Remifentanil PCA should be considered as a first line alternative for analgesia during labour.

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Alternative to what and when ?

- To what ?
  - To other parenteral or inhalational analgesia ?
  - To epidural analgesia ?
- When ?
  - Always ?
  - Or in certain situations ?

Remember ……

- Most studies performed in early labour, following only 60 – 180 minutes of labour and not in the second stage !!!!!

Remifentanil PCA should not routinely be used in labour.

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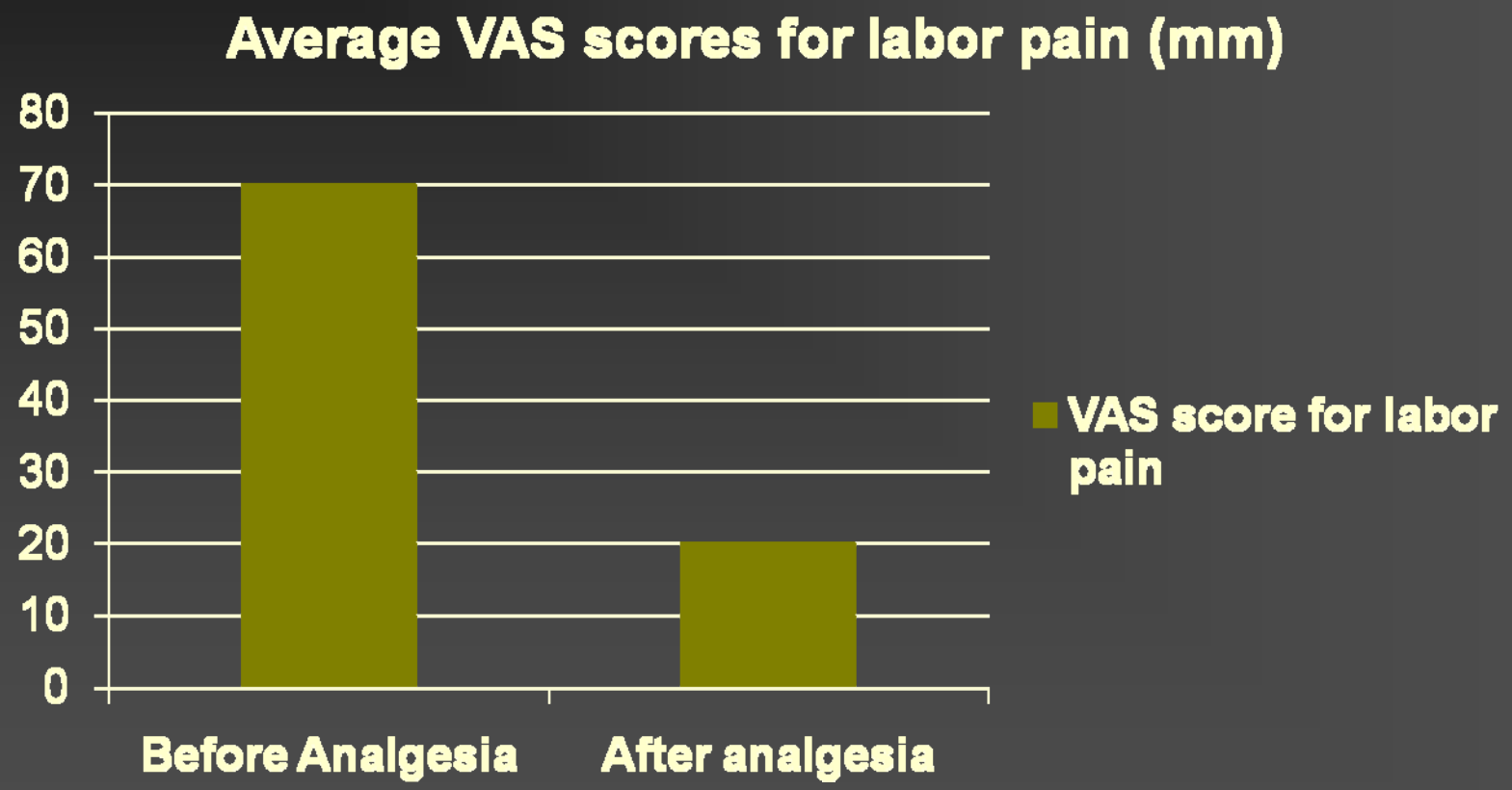
Quality of pain relief.



Epidural versus pethidine and tramadol.

