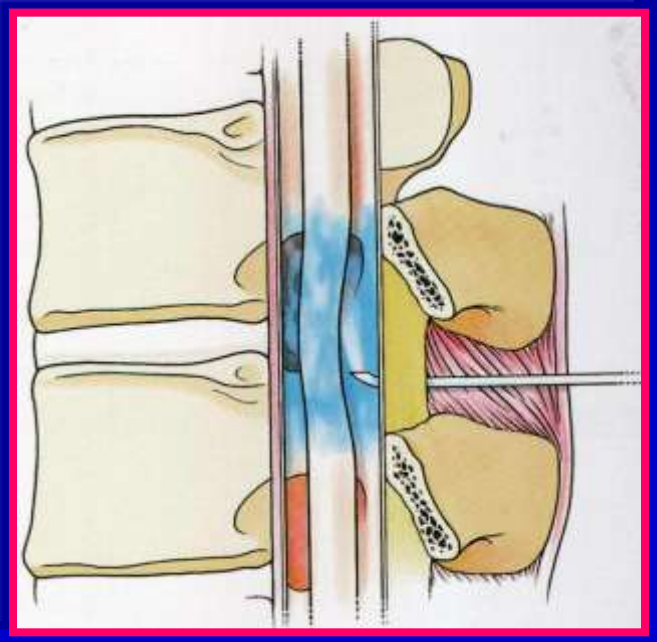
- No perioperative complications
- Improved Postoperative Pain
- Haemodynamic Stability



Jellish WS et al, 2003

Clonidine + Opioids
(Continuous Epidural Infusion)

↓ 20 – 30 % of opioid dose



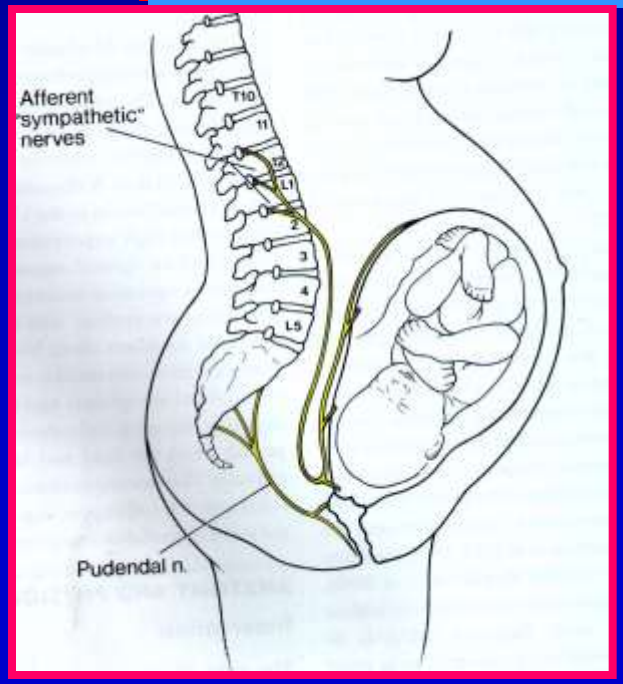
Eisenach JC, 1998

LA + Clonidine

Labour Analgesia

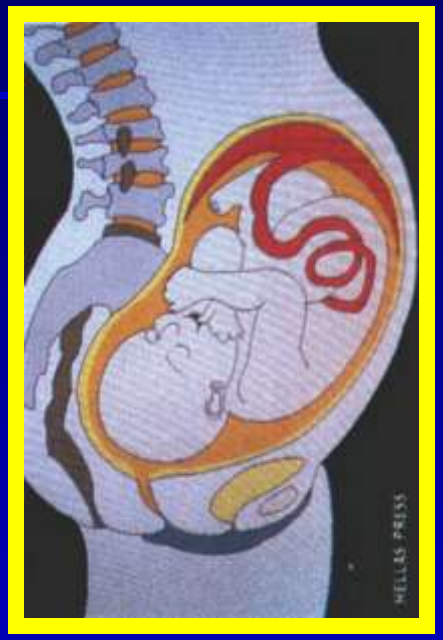
INCREASED:

