

---

# Proceedings of the Residents' Meeting of the Belgian Society of Anesthesia and Reanimation

8 September 2007

---

*Weight-related aprotinin regimen in cardiac surgery : effects on blood loss and transfusion needs.*

Liesbeth BATENS, Gerdy DEBEUCKELAERE, Stefanie CROMHEECKE, Stefan DE HERT. Department of Anesthesiology, University Hospital Antwerp, Belgium.

## Introduction

Aprotinin is a serine protease inhibitor, whose advantages when given for heart surgery are : reduced perioperative bleeding, decreased reintervention rates and lesser needs for transfusion. The current high-dose regimen gives a fixed dose to all patients regardless of weight, age, gender or medical antecedents. This approach may result in highly variable plasma concentrations (1, 2). To avoid this a weight-related protocol has been proposed, but its efficacy awaits clinical confirmation. We hypothesized that the use of a weight-related regimen would be associated with lower blood loss.

## Methods

After institutional ethical committee approval and written informed consent, one hundred and twenty eight

patients scheduled to undergo elective cardiac surgery and allocated to aprotinin treatment according to institutional guidelines (combined procedures and recent antiplatelet drug therapy) were randomly assigned to two aprotinin dosage regimens : high-dose (n = 78) : 280 mg pump prime load, 280 mg bolus and a maintenance infusion of 70 mg/h until the completion of the operation, or a weight-related protocol (n = 50) : 52.5 mg in the pump prime, 3.5 mg/kg bolus and 3.5 mg/kg/h maintenance infusion. Postoperative blood loss and need for transfusion of allogenic blood products was assessed and the total aprotinin dosage was calculated. Data were compared using Student-t test,  $\chi^2$  square test or Mann-Whitney-U test where appropriate.

## Results

	high dose	weight related
blood loss after 12 h (ml)	431 $\pm$ 299	404 $\pm$ 280
blood loss after 24 h (ml)	577 $\pm$ 346	579 $\pm$ 444
patients receiving packed cells (%)	17 (21%)	19 (38%)
transfused products : median (range)		
packed red blood cells (units)	0 (6)	0 (3)
platelets (donor units)	0 (15)	0 (2)
fresh frozen plasma (units)	0 (6)	0 (7)
amount of aprotinin (mg/kg)	8.9 $\pm$ 1.7	8.8 $\pm$ 2.3

## Conclusion

Weight-related aprotinin regimen is as effective as high-dose regimen with regard to postoperative blood loss and transfusion needs. Because of the small number of patients included, this study is not sufficiently powered to make a definite conclusion about the efficacy of aprotinin.

## References

1. Royston D., Cardigan R., Gippner- Steppert C., Jochum M., *Is Perioperative Plasma Aprotinin Concentration More Predictable and Constant After a Weight-related Dose Regimen ?*, ANESTH. ANALG., **92**, 830-6, 2001.
2. Nuttal G., Fass D., Oyen L., Oliver W., Ereth M., *A Study of a Weight-adjusted Aprotinin Dosing Schedule During Cardiac Surgery*, Anesth. Analg., **94**, 283-9, 2002.

*Neonatal outcome following vaginal delivery in normal, term, vertex presenting pregnancies : effect of combined spinal epidural analgesia.* L. BEQUE, F. DE BUCK, E. VANDERMEERSCH, M. VAN DE VELDE. Department of Anaesthesiology, UZ Gasthuisberg, Leuven, Belgium.

### Introduction

Recent evidence, compiled from randomised, prospective trials, suggests that epidural labor analgesia improves fetal acid base status when compared to parenteral opioid analgesia (1). However, no data is available comparing labor with neuraxial analgesia to labor without any pharmacological analgesia. The present retrospective study compares the effects of combined spinal epidural analgesia or no analgesia on fetal acid base status and neonatal outcome in term, vertex presenting, healthy pregnancies.

### Methodology

Following ethics committee approval, the obstetric and anesthetic database was searched to identify all patients that delivered a term, vertex presenting, singleton pregnancy between January 1<sup>st</sup> 2000 and December 31<sup>st</sup> 2002. Demographic data, relevant obstetric data, type of analgesia, neonatal outcome (blood gas analysis and Apgar scores) were recorded. Data were analysed according to type of analgesia used. Data were analysed

using repeated measures ANOVA with appropriate post-hoc testing. Categorical data were analysed using Chi square analysis. A  $p < 0.05$  was considered to be statistically significant.

### Results

A total of 2611 mothers were identified. Only 1366 full datasets could be completed. Regional analgesia, using the combined spinal epidural technique, was administered to 852 mothers, while no pharmacological analgesia was given to 514 patients. Demographic and obstetric data were similar between the two groups. Outcome of labour was similar between treatment groups. Umbilical artery pH was lower in the group treated with combined spinal epidural analgesia (Table 1). However the number of patients with extremely low pH values or a high base deficit was similar between the two treatment groups (Table 1). In the regional analgesia group more low Apgar scores were noted as well as more babies that needed admittance to the neonatal intensive care unit (Table 1).