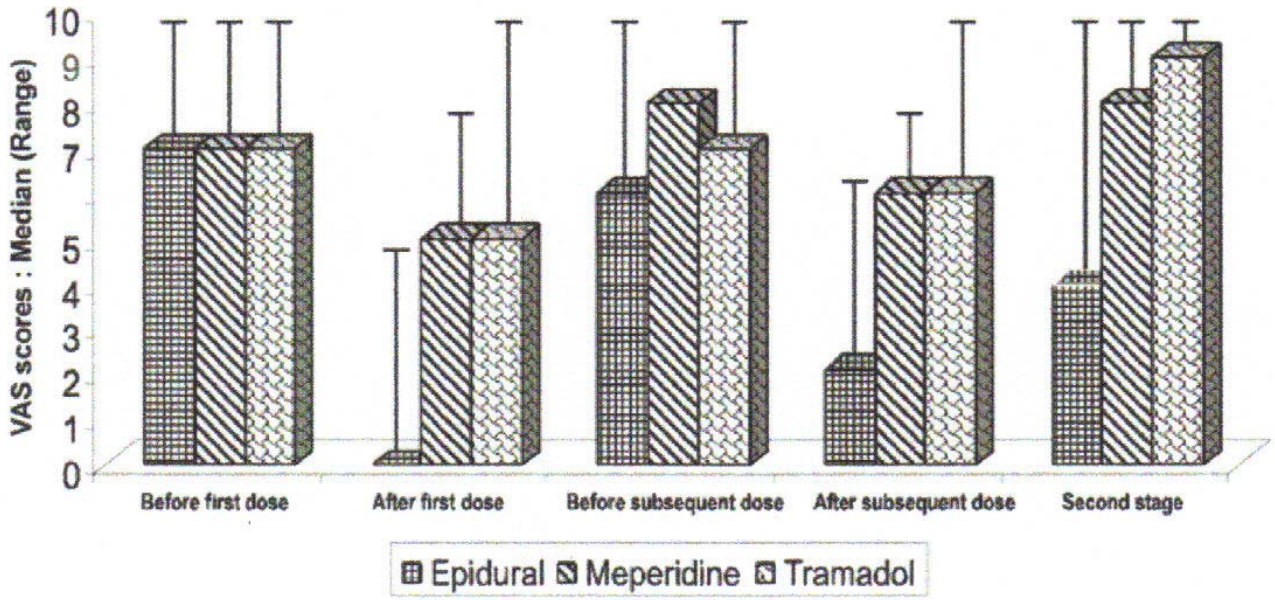


Fig. 1. Median VAS scores at various stages of labor.

Jain et al. Int J Obstet Gynecol Obstet 2003; 83, 19 – 27.

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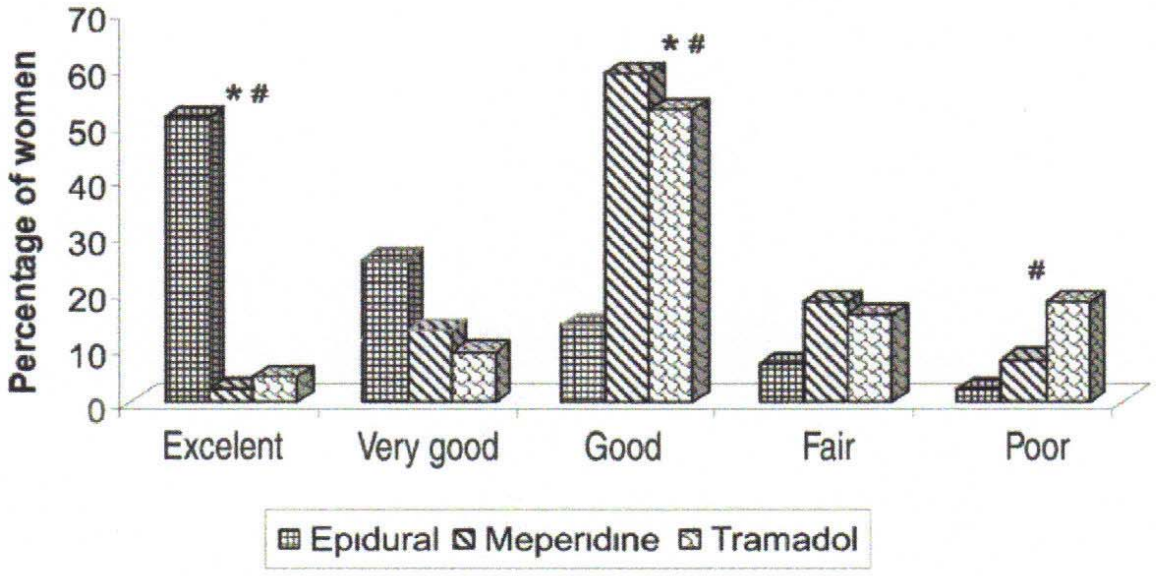
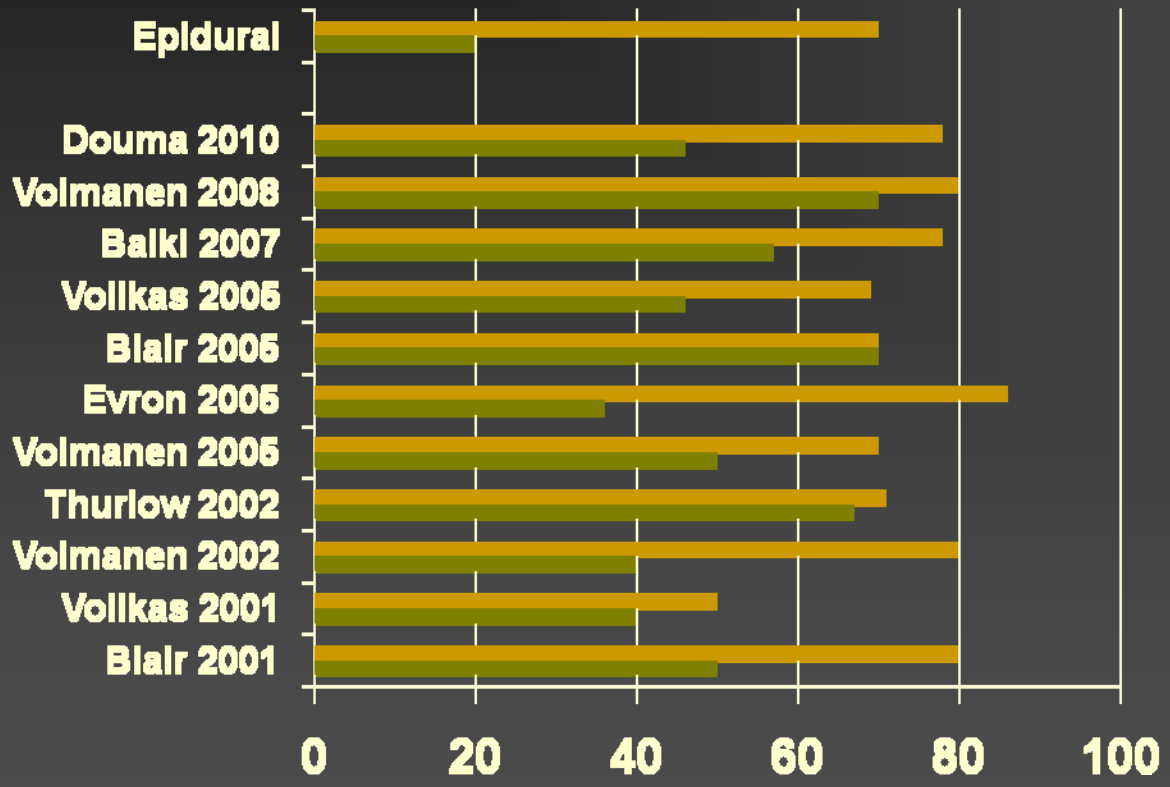