- Risk of maternal hypotension
- Risk of maternal sedation
- Risk of neonatal sedation



Eisenach JC, 2000

Clonidine in obstetrics (Labour)



PCEA

bupivacaine

+

clonidine

+

fentanyl

Reduce

Supplementation rate of analgesics

Shivering

Paech JM et al, 2000

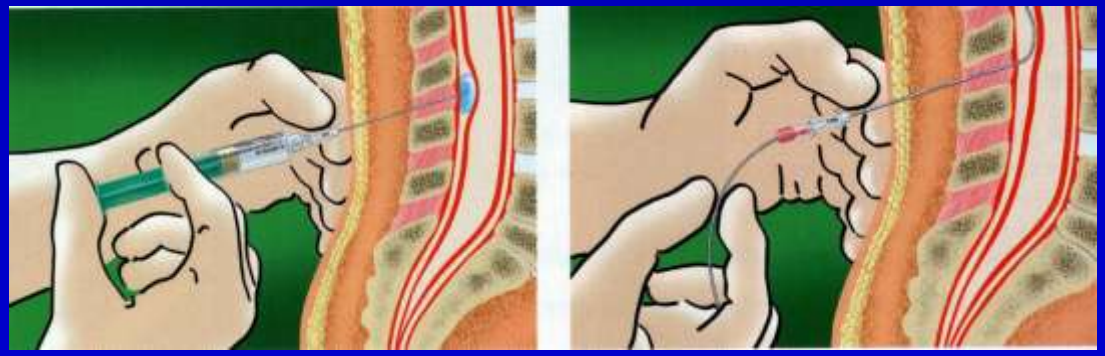
CSE in Obstetrics

- 9 – 10 mgr ropivacaine
  +
  25 mcg fentanyl

Spinally

- 100 mcg fentanyl
  +
  30 mcg clonidine

Epidurally



Vadalouca A et al, 2000

Other uses of clonidine as an adjuvant

- Local infiltration with LA + clonidine: better results in comparison with plain LA
- During iv anaesthesia clonidine improves the tolerance of tourniquet

Elliot S et al, 1997

Gentilli M et al, 1998

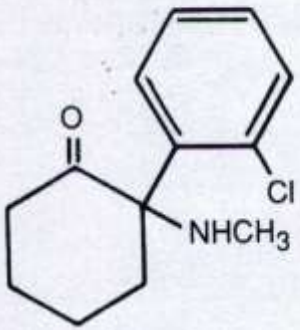
Dexmetomidine

Characteristics	Clonidine	Dexmetomidine
Type of action	a_2 selective adrenergic agonist	a_2 selective adrenergic agonist
Cardiovascular blood pressure effects	moderate	minimal in comparison with clonidine
Side effects	few	fewer
Selectivity for a2 receptors	a_2 - agonist	7 times more selective
Duration of action	short	shorter
Use in obstetrics	few references	not yet

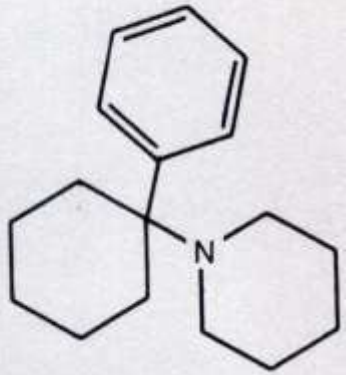
Ketamine as an adjuvant in RA

- Classic iv drug
- Anaesthetic
- Sedative
- Amnesic
- Analgesic
- Phenylcyclidine derivative
- Produces dissociative anaesthesia
- S+ & R- isomers
- NMDA receptor antagonist
- 1984 first use intrathecally (Bion)