	CSE (n = 852)	No analgesia (n = 514)
Umbilical artery pH	7.264 ± 0.074	7.297 ± 0.076*
Umbilical artery pCO <sub>2</sub> (mmHg)	55 ± 10	51 ± 10*
Umbilical artery pO <sub>2</sub> (mmHg)	17.2 ± 13.8	18.8 ± 17.7
Umbilical artery base deficit	-1.96 ± 3.9	-1.76 ± 3.0
Umbilical artery pH < 7.04 (n)	5	2
Umbilical artery base deficit > -12 (n)	3	2
NICU admittance (n)	42	13
Apgar < 7 (n)	42	13

NICU : neonatal intensive care unit ; CSE : combined spinal epidural analgesia ; \* $p < 0.05$  versus CSE.

### Discussion

Based on this retrospective study, fetal acid base status is reduced when patients receive regional analgesia. This effect seems to be a respiratory effect. Severe fetal acidosis, risking neonatal encephalopathy, is not increased in our study population. Since the study is retrospective, we are unable to conclude that the effects on fetal acid base status are causally related to the analgesic technique used. As with many so-called side-

effects of labour analgesia, the factors influencing patient choice to opt for regional analgesia are also causally related to more prolonged second stage labours and thus impaired fetal acid base status. A prospective, properly randomised trial should now follow this retrospective audit.

### References

1. Reynolds F., BJOG, **109**, 1344-1353, 2002.

*Pain processing in hypnosis studied by functional magnetic resonance imaging (fMRI).* P. BOVEROUX, M. BOLY, A. VANHAUDENHUYSE, SCHNAKERS, A. LUXEN, P. MAQUET, S. LAUREYS, M. FAYMONVILLE. University of Liège, Liège, Belgium.

### Introduction

The neural mechanisms underlying the antinociceptive effects of hypnosis remain badly understood. We here used fMRI to study the effect of hypnosis on thulium-YAG laser induced pain in volunteers. Thulium-YAG laser emits near-infrared radiation with a penetration depth of 360  $\mu\text{m}$  into the human skin. The laser stimulation allows precise targeting of the emitted heat energy to the termination area of primary nociceptive afferents without damaging the epidermis or affecting the subcutaneous tissue. Additionally, the temperature rise in the superficial skin is fast enough to elicit activation of thinly myelinated A $\delta$ - and unmyelinated C nociceptors (1).

### Methods

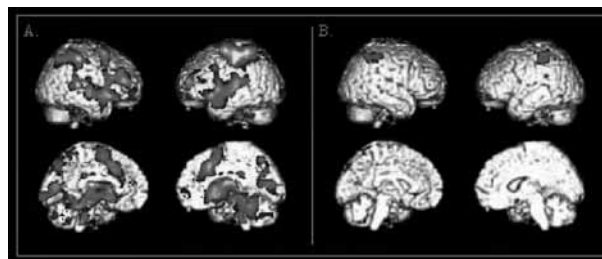
13 healthy volunteers were recruited from Liège University and gave their written informed consent to participate in the study. The study was approved by the Ethics Committee of the University of Liège and was conducted according to the declaration of Helsinki (\*) and to the International Association for the Study of Pain Ethical Guidelines for Pain Research in Humans (\*). Subjects were pre-selected for their high hypnotizability by an experimented anesthesiologist (Pr Faymonville). They underwent 2 randomized fMRI sessions, one in normal, and one in hypnotic state induced by a validated clinical protocol (\*). During each session, 200 laser stimuli with intensity ranging from 300 to 600 mJ were administered on the left hand. Subjects rated their sensations as P0 : nothing perceived, P1 : perceived, non painful, P2 : mild pain, P3 : moderate pain, P4 : intense pain. fMRI data were preprocessed and analyzed using statistical parametric mapping (SPM2) (<http://www.fil.ion.ucl.ac.uk/spm/software/spm2/>; Wellcome Department of Imaging Neuroscience, London, UK). Analyses compared activation induced by matched intensity laser stimulation in normal and in hypnotic state. Results were thresholded at small-volume corrected  $p < 0.05$  within the previously identified pain matrix (2).

### Results

A significant difference in sensation was found between normal and hypnotic state for the painful intensity range of stimulation (mean score  $1.9 \pm 0.3$  SD vs.  $1.2 \pm 0.4$ , respectively), but not for the non-painful range of intensity (mean score  $0.5 \pm 0.2$  SD vs.  $0.4 \pm 0.3$ , respectively). In the normal state, high intensity (painful) compared to low intensity (non-painful) stimuli activated bilateral thalamus, primary somatosensory cortex (S1), insula, and anterior cingulate cortex (i.e., the pain matrix). In the hypnotic state, high intensity compared to low intensity stimuli only identified significant activation in S1. Bilateral thalamus, left insula and bilateral anterior cingulate cortex showed significant less activation in the hypnotic state as compared to the normal state.

### Conclusion

Our parametric event-related fMRI study investigating the effects of hypnotic suggestion on pain intensity perception in healthy volunteers demonstrated decreased pain perception during hypnosis, while leaving sensory non-painful perception unaltered. This hypnosis-induced decreased pain perception correlates with a decreased activation in thalamus, insula and anterior cingulate cortex.



Brain activation induced by high intensity painful laser stimulation in our volunteers in A : normal awake state ; B : hypnotic state. Results of random-effect group analyses thresholded for display purposes at uncorrected  $p$  value  $< 0.0001$  on a standard surface T1 template.