Fig. 2. Maternal opinion about analgesia. *$P < 0.05$ epidural vs. meperidine; #$P < 0.05$ epidural vs. tramadol.

Jain et al. Int J Obstet Gynecol Obstet 2003; 83, 19 – 27.

Pain relief with remifentanil.

VAS for labour pain (mm).



Remifentanil versus epidural.

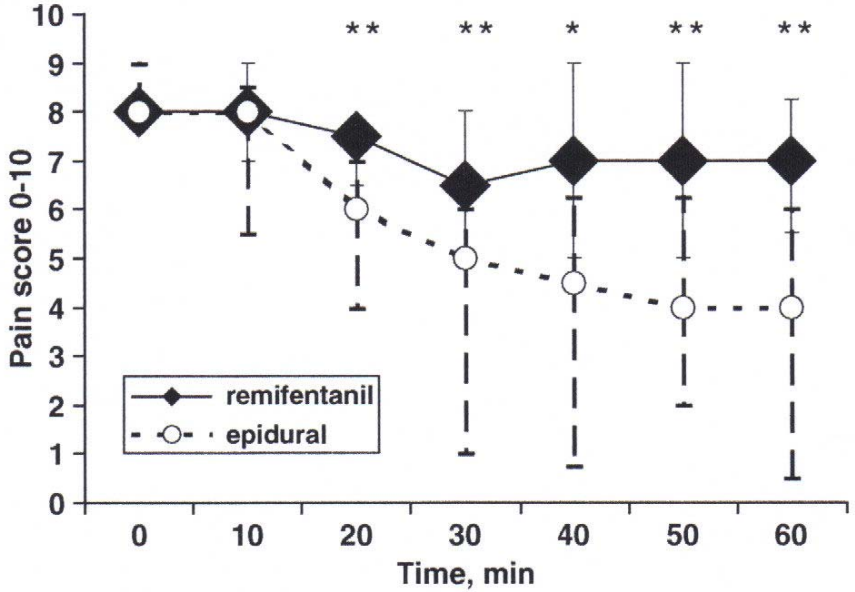


*Fig. 2. Pain scores (median and 25th and 75th percentiles) during intravenous patient-controlled analgesia with remifentanil or epidurally given 20 ml levobupivacaine 0.625 mg/ml and fentanyl 2 μg /ml in saline. *P < 0.05, **P < 0.01.*

Volmanen et al. Acta Anaesth Scand 2008; 52, 249 – 255.

Quality of pain relief.

- 5 – 40% conversion to regional analgesia in various studies.
- 35% dissatisfied with opioid analgesia: Jain et al. 2003.

- Blair et al. 2001:
  - 90% of women used remifentanil + nitrous oxide !
- Thurlow et al. 2002:
  - 55% of women used remifentanil + nitrous oxide !
- Volikas et al.2001:
  - 45% of women used remifentanil + nitrous oxide !

- A quote: « remifentanil has been shown to provide modest analgesia in labor …. »
- David Hill, 2008

THE BEST LABOUR PAIN RELIEF STRATEGY IS A NEURAXIAL BLOCK !

THE BEST LABOUR PAIN RELIEF STRATEGY IS A NEURAXIAL BLOCK !

IF ONE OPTS FOR OPIOID ANALGESIA OR NITROUS OXIDE PERHAPS REMIFENTANIL IS SLIGHTLY BETTER IN TERMS OF PAIN RELIEF.

Fentanyl – meperidine – remifentanil.