Ketamine

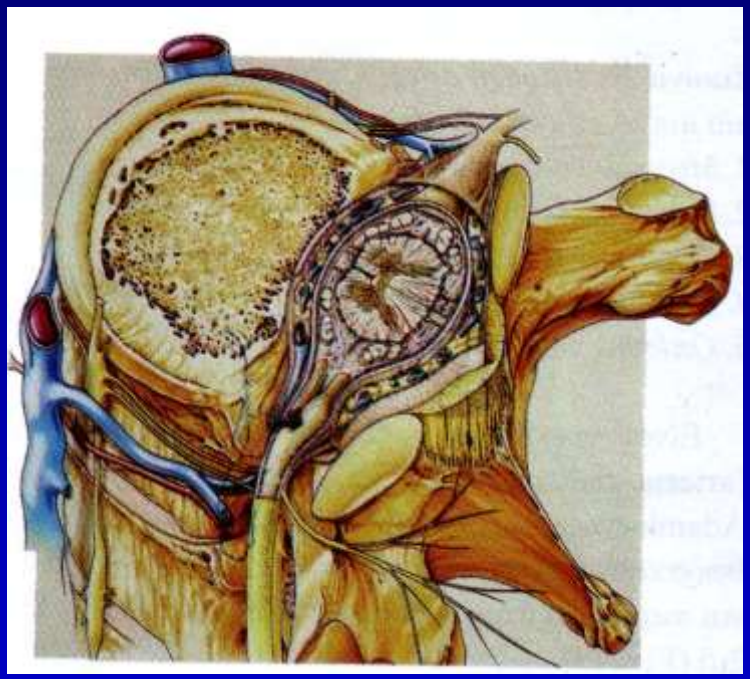


Phenylcyclidine



Use of ketamine Intrathecally

- Surgical anaesthesia can be achieved by intrathecal *ketamine*
- Intraspinal ketamine in pigs produced lower haemodynamic alterations in comparison with lignocaine.
- Haemodynamic alterations, not dose - dependent
- ?? Neuraxial Ketamine in hypovolaemic patients



Errando CI et al, 2000, 2004

Intrathecal ketamine: a promising analgesic alternative for women in labour, although its use is still at an early clinical stage

Mercier FJ et al, 1998

Ketamine as an adjuvant in children

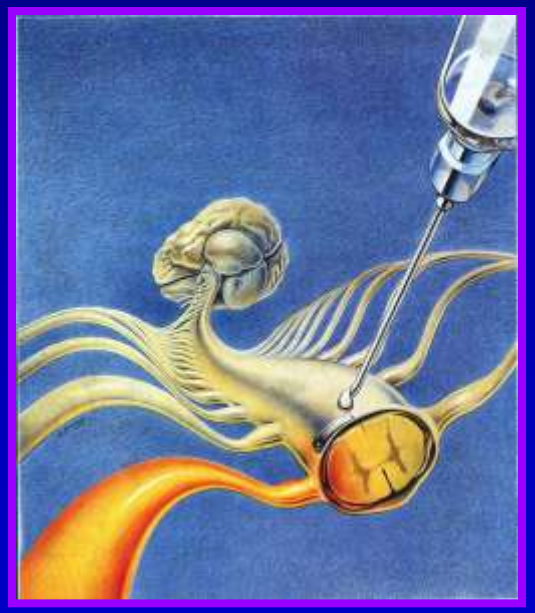
- Epidural route
  Caudal route → ***0.5 mg/kg*** Postoperative analgesia
- Sedation / Analgesia → ***1 – 2 mg/kg iv***
- ICU → ***0.5 mg/kg/h***
  (continuous infusion)

Ivani G et al, 2003

Ketamine (spinally – epidurally)

- *Intrathecal* Ketamine + Bupivacaine (spinal anaesthesia)