Brain area	x	y	z	Z value	P value
Medial thalamus	-4	-10	12	3.44	0.033
	16	-18	6	3.56	0.025
Insula	-32	-2	13	3.35	0.042
Anterior cingulate cortex	8	8	30	3.68	0.018
	-4	10	60	3.39	0.037

Areas significantly more activated in normal awake state compared to hypnosis, in response to painful compared to non painful stimulation. Results thresholded at 10-mm radius sphere small volume corrected  $p < 0.05$  on a priori pain matrix areas coordinates.

### References

1. Buchel *et al.*, J. NEUROSCI., **22** (3), 970-6, 2002, Bornhovd.
2. Craig A. D., ANNU. REV. NEUROSCI., **26**, 1-30, 2003.

*Assessment of the coagulation tests sparing effect of a standardized oriented questionnaire in pregnant women.* D. CERFONT, E. VAN BRUSSEL, P. Y. DEWANDRE, V. BONHOMME, P. HANS, J. F. BRICHANT.  
Department of Anaesthesia & ICM, CHU Liege and CHR de la Citadelle, Liege, Belgium.

### Background

Spinal haematoma is a rare but potentially severe complication of neuraxial blockade. Abnormal coagulation is a risk factor for this complication. Although current guidelines recommend that the decision to order coagulation tests in parturient wishing to benefit from labor epidural analgesia should be individualized and based on patient history, these tests are required for every such patient in numerous hospitals (1).

### Aim

The goal of this study was to estimate the coagulation test sparing effect of a standardized questionnaire aiming at detecting coagulation disorders.

### Material & methods

After approval of the study protocol by the Institutional Ethics Committee, 808 consenting pregnant women in late pregnancy were recruited between February and December 2006. They were asked to answer, by yes or no, to a standardized written questionnaire containing seven questions regarding bleeding disorders. These questions were : 1) Do you or does one of your relatives have a coagulation disorder ? 2) Did you already have had a prolonged bleeding after a bite of tongue ? 3) Do you have bruises without obvious cause ? 4) Did you already have bled for a long time after a tooth extraction ? 5) Do you have heavy periods ? 6) Did you already have had abnormal bleeding during or after a delivery or a surgical procedure ? 7) Did a relative have had any abnormal bleeding during or after a delivery or a surgical procedure ?

Should a patient answer "yes" to any of these seven questions, a set of coagulation tests was ordered by the attending anesthesiologist.

### Results

Among the 808 patients, 266 answered "yes" to at least one question. After further questioning by the attending anesthesiologist, it was deemed not necessary to perform coagulation tests in 26 patients. Among the remaining 240 patients, only 3 patients had an abnormal coagulation test but a neuraxial anesthesia was performed in these 3 parturients as the alterations were not clinically significant.

### Conclusion

A standardized questionnaire allows to spare coagulation tests in 70 percent of the pregnant women who wish to deliver with neuraxial analgesia. Such a reduction has also been demonstrated in a general surgical population (2). Also, this is in agreement with the estimation of 35% of pregnant patient requiring coagulation tests after systematic preanesthetic assessment in France (3). This would result in a significant cost reduction.

### References

1. The BARA Working Party on Obstetric Anesthesia, *Belgian Guidelines and recommendation for safe practice on obstetric anesthesia*, ACTA ANAESTHESIOL. BELG., **54**, 119-125, 2003.
2. Koscielny J., *et al.*, *Preoperative identification of patients with impaired haemostasis. A practical concept*, HÄMOSTASEOLOGIE, **27**, 177-184, 2007.
3. Simon L., *et al.*, *Evaluation of hemostasis before obstetrical epidural anesthesia: a survey in 435 French obstetric departments*, ANN. FR. ANESTH. REANIM., **16**, 107-113, 1997.

## Postoperative analgesic effect of epidural Neostigmine after non-elective Cesarean Section.

P. CHAMORRO, M.D., F. ROELANTS, M.D., P. LAVAND'HOMME, M.D., Ph.D. St Luc Hospital, Université Catholique de Louvain, Brussels, Belgium.

### Background

Epidural Neostigmine, a cholinesterase inhibitor, produces antinociceptive effects without the bothersome side effect which are usually associated to the intrathecal administration. At dose up to 4 µg/kg, epidural Neostigmine provides limited analgesia after elective cesarean section (CS) (1). Pain may activate spinal noradrenergic inhibitory system and hence spinal cholinergic pathways (2) and Neostigmine displays greater analgesic effect in experimental postoperative conditions (3), the study sought to evaluate the postoperative effects of epidural Neostigmine administered in laboring women who have undergone a semi-urgent CS under epidural anesthesia.