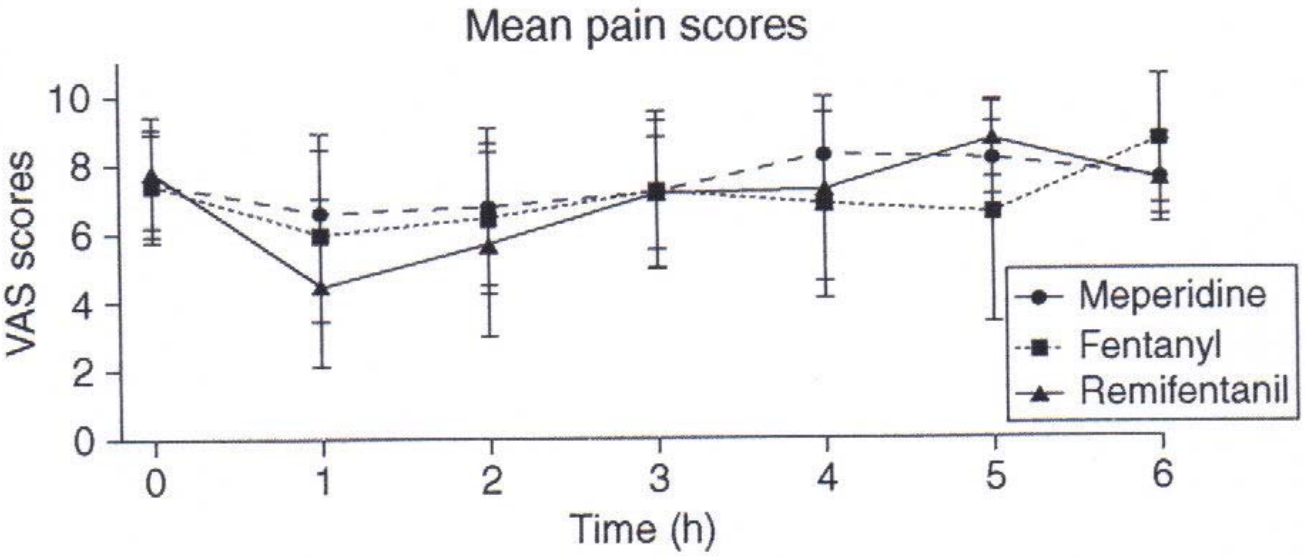


Fig 1 Mean VAS pain scores as a function of time for meperidine, remifentanil, and fentanyl. Vertical bars represent SD.

Douma et al. Brit J Anaesth 2010; 104, 209 – 215.

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Maternal side-effects.

- Sedation.
- Nausea and vomiting.
- Pruritus.
- Respiratory depression and desaturation.

Sedation.

- Blair: VAS scores for sedation.
  - 2001: from 20 to 40 and 60 mm.
  - 2005: from 30 to 80 mm.
- Volmanen: four point scale 0 – 3.
  - 2005: sedation score of 2.
  - 2008: sedation score of 2.3.

Nausea and vomiting.

- Volikas: VAS score (mm).
  - 2005: 9 mm.
  - 2001: 20 mm and 2/9 patients required ondansetron.
- Reported incidence in various remifentanil studies: 30 – 60%.
  - Example: Douma et al. 2010: 39% !
- Epidural analgesia: < 5% incidence.

Pruritus.

- Reported incidence in various remifentanil studies: 10 – 50%.
- Epidural analgesia: similar incidence.

Respiratory depression and desaturation.

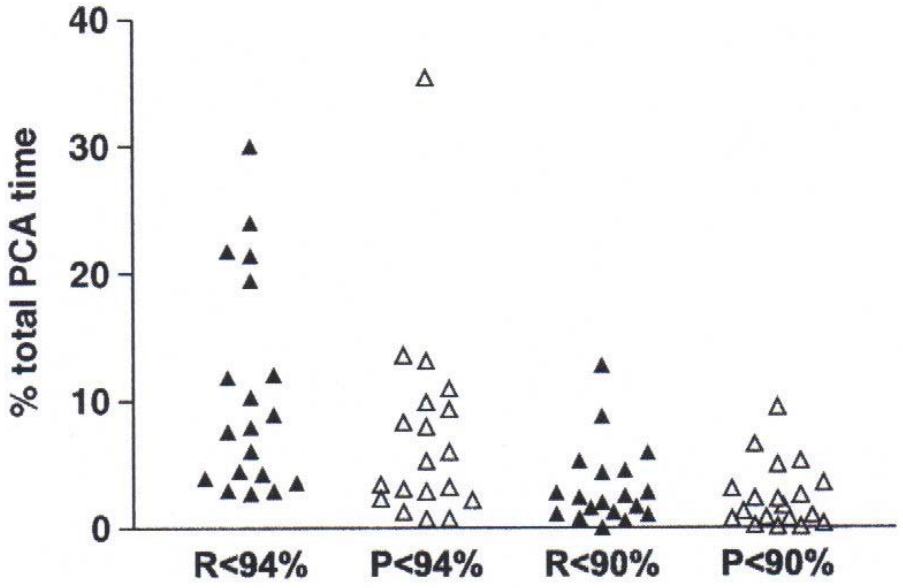
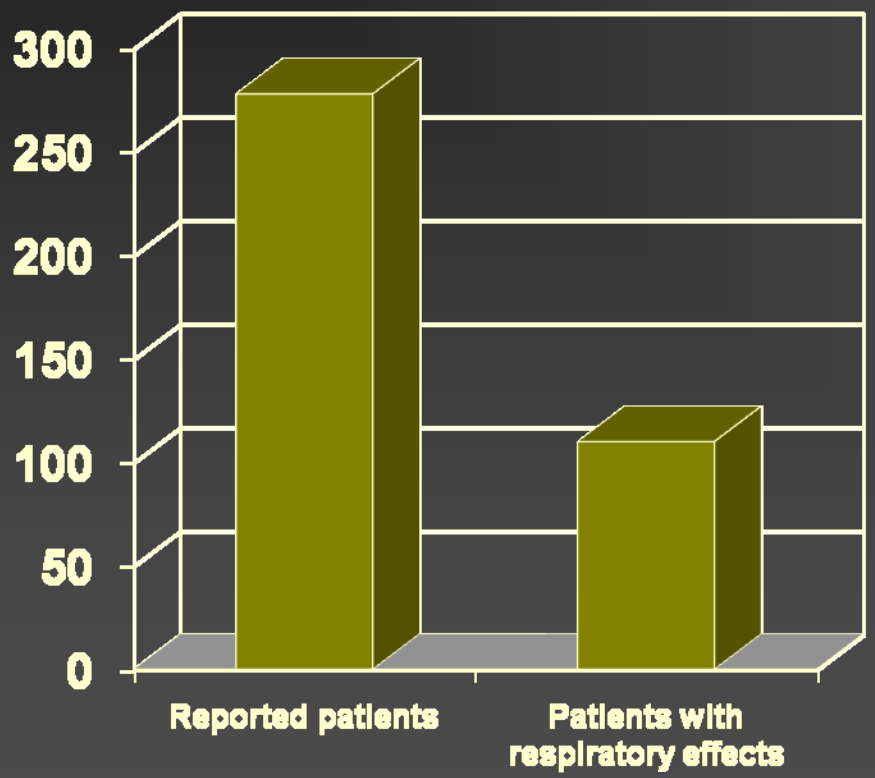


Figure 2 Percentage of total PCA time spent with SpO_2 < 94% or < 90% for each woman during labour using remifentanil (R; closed triangles) or pethidine (P; open triangles) PCA.