- Epidural Ketamine + LA



↓

- Better post-op analgesia
- Alternative to opioids for obstetric anaesthesia

Kethirrel S, 2000
Himmelscher, 2001

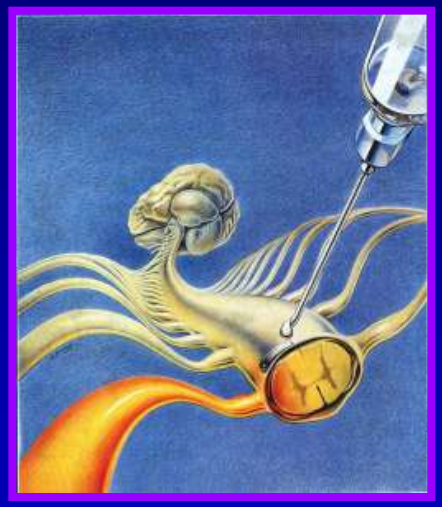
S (+)Ketamine (spinally – 0.1 mgr/kgr)

+

hyperbaric bupivacaine 7.5 mgr

- *Patients > 60 years*

Provide



- shorter motor / sensory block
- shorter duration of action
- less motor blockade in elderly males

Togal et al, 2004

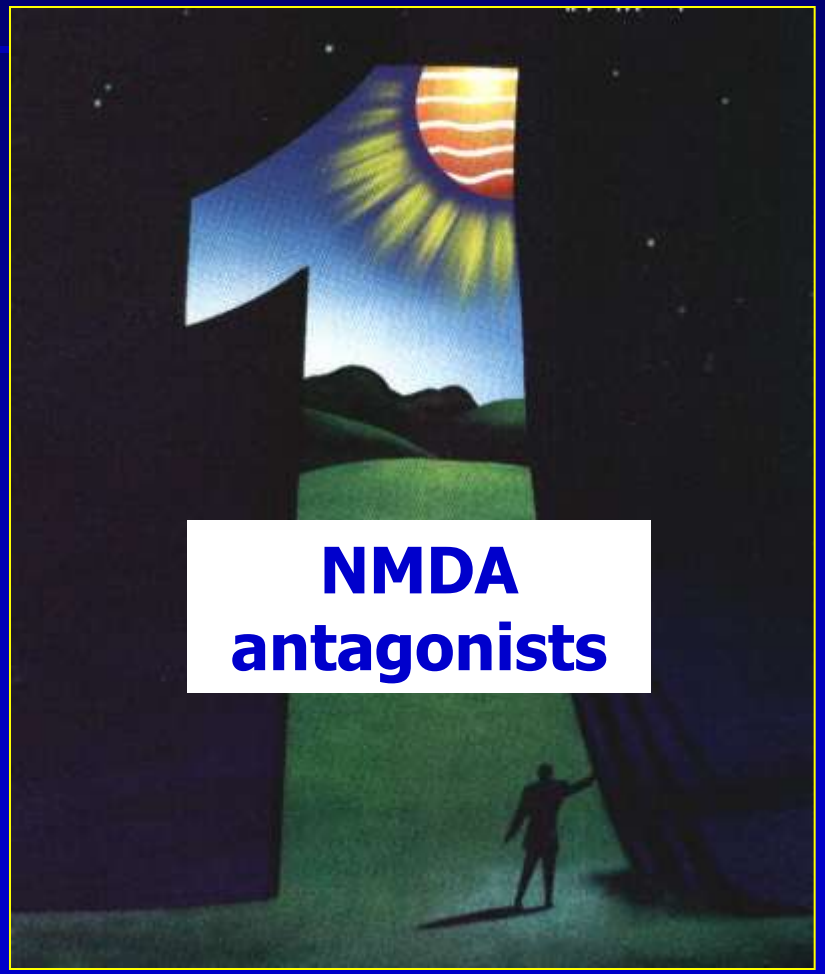
Analgesic Affinity of Ketamine

- Antioxidative Properties

Lupp A et al, 1998

NMDA antagonists
as antioxidants

- Antioxidants play a role in pain relief
- New horizon for analgesic properties of NMDA antagonists