### Materials and methods

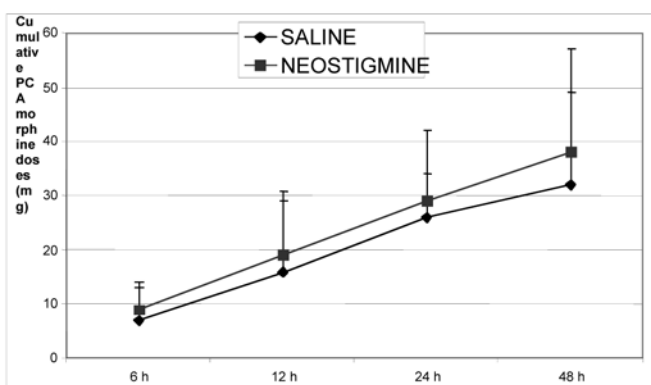
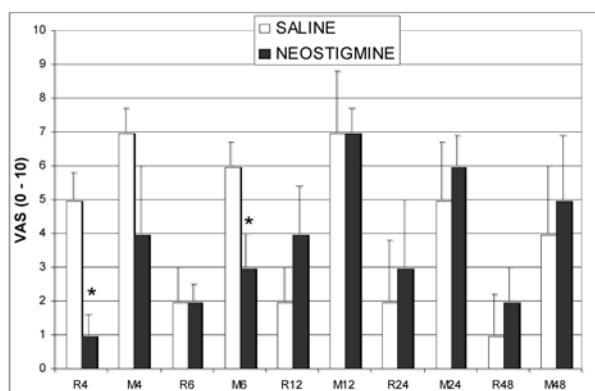
After Ethical Committee approval and informed consent, healthy parturients in labor with indwelling epidural catheter (receiving ropivacaine/sufentanil analgesia) who needed a semi-urgent CS (anesthesia Th4 level with epidural administration of ropivacaine 0.75%) were randomly assigned to receive after cord clamping : either saline 5 mL (n = 13) or Neostigmine 500 µg dilut-

ed in 5 mL saline (n = 12). Postoperative pain scores at rest and movement (VAS : 0-10), time to first analgesic request and PCA morphine needs were recorded at 4,6,12,24 and 48 h after injection. Hemodynamic parameters and side effects (sedation, nausea) were also noticed.

Statistical analysis used one way ANOVA,  $P < 0.05$  (\*) was considered to be significant.

### Results

Demographic data did not differ (age, pregnancy term, history of previous CS). Labor duration ( $400 \pm 200$  min), cervical dilatation ( $5 \pm 1.7$  cm) and epidural doses of ropivacaine ( $77 \pm 49$  mg) and sufentanil ( $17 \pm 5$  µg) received at the time of CS were similar in both groups. Evaluation of labor analgesia demonstrated similar maximal VAS scores in saline ( $3 \pm 2.9$ ) and the Neostigmine group ( $3 \pm 2.3$ ). Early postoperative pain scores were significantly decreased in the Neostigmine group. Time for first PCA use was similar ( $174 \pm 103$  min and  $157 \pm 123$  min) as well as total 48h consumption. No particular side effects occurred in relation to epidural Neostigmine administration between both groups.



### Discussion and conclusion

As previously reported for elective CS (1), epidural Neostigmine only provides a short-lasting postoperative analgesia in laboring women undergoing semi-urgent CS. The results confirm a previous investigation results and the lack of evidence for a spinal cholinergic system activation during labor (4).

### References

1. Kaya, *et al.*, ANESTHESIOLOGY, **100**, 381-5, 2004.
2. Eisenach, *et al.*, PAIN, **43**, 149-54, 1990.
3. Bouaziz, *et al.*, REG. ANESTH. PAIN MEDICINE, **80**, 1140-4, 1995.
4. Eisenach, *et al.*, ANESTH. ANALG., **82**, 621-6, 1996.

*Influence of lateral tilt on the hemodynamic variables after spinal anaesthesia for caesarean delivery.* P. DEPAUW, E. DEFLANDRE, D. LEDOUX, E. LANGLET, J. F. BRICHANT. Department of Anaesthesia & ICM, CHU Liege and CHR de la Citadelle, Liege, Belgium.

### Background

In late pregnancy, the gravid uterus compresses the inferior vena cava. This can contribute to the hypotension associated with spinal anaesthesia for caesarean section. Therefore, it is recommended to tilt the patients undergoing caesarean section to the left. However the ideal amount of tilt has not been determined so far. Hence, we investigate to what extent the use of different left lateral tilts alter hemodynamic during caesarean section under spinal anaesthesia.

### Methods

After IRB approval, 39 (ASA 1-2) pregnant women (GA > 36 weeks) scheduled to undergo caesarean section under spinal anaesthesia were enrolled in this randomised prospective study. All had normal monofoetal pregnancy. All were premedicated with ranitidine and sodium citrate. Upon admission in the operating theatre, women were equipped with standard monitoring (ECG, NIBP, SpO<sub>2</sub>). A second NIBP device was placed on the

right lower limb. Baseline haemodynamics variables were recorded. An 18G catheter was inserted in a forearm vein and a crystalloid infusion was started. Thereafter, a spinal mixture containing a bupivacaine 0.5% 10 mg + sufentanil 10 µg was injected at the L3-L4 levels with the patient in sitting position. The women were then placed in the supine position on a table tilted to the left. The amount of tilt angle (2.5°, 7.5°, 12.5°) was assigned randomly. A continuous infusion containing ephedrine (2 mg/min) and phenylephrine (10 µg/min) was started. The infusion rate was adjusted according to systolic blood pressure of the upper limb using a predetermined algorithm. The neonates' Apgar scores were recorded at 1 and 5 minutes. Data were analysed using two way repeated measures ANOVA.

### Results

Patients' characteristics were similar in the 3 groups. Haemodynamics variables, vasoconstrictor administration and Apgar scores were not different between the 3 groups.