Blair et al. Anaesthesia 2005; 60, 22 - 27.

Respiratory effects.

40 % respiratory problems



Respiratory effects:

SaO2 < 90%

SaO2 < 94%

SaO2 < 95%

RR < 12

RR < 8

« Remifentanil is no worse then pethidine……. »

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« Remifentanil is no worse then pethidine……. »

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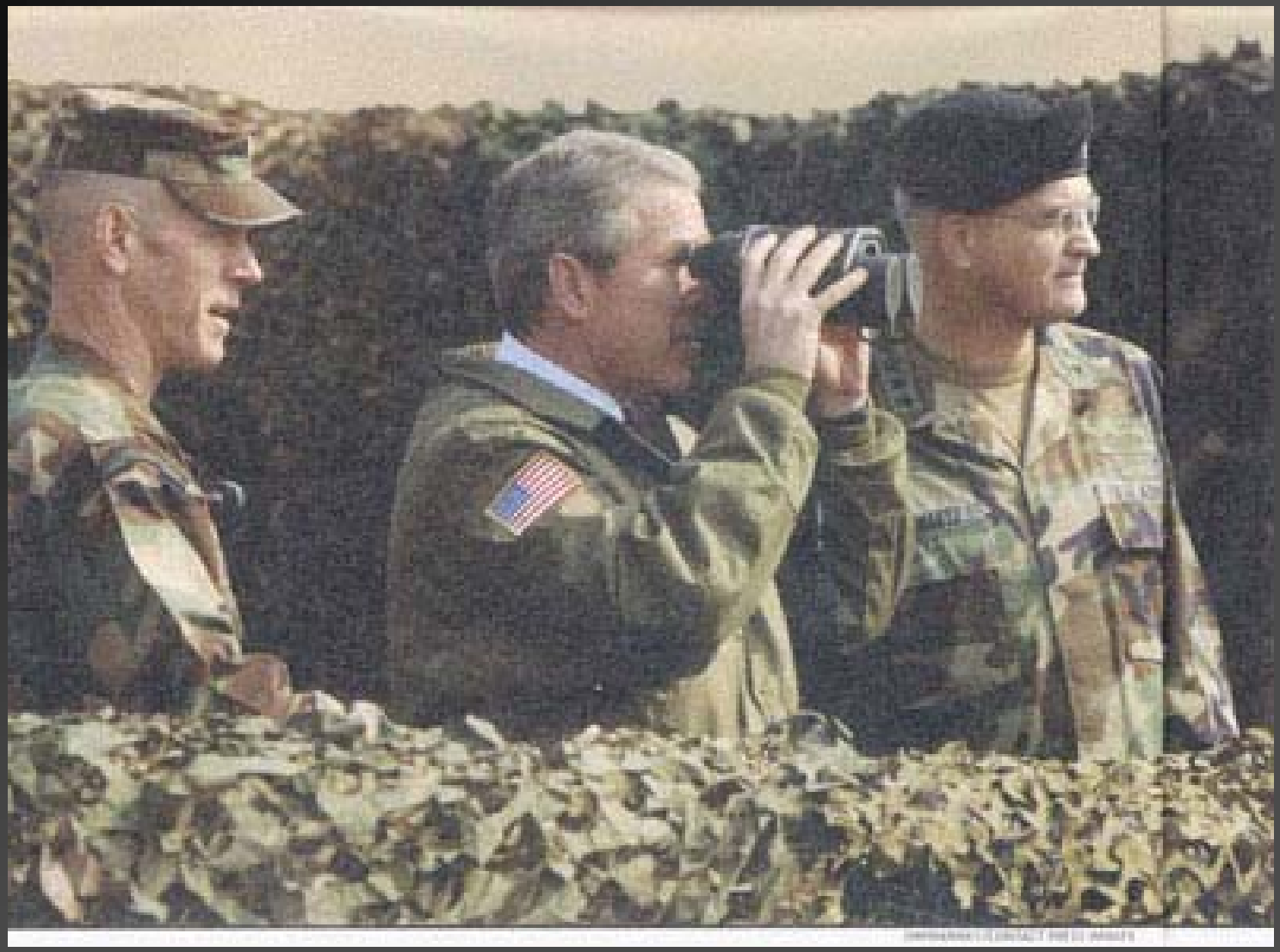
In the land of the blind, one-eye is king !

Respiratory depression and desaturation.

- Balki 2007: « We further recommend continuous oxygen saturation monitoring, one-on-one nursing, and the use of supplemental oxygen if the oxygen saturation falls below 95%. »
- Thurlow 2002: « Remifentanil is a potent respiratory depressant and adequate continuous monitoring is advisable. »
- Douma 2010: « Because remifentanil is a potent respiratory depressant, continuous monitoring is required. Further studies are needed to determine the safety of remifentanil especially with relation to its respiratory effects. »

- Are we really willing to give supplemental oxygen and continuous oxygen saturation montoring to all our labouring patients ?