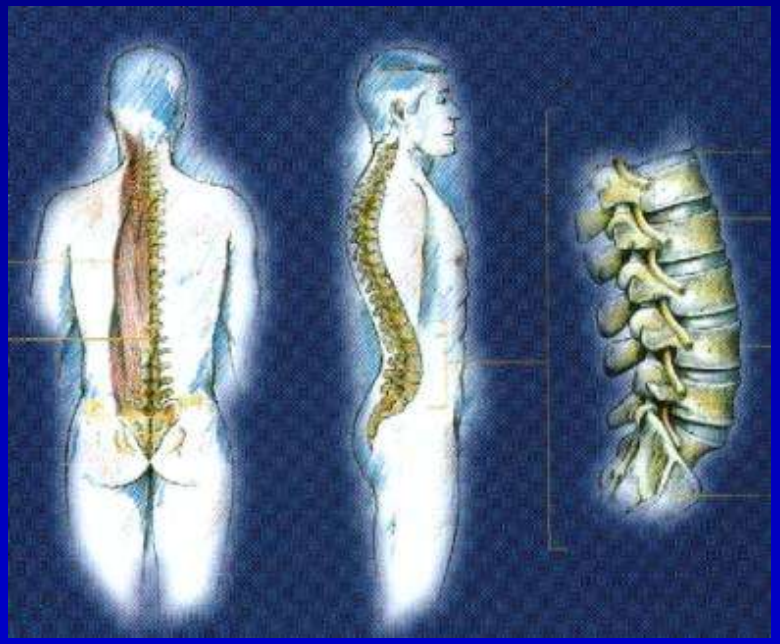


Evagelou A et al, 1998, 2000
Kahlil z et al, 1999

Neostigmine as an adjuvant in RA

- Neostigmine administered spinally

inhibits nociception in a dose-dependent manner by increasing the endogenous neurotransmitter acetylcholine



Hood DD et al, 1996

Neostigmine as an adjuvant in RA

- However: scepticism about side effects
- Need to investigate the ultra low doses of neostigmine combined with other analgesics in order to avoid adverse effects

Eisenach JC, 2000

Low – Dose Spinal Neostigmine: Morphine Analgesia Improvement

- 1 – 5 mcg neostigmine

  +

  100 mcg morphine

- Doubled the duration to first rescue analgesic
- ↓ analgesic consumption in 24 h
- No increase in adverse effects

Almeid RA et al, 2003

Neostigmine as an adjuvant in obstetrics (labour)

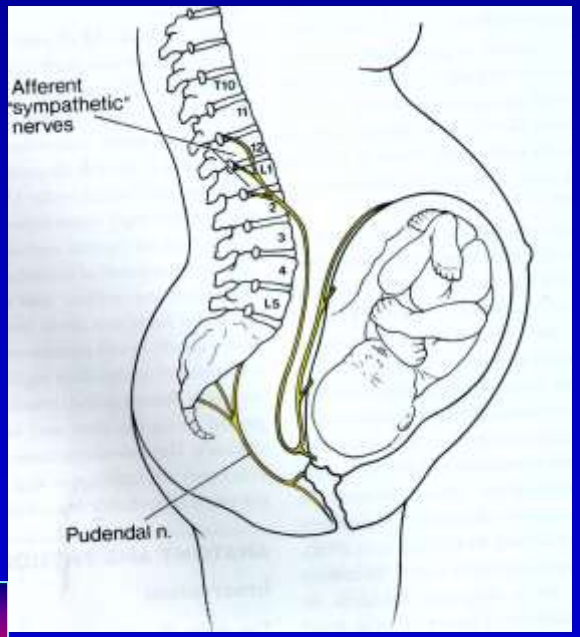
- bupivacaine + fentanyl

  +

  neostigmine + clonidine

Intrathecally

- ↑ duration of labour analgesia
- ↑ nausea



Owen MD et al, 2000

Adenosine receptors and pain signaling

- Adenosine receptors: in the superficial layers of the dorsal horn of the spinal cord
- Antinociceptive effect of adenosine: probably mediated through A_1 subtype receptors
- ***It increases the pain threshold***

Sjolund KF et al, 1998

Adenosine intrathecally

- 2000 mcg intrathecally: transient lumbar pain
- Adenosine: no motor block, no hypotension, no sedation
- Analgesia in hypersensitivity states
- Uncertain role in acute obstetric pain