	SBP Control (mm Hg)	SBP Inc. Cut. (mm Hg)	SBP Inc. Ut. (mm Hg)	SBP Ext. (mm Hg)	Vaso const. cont. (ml/h)	Vaso const. inc.cut. (ml/h)	Vaso const. inc.ut. (ml/h)	Vaso const. ext. (ml/h)	APGAR 1'	APGAR 5'
2.5°	124.29	132.29	137.00	138.86	56.25	45.00	45.00	30.00	8.88	9.63
7.5°	126.08	129.75	134.25	135.92	57.50	50.00	45.50	45.00	9.08	9.75
12.5°	125.18	125.27	135.18	135.18	50.00	45.00	30.00	32.50	9.27	9.92

### Discussion

Our results are in agreement with previous studies finding that moderate amount of left tilt does not improve maternal haemodynamics (1, 2). This lack of significant effect could be explained by an insufficient amount of tilt, inadequate power of the study. Also it would be interesting to obtain neonatal pH and SpO<sub>2</sub> values.

### References

1. Bamber J. H., Dresner M., *Aortocaval compression in pregnancy : the effect of changing the degree and direction of lateral tilt on maternal cardiac output*, ANESTH. ANALG., **97**, 256-8, 2003.
2. Wilkinson C., Enkin M. W., *Lateral tilt for caesarean section*, COCHRANE DATABASE SYST. REV., (2) : CD 000120, 2000.

*Effect of Anesthesia Technique on Neonatal Outcome following Cesarean Section in Premature Infants : a Retrospective Study.* M. DIERCKX, F. DE BUCK, E. VANDERMEERSCH, M. VAN DE VELDE.  
Department of Anaesthesiology, UZ Gasthuisberg, Leuven, Belgium.

### Introduction

Worldwide, spinal anesthesia is the preferred technique for non-urgent Cesarean section (CS) (1). The effect of the type of anesthesia for CS on the premature fetus and neonate is poorly investigated. This retrospective study evaluated the effect of the type of anesthesia (combined spinal epidural anesthesia (CSE), general anesthesia (GA) or epidural anesthesia (EA)) on fetal and neonatal outcome following CS, performed pre-term.

### Methodology

Following ethics committee approval, the obstetric and anesthetic database was searched to identify all patients that delivered prematurely (25-35 weeks) via CS between January 1<sup>st</sup> 2000 and December 31<sup>st</sup> 2005. If urgent CS was performed for reasons of fetal distress, patients were excluded from data analysis. Demographic data, relevant obstetric data, type of anesthesia, maternal hemodynamics, neonatal outcome (weight, blood gas analysis and Apgar scores) were recorded. Data were analysed according to type of anesthesia used for CS. Data were analysed using repeated measures ANOVA with appropriate post-hoc testing. Categorical data were analysed using Chi square analysis. A  $p < 0.05$  was considered to be statistically significant.

### Results

A total of 395 mothers were identified that delivered via CS, giving birth to 566 children. Fifty-three mothers and 91 children were excluded from data-analysis because CS was performed for reasons of acute fetal compromise. So 342 mothers and 475 children remained for final analysis. One third of patients (37%) were delivered because of preeclampsia. Of the 342 mothers that were included, 37% delivered a twin or triplet pregnancy. No differences in age, height and weight were identified between the groups. Patients undergoing general anesthesia (GA), were more premature than those having EA or CSE anesthesia. Baseline hemodynamics as well as hemodynamics during CS were comparable between the groups. Neonatal weight in the GA-group was lower than in the CSE- and EA-groups ( $1470 \pm 590$  versus  $1690 \pm 600$  and  $1660 \pm 620$  g respectively). Umbilical artery pH values were significantly better in the CSE- and EA-groups (Table 1). Compared to the CSE- and EA-groups, more patients in the GA-group had Apgar scores  $< 7$  and umbilical artery pH values below 7.2 and 7.1 (Table 1). Also in the EA-group more patients had low Apgar scores when compared to the CSE-group (Table 1). No differences in neonatal mortality were identified.

Table 1

	CSE-group (n = 337)	GA-group (n = 66)	EA-group (n = 74)
UA pH	$7.300 \pm 0.077$	$7.237 \pm 0.119$ * #	$7.282 \pm 0.069$
Apgar $< 7$ n (%)	65 (19)	43 (65) * #	23 (31) #
UA pH $< 7.2$ n (%)	25 (7)	15 (23) * #	6 (8)
UA pH $< 7.1$ n (%)	10 (3)	5 (8) * #	1 (1)
UA pH $< 7.0$ n (%)	2 (1)	2 (3)	0 (0)

UA : umbilical artery. \*  $p < 0.05$  versus epidural group ; #  $p < 0.05$  versus spinal group.

### Discussion

Based on this retrospective study, GA results in worse neonatal outcome in terms of Apgar scores and umbilical artery blood gas analysis, as compared to CSE or EA anesthesia. However, the need for GA may just be indicative of more severe maternal or fetal pathology.

### Reference

1. Jenkins and Khan, ANAESTHESIA, **58**, 1101-1118, 2003.

*Paraplegia after epidural steroid injection : a case report.* A. GILBEAU, C. SADIS, A. DUCART.  
Anaesthesiology Department, ULB Erasme Hospital, Brussels, Belgium.

### Introduction

Lumbar epidural steroid injections (ESIs) may be indicated to treat chronic spinal pain from disk herniation, canal stenosis, lumbago sciatica pain, radiculopathy and postlaminectomy syndrome.