« Is David Bush or George Hill really letting us believe he is monitoring routinely for desaturation ? »

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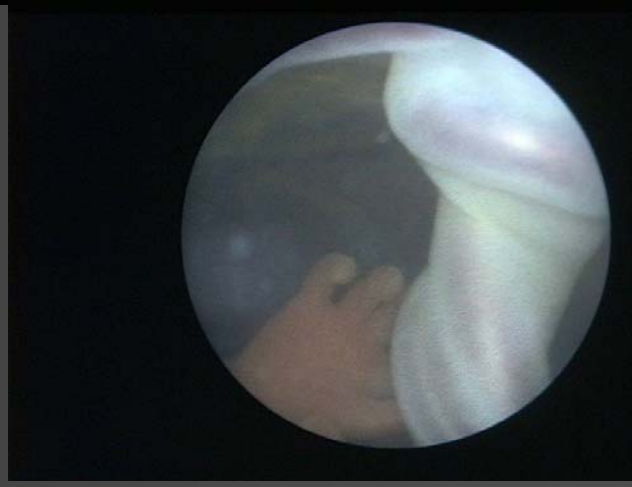
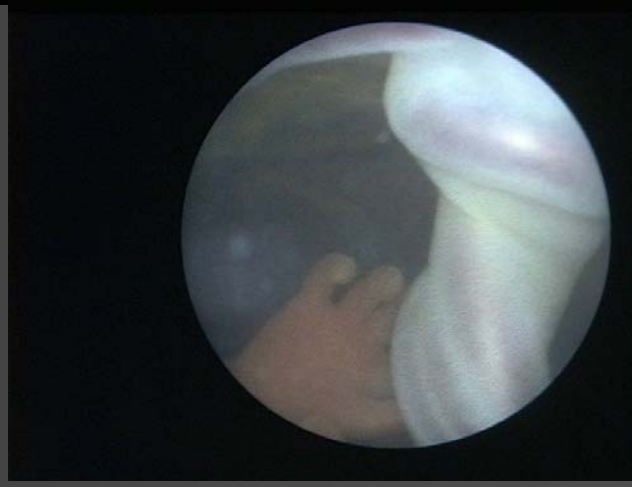
Remifentanil sedation in second trimester pregnancies.



- 54, second trimester pregnancies.
- CSE anesthesia: 8 mg hyperbaric bupivacaine.
- Two groups:
  - Diazepam (DZP): 10 mg IV + a further bolus 2.5 mg if required.
  - Remifentanil (REMI): 0.1 µg/kg/' and increments of 0.025 µg/kg/' if required.
- Maternal and fetal hemodynamics, fetal immobilization, maternal sedation, maternal blood gas analysis.
  - Fetal immobilization:
    - VAS score of mobility: 100 is baseline mobility and 0 is no mobility.
    - Number of limb and gross body movements per 5 minutes.
    - Overal appreciation by endoscopic surgeon.

Van de Velde et al. Anesth Analg 2006.

Remifentanil sedation in second trimester pregnancies.



- Loss of beat-to-beat variability in the CTG !
- There have been cases of urgent C-section for opioid induced loss of FHR variability.

Van de Velde et al. Anesth Analg 2006.

Remifentanil for general anesthesia: Case reports.

Case report + year	A1	A5	A10	Weight (g)	Mask	Duration mask	ETT	Naloxone	NICU
Scott et al. 1998	6	8	8	NR	No	0	No	No	NR
Bedard et al. 1999	7	8	NR	2970	No	0	No	No	Yes
Johannsen et al. 1999	3	5	10	635	Yes	NR	Yes	No	Yes
Johnston et al. 2000	8	10	NR	1960	No	0	No	No	No
Manullang et al. 2000	6	9	NR	NR	No	0	No	No	No
Mertens et al. 2001	3	7	9	NR	Yes	1 minute	No	No	NR
McCarroll et al. 2001	6	8	NR	NR	NR	NR	NR	Yes	NR
Imarengiaye et al. 2001	6	9	NR	2830	Yes	4 minutes	No	Yes	NR
Wadsworth et al. 2002	3	9	NR	3100	Yes	6 minutes	Yes	No	Yes
Wadsworth et al. 2002	3	7	NR	2150	Yes	NR	No	No	Yes
Orme et al. 2004	10	10	NR	3500	No	0	No	No	Yes
Orme et al. 2004	9	10	NR	3200	No	0	No	No	No
Orme et al. 2004	6	10	NR	3000	Yes	1 minute	No	No	No
Orme et al. 2004	5	10	NR	2400	No	0	No	No	Yes
Carvalho et al. 2004	7	9	NR	3027	Yes	2 minutes	No	No	No
Richa et al. 2005	8	10	10	2050	No	0	No	No	Yes
Restrepo et al. 2005	7	10	NR	NR	No	0	No	No	NR
Restrepo et al. 2005	8	10	NR	NR	No	0	No	No	NR
Alexander et al. 2005	8	10	NR	NR	No	0	No	No	No

10/19 neonates Apgar at 1' < 7 (53%); at 5' only 1/19 neonates (5%); 7/19 required mask ventilation (37%).

Remifentanil for general anesthesia: Prospective case series.

Base Exc: base excess; ND: not done, UA: umbilical artery.

Patient	Apgar 1'	Apgar 5'	Apgar 10'	Weight (g)	Mask (min)	UA pH	UA pCO2	Base Exc
1	7	9	10	1250	1	7.364	50.2	2.1
2	3	6	9	1410	5	7.233	64.5	- 2.6
3	7	9	9	3830	None	7.370	54.2	4.3
4	7	8	9	1187	None	7.318	52.9	- 0.2
	9	9	9	1750	None	7.340	45.1	- 1.8
5	5	9	10	3100	2	7.297	57.0	- 0.3
6	5	9	10	3050	3	ND	ND	ND
7	9	9	10	3370	None	7.319	53.3	- 1.7
8	8	9	9	1750	None	7.270	54.2	- 3.0
	8	9	10	1650	None	7.300	57.0	- 0.3
9	2	6	8	2135	3	7.322	50.1	- 1.1
	4	7	8	1660	None	7.300	57.3	- 0.2
10	1	9	9	3600	2	7.205	52.8	- 1.3

Van de Velde et al. Int J Obstet Anesth 2004; 13, 153 – 158.