Karlsten R et al, 1995
Rane K et al, 1998
Chiari A et al, 1999

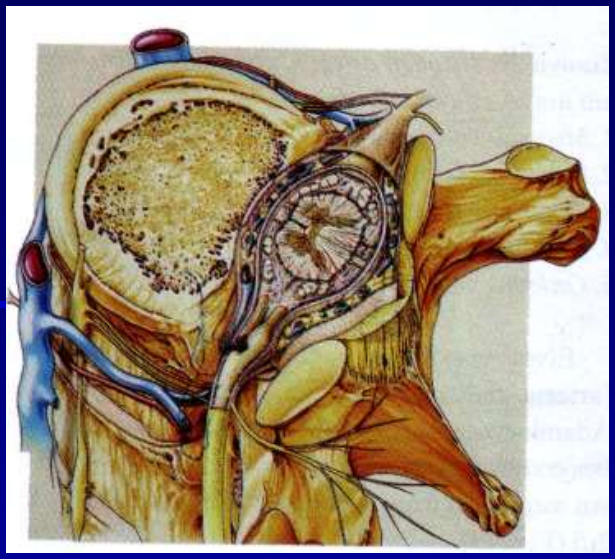
Somatostatin - Octreotide

- Reports: Alleviation of post-operative and severe cancer pain if given epidurally - intraspinally

Chrubasic, 1989

Vadalouca A, 1993

Epidural – Spinal Calcitonin



- Rich literature regarding spinal and epidural administration for cancer pain
- Few references regarding its successful use in post-op pain

Fiore CE et al, 1983

Vadalouca A et al, 1999

Vadalouca A et al, 2003

Antioxidants

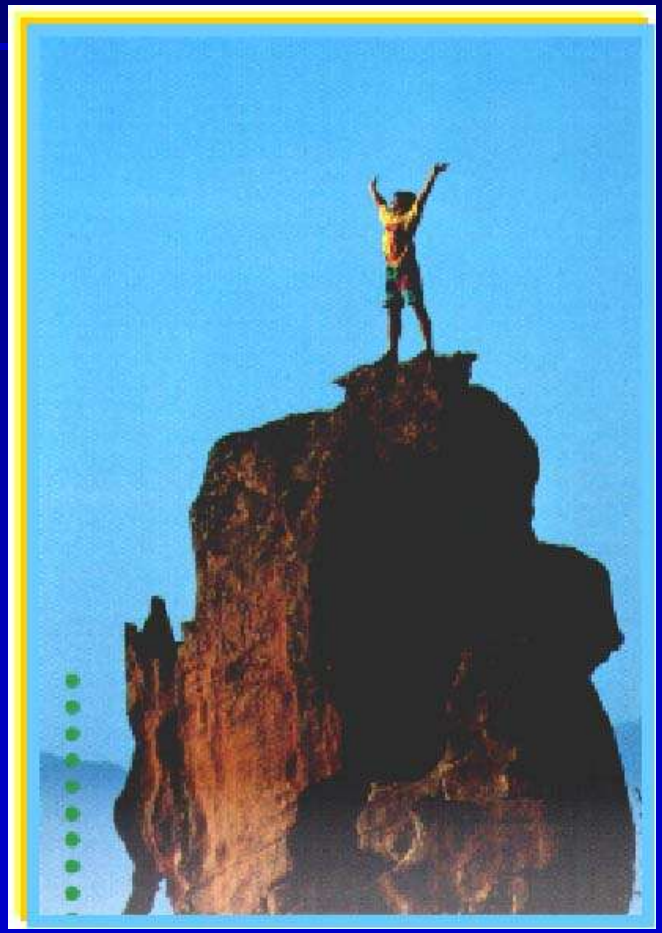
- They may indicate a new horizon for analgesia
- Can be easily used in some kinds of chronic pain