### Case report

A 68-yr old woman of 90 kg, with diabetes, hypertension and ischemic cardiomyopathy, was scheduled for an ESIs. After a laminectomy (L3-L4) 6 years ago, she presented with leg's weakness and attenuation of reflexes. A CT Scanner revealed a canal spinal stenosis from L1 to S1. Her coagulation tests were normal and her drugs, particularly aspirin and diclofenac, were not stopped before ESIs. An attempt to reach the L4-L5 intervertebral space with an interlaminar technique under fluoroscopy was unsuccessful, provoking paraesthesia. The epidural space was identified with another attempt at the L1-L2 level and a dose of 2% lidocaine (3 ml) with depo-steroid methylprednisolone (80 mg) was injected through a 17 G-Tuohy needle. The patient showed neither haemodynamic change nor weakness. Eight hours later after ESIs, the patient complained of acute pain in the left hip and loss of bladder control, after standing up. The neurological examination revealed a complete loss of motor function and tendon reflexes. Pinprick sensation was reduced but still preserved with a level at T11-12. Magnetic resonance imaging (MRI) demonstrated an increased central signal in the spinal cord from T6 to T10, on T2-weighted images, compatible with an oedema. The patient's symptoms slightly improved over the next few days. An early rehabilitation program was begun, her motor and sphincter functions recovered gradually.

### Discussion

Reported worrisome neurological complications after epidural are haematoma, spinal cord trauma and intracord injection of steroid, infection, intrathecal injection of steroid, nerve damage, cauda equina syndrome and vascular injury (1). The dissociated sensory loss and the MRI images suggested a possible aetiology of an anterior spinal artery (ASA) syndrome. Coexisting causes of elevated epidural pressure such as degenerative spine disease, epidural injection and atherosclerotic vascular disease, involving the ASA, might have compromised blood flow as well as some hypotension due to the upright position (2). Epidural anaesthesia is a rare cause : 1,8% in a series of 57 patients admitted for an acute spinal cord ischemia (3). The transient symptoms suggested an ASA vasospasm rather than ASA direct injury or injection of particulate matter into it, causing a persisting paraplegia.

### Conclusion

Complications associated with ESIs are rare but vigilance for neurological deterioration is important.

### References

1. Abdi S., et al., *Epidural steroids in the management of chronic pain : a systematic review*, PAIN PHYSICIAN, **10**, 185-212, 2007.
2. Crystal Z., et al., *Postoperative epidural analgesia and possible transient anterior spinal artery syndrome*, REG. ANESTH. PAIN MED., **26**, 274-277, 2001.
3. Nedeltchev K., et al., *Long-term outcome of acute spinal cord ischemia syndrome*, STROKE, **35**, 560, 2004.

*Effects of perioperative i.v. infusion of low dose ketamine associated with thoracic epidural analgesia for abdominal aortic surgery on postoperative analgesia and early postoperative outcome.*

A. GILLON, M. SENARD, E. AERTGEERTS, D. LEDOUX, L. ROEDIGER, B. HUBERT, M. LAMY, J. JORIS.  
Department of Anaesthesia and Intensive Care Medicine. CHU Sart Tilman, Liège, Belgium.

*Background and Goal of Study*

Thoracic epidural analgesia (TEA) provides effective analgesia and improves postoperative outcome after abdominal surgery (1). However, some peritoneal nociceptive inputs are not blocked by TEA (2). Ketamine (KET) prevents postoperative hyperalgesia through central and peripheral mechanisms (3). We investigated effects of the adjunction of perioperative iv KET to TEA, on early postop. analgesia and outcome after open abdominal aortic surgery (AAS).

*Material and methods*

After approval of ethic committee and informed consent, 36 patients scheduled for open AAS were included in this randomized study. Combined general anaesthesia with TEA were used in all the patients. TEA (T9-T10) was started before surgical incision and maintained for the first 60 h postop (ropivacaine 0.2% + 0.5 mg/ml sufentanil). After induction of anaesthesia,

patients were randomly allocated in two groups (n = 18 in each group) : patients were given an iv bolus of KET (225 mg/kg) followed by an infusion (100 mg/kg/h) during the first 24 h postop (KET) or same volume of saline (SAL). All patients were provided with a piritramide PCA pump for 96 h. Pain scores at rest and during activity (100 mm VAS), piritramide consumption, respiratory function, postop outcome (PONV, satisfaction, fatigue, time to first flatus, ambulation, hospital stay, stress response, and morbidity) were recorded. ANOVA for repeated measures, Student's t test, Mann-Whitney test and Fischer exact test were used with  $p < 0.05$  as significant.

*Results*

Demographic data, pain scores at rest ( $p = 0.1$ ), coughing ( $p = 0.2$ ) and mobilization ( $p = 0.24$ ) and piritramide consumption ( $p = 0.56$ ) (Table) were not significantly different between the two groups.

Piritramide consumption	Day 1	Day 2	Day 3	Day 4
KET	8.4 ± 12	16.6 ± 20	12.8 ± 14	8.4 ± 9
SAL	5.8 ± 7	15.2 ± 16	14.7 ± 13	3 ± 5.2

There was no difference with regards to morbidity or postop. outcome parameters between the two groups.

*Conclusions*

Compared to previous studies, when associated with TEA using local anaesthetic and opioid, perioperative iv infusion of low dose ketamine does not improve analgesia nor early postop. outcome after open AAS. It differs with previous published data in abdominal surgery where the use of higher doses ketamine

improves level of postoperative analgesia provided with TEA.