Opioids and fetal acid-base status.

BJOG: an International Journal of Obstetrics and Gynaecology
December 2002, Vol. 109, pp. 1344–1353

Analgesia in labour and fetal acid–base balance: a meta-analysis comparing epidural with systemic opioid analgesia

Felicity Reynolds[a,*], Shiv K. Sharma[b], Paul T. Seed[c]

Opioids and fetal acid-base status.

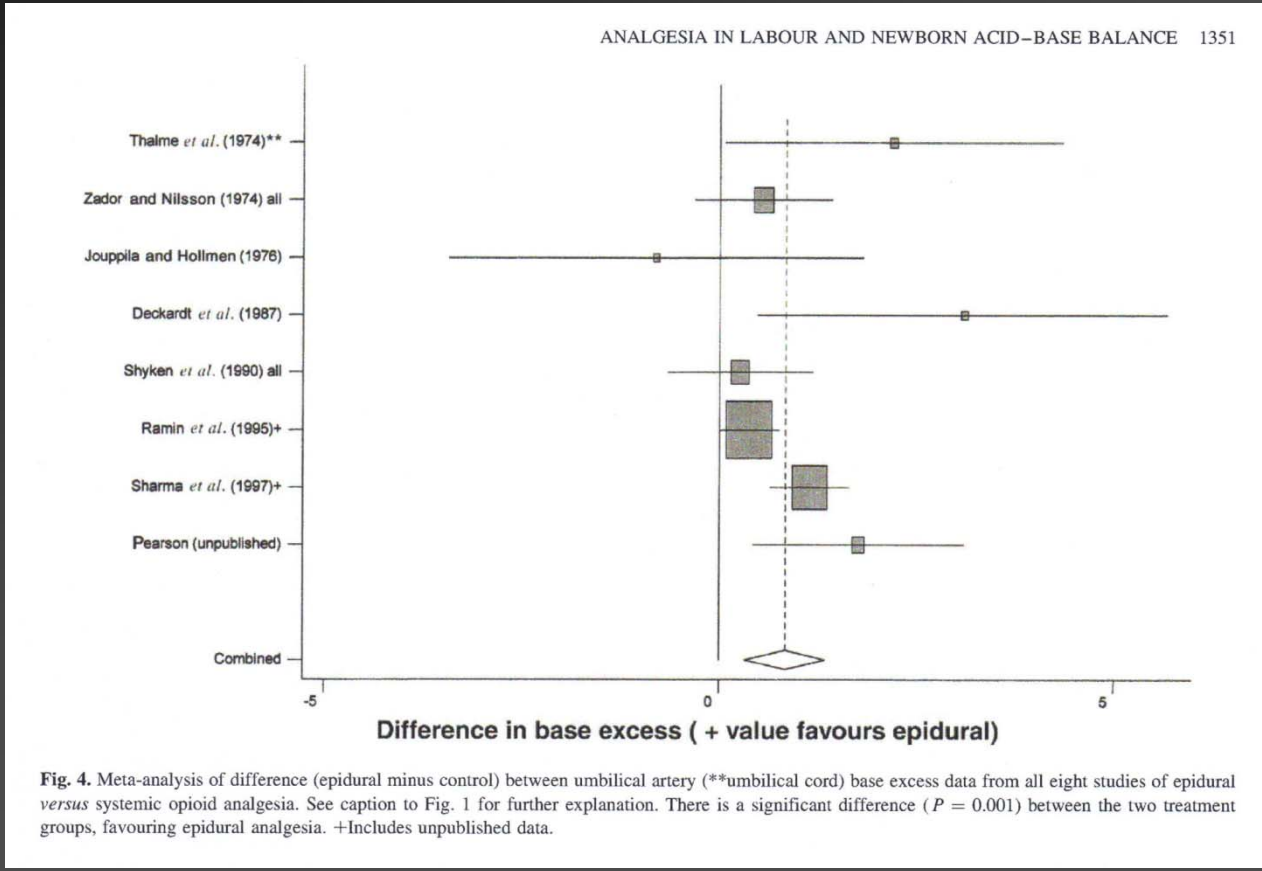


Fig. 4. Meta-analysis of difference (epidural minus control) between umbilical artery (**umbilical cord) base excess data from all eight studies of epidural *versus* systemic opioid analgesia. See caption to Fig. 1 for further explanation. There is a significant difference ($P = 0.001$) between the two treatment groups, favouring epidural analgesia. +Includes unpublished data.

Reynolds et al. BJOG 2002; 109, 1344 - 1353.

Remifentanil and fetal acid-base status.

- Only four studies looked at UA BE !
- Only 1 study looked specifically at side-effects (n = 50, n = 37 for umbilical artery samples; Volikas et al. BJA 2005).
- UA BE: -5.19 ± 5.02 (mean ± SD).
- 2/34 subjects UA BE worse then -10 mEq/L.