Davis RH et al, 1990

Alindon TE et al, 1992

Kahlil Z et al, 1999

Evagelou A et al, 1998, 2000



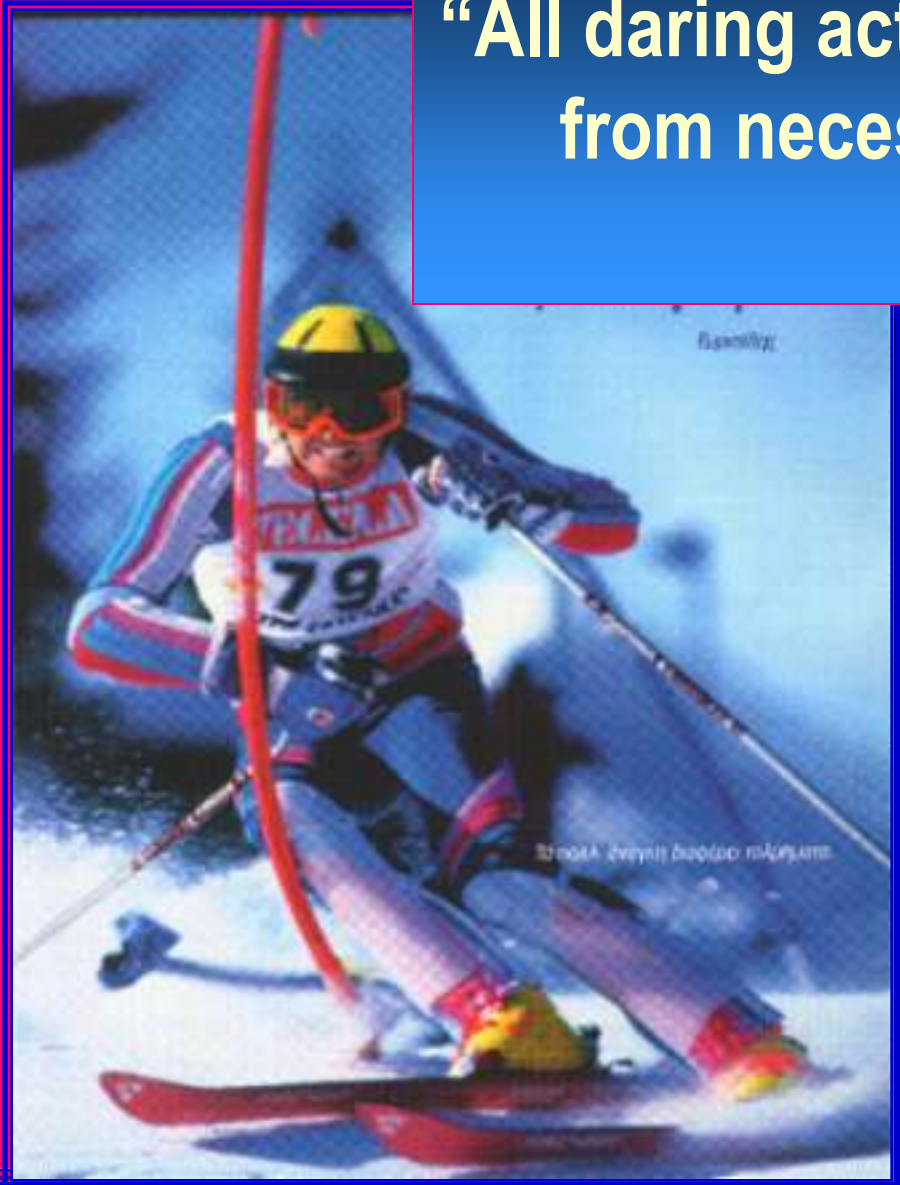
Perioperative & post-operative pain is a definite fact

Adjuvants ???

- Regional anaesthesia:
  mostly achieved with LA

Adjuvant drugs:

- ★ Better analgesia
- ★ Prolonged analgesia



“All daring actions begin from necessities”

Evripides

When safer & better RA is the primary goal

↓

non-traditional adjuvants

Future studies
are increasingly important to monitor the **risk-to-benefit ratio** from the use of **Novel Adjuvant Drugs**