*References*

1. Ballantyne J. C., ANESTH. ANALG., **86**, 598-612, 1998.
2. Aida S., ANESTH. ANALG., **89**, 711-6, 1999.
3. De Kock M., PAIN, **92**, 373-80, 2001.
4. Suzuki M., ANESTHESIOLOGY, **105**, 111-9, 2006.
5. Kararmaz A., ANESTH. ANALG., **97**, 1092-6, 2003.

*Haemodynamic effects of sevoflurane versus propofol sedation after coronary artery bypass grafting.*

G. JONCKHEERE, L. FOUBERT, I. DEMEYER, J. VERBEKE, T. DELOOF, G. NOLLET. Dept. of Anaesthesia and Intensive Care, Onze Lieve Vrouwziekenhuis, Moorselbaan 164, 9300 Aalst, Belgium.

*Introduction*

Although prolonged isoflurane sedation of ICU patients with the Anesthetic Conserving Device Anaconda® has been studied, there is no information on sevoflurane sedation with the Anaconda® device in post-operative sedation of cardiac surgical patients. We studied the haemodynamic effects and extubation times of sevoflurane sedation after coronary surgery.

*Methods*

In a prospective randomized study the haemodynamic effects of sedation with propofol (0.5-2 mg/kg/hr) plus remifentanyl (0.05-0.2 µg/kg/min) were compared with sevoflurane sedation (0.4-0.6%) via the Anaconda® plus remifentanyl (0.05 -0.2 µg/kg/min). In both groups 15 ventilator dependent ICU patients (21 to 80 years

old), expected to need 6 hours sedation after elective CABG with cardiopulmonary bypass, were studied. Haemodynamic evaluation with a thermodilution catheter was performed at hourly intervals during sedation and at 1, 4 and 8 hours after extubation. Time of extubation after cessation of sedation was noted in both groups. Statistical analysis was performed with an unpaired T-test.  $P < 0.05$  was considered significant.

*Results*

Haemodynamic data are shown in table 1. There was no statistically significant difference in any of the parameters. Extubation times after arrival in ICU were 404 (35) and 412 (44) min in the sevoflurane and propofol group, respectively ( $P = 0.59$ ). Extubation times after cessation of sedation were 32 (16) vs. 46 (28) min, respectively ( $P = 0.13$ ).

	T0	T1	T2	T3	T4	T5	T6	TE1	TE4	TE8
<b>SEVO</b>										
HR	74 (9)	75 (8)	74 (9)	77 (10)	78 (12)	79 (13)	79 (16)	98 (31)	85 (13)	82 (14)
MAP	82 (12)	71 (8)	74 (8)	71 (6)	73 (11)	71 (9)	67 (11)	85 (14)	81 (12)	81 (18)
CO	4.7 (0.8)	5.4 (1.2)	5.5 (0.9)	5.5 (1.2)	5.3 (0.7)	5.3 (1.0)	5.4 (0.9)	6.4 (1.8)	5.3 (1.5)	5.2 (1.2)
<b>PROP</b>										
HR	82 (15)	78 (12)	80 (13)	82 (14)	82 (15)	82 (14)	83 (15)	95 (16)	89 (12)	87 (14)
MAP	87 (22)	82 (20)	80 (15)	79 (15)	69 (10)	66 (8)	66 (13)	77 (11)	75 (9)	73 (12)
CO	5.1 (1.6)	5.0 (1.3)	5.6 (1.9)	5.2 (1.4)	5.4 (1.5)	5.5 (1.2)	5.7 (1.4)	7.4 (2.5)	5.8 (1.0)	5.5 (1.1)

SEVO : sevoflurane ; PROP : propofol ; HR : heart rate (beats/min ; SD) ; MAP : mean arterial pressure (mmHg ; SD) ; CO : cardiac output (L/min ; SD).

*Discussion*

The haemodynamic effects of postoperative sedation with sevoflurane are similar to propofol. After extubation haemodynamics were not altered in any of the groups. Extubation times after cessation of sedation were short, but there was no statistically significant difference in extubation times between both sedation regimen.

*Conclusion*

Postoperative haemodynamic stability after coronary bypass is similar for sevoflurane and propofol

based sedation. Using sevoflurane with the Anaconda® device offers a possible alternative and allows rapid extubation once sedation is stopped.

*Reference*

1. Sackey, *et al.*, CRIT. CARE MED., **32**, 2241-6, 2004.

*Post-operative analgesia for minor hand surgery : comparison between two dosages of paracetamol.*

A. LEGRAND, M. KIRSCH, C. DRESSE, E. DEFLANDRE, D. LEDOUX, G. HICK, M. LAMY, M. SENARD.  
Department of Anaesthesia and Intensive Care Medicine, CHU Sart Tilman, 4000 Liège, Belgium.

*Introduction*

Paracetamol is widely used for post-operative analgesia (1). A classic dose of 1 g per six hours is recommended for adult. Recently, some authors proposed the use of 2 g as first dose administered (2). The maximum plasmatic concentration reached after administration of 2 g paracetamol iv at healthy subjects (going from 235 to 521 umol/l) would remain largely in lower part of the definite threshold of 1.000 umol/l like threshold of hepatic toxicity (3). However, there are few data in the literature that confirm this hypothesis. In this prospective randomised study, we compare two dosages for peroperative use of iv paracetamol : 1 g versus 2 g.