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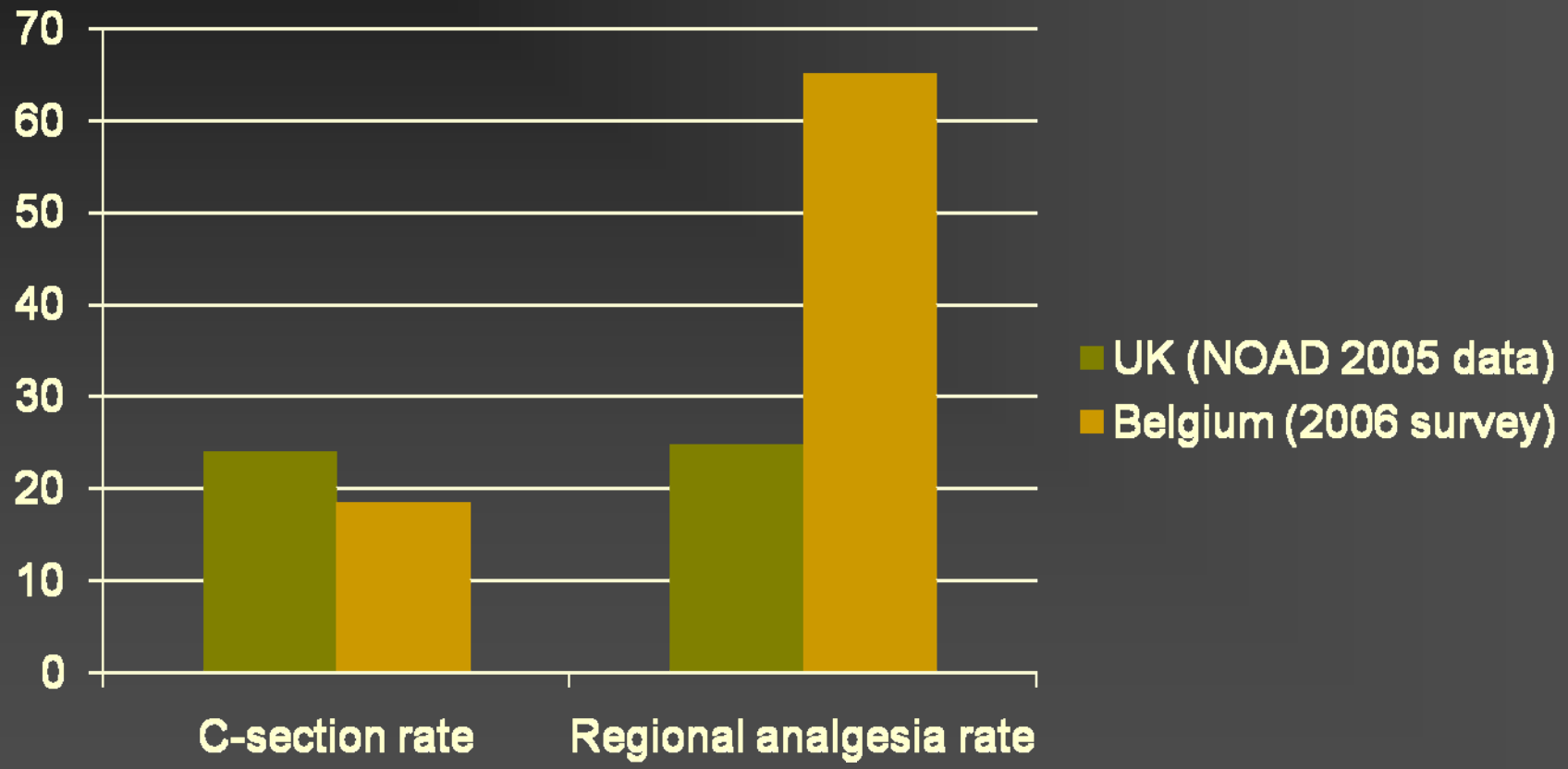
Remifentanil versus neuraxial analgesia: C-section rate.



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Rat studies: remifentanil decreases uterine muscle activity following oxytocin infusion in vitro.

	n	pD_2	E max %
Meperidine	10	3.7 ± 0.2	39.5 ± 7.8
Remifentanil	10	3.9 ± 0.2	20.5 ± 7.6
Alfentanil	10	3.6 ± 0.5	42.3 ± 8.9
Mepivacaine	10	4.7 ± 0.2	33.1 ± 7.3
Ropivacaine	10	4.1 ± 0.4	9.5 ± 3.7
Bupivacaine	10	4.2 ± 0.2	20.4 ± 7.4
Clonidine	10	ND	4.7 ± 10.4
Midazolam	10	5.3 ± 0.6	41.0 ± 11.0

The sensitivity (pD_2) and maximal responses (E_{max}) of isolated pregnant rat uterine preparations to agents tested.

Nacitarhan et al. Methods Find Exp Clin Pharmacol 2007; 29, 273-276.
Kayacan et al. Adv in Therap 2007; 24, 368 – 375.

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Sometimes bonafide information can be misleading or untrue…..

What is the scientific basis to advocate routine use ?

- 65 hits.
- 8 were unrelated.
- 2 were experimental studies.
- 29 were letters and reviews.
- 12 were case reports.
- 14 prospective studies.

What is the scientific basis to advocate routine use ?

- 10 groups (7 groups have done only 1 study). 3 groups have done 7 studies (Volmanen, Blair and Volikas).
- Involving 358 parturients that received remifentanil in labour.
- Most patients: remifentanil was stopped after 60 – 180 minutes.

Who apart from Dr. Hill is using it ?

- In Belgium: High epidural zone ! >65%
  - Only if epidural is contraindicated
  - Only in 50% of centers.
- In Norway: Low epidural zone ! <30%
  - Only 2 units offer remifentanil !
  - Meperidine still preferred.

Any alternatives for remifentanil when Epidurals are contraindicated ?

TRAMADOL !!!!!!!

Conclusion.

- Remifentanil is worse in terms of pain relief and maternal and fœtal side-effects as compared to epidural analgesia.
- Remifentanil is marginally better then pethidine or entonox.
- Opinion leaders state that routine oxygen saturation monitoring and supplemental oxygen are required, combined with one-to-one care.

Conclusion.

- At the moment, I can not recommend remifentanil for FIRST LINE use, because:
  - There are better alternatives.
  - It has potent maternal and fœtal side-effects and adequately powered studies evaluating it's safety are non-existing.
- What we need are good prospective LARGE studies demonstrating maternal and fœtal/neonatal safety. I encourage the opinion leaders in the field to act according to what they say. That is to do the large, well-designed safety studies !!!!