*Methods*

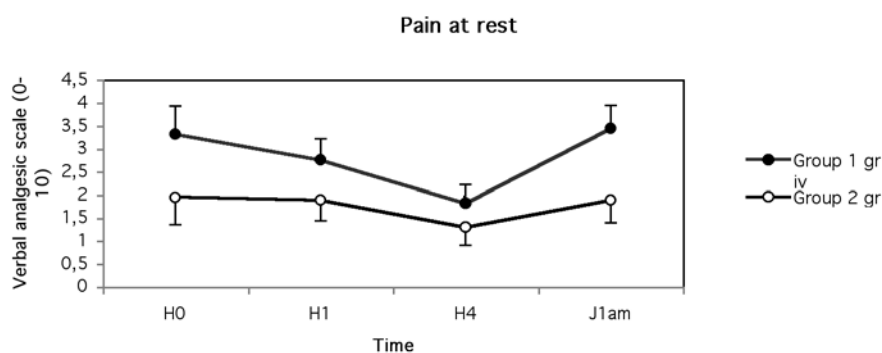
After IRB approval, we enrolled 34 consenting ASA I or II consecutive adult patients scheduled for minor hand surgery (carpal tunnel releases or arthro-synovial cysts). All patients admitted to one day clinic. Excluded were patients treated with chronic high dose analgesic use, NSAIDs use, paracetamol allergy or intolerance and patients with a weight < 50 kg or > 100 kg. Anesthesia was achieved with intravenous regional anesthesia by using 40 ml of lidocaine 0.5%. Patients were randomised in two groups. The first group (n = 17) received a peroperative dose of paracetamol of 1 g and the second group

(n = 17) received 2 g. The relay of analgesia was ensured by 1g paracetamol po every 6 hours if necessary. If analgesia was unsatisfactory, an oral dose of 50 mg tramadol was given to the patient. Analgesic consumption and verbal analgesic scale (0-10 : 0 = no pain and 10 = most awful imaginable pain) were noted : at the arrival in recovery room (H0), after 1 hour (H1), after 4 hours (H4) and 24 hours later (J1am) by phone investigation. Sleep quality and patient's satisfaction score (0-10) at H24 was also recorded.

ANOVA for repeated measures, t-test, Mann Whitney test and Fisher exact test were used as appropriate. Differences were considered as significant if p value was < 0.05.

*Results*

Demographic data didn't differ between the two groups. No difference was found between the two groups in operative time. We didn't observe any significant difference in the analgesic consumption between the two groups. However the verbal analgesic scale shows a significant reduction in the group who received 2 g paracetamol per-operatively (p < 0.045). These data are illustrated in Figure 1. Sleep efficiency and patient's satisfaction didn't differ between the two groups. We didn't observe any adverse event for both groups.



*Conclusions*

In our study, we observed an improvement of quality of postoperative analgesia after minor hand surgery with the peroperative use of 2 g paracetamol compared to 1 g. After this preliminary work, we could consider the use of a first peroperative dose of 2 g paracetamol iv to initiate analgesia after minor adult surgery.

*References*

1. Conférence de consensus, Société Française d'Anesthésie et Réanimation, ANN. FR. ANESTH. REA., **17**, 444-49, 1998.
2. Juhl G. I., Norholt S. E., Tonnessen E., *et al.*, EUR. J. PAIN, **10**, 371-7, 2006.
3. Rose S. R., AM. J. HOSP. PHARM., **51**, 3065-8, 1994.

*The enhanced Model Predictive Control Algorithm using time variant sampling for Tight Glycemic Control in the ICU.* D. LEROUGE<sup>1</sup>, S.J. VAN CROMPHAUT<sup>1</sup>, I. VAN DEN HEUVEL<sup>1</sup>, D. VLASSELAERS<sup>1</sup>, P. J. WOUTERS<sup>1</sup>, R. HOVORKA<sup>2</sup>, G. VAN DEN BERGHE<sup>1</sup>. Intensive Care medicine<sup>1</sup>, University Hospital, Leuven, Belgium ; Paediatrics<sup>2</sup>, Addenbrooke's Hospital, Cambridge, United Kingdom.

### Introduction

Tight glycemic control (TGC) with intensive insulin therapy (IIT) in critically ill patients saves lives and decreases morbidity (1, 2). However current algorithms to implement TGC are not always efficient.

We therefore developed a fully automated algorithm based on an enhanced model predictive controller (eMPC) driving the insulin infusion. This study evaluates the second version of this eMPC (eMPC2) in mechanically ventilated ICU patients following the comparison between the first eMPC (eMPC1) with the routinely used insulin algorithm.

### Methods

To evaluate the eMPC1 algorithm, patients were included for 72 consecutive hours and randomized either to the control group (n = 10) treated by our routine insulin algorithm or to the eMPC1 group (n = 10). The study protocol was approved by the hospital ethics com-

mittee and informed consent was obtained. A follow-up study evaluated an adapted eMPC2 algorithm in 16 patients for 120 consecutive hours. Target range for blood glucose (BG) was 80-110 mg/dl for all groups. Safety was assessed by the number of hypoglycemic events (BG < 40 mg/dl). Efficacy was assessed by calculating time-to-Bgtarget (BG < 110 mg/dl), sampling frequency (SF) and hyperglycemic index (HGI) (3).

### Results

There were no hypoglycemic events and time-to-BG-target was not significantly different in the 3 study groups. HGI was significantly higher at day 1 (p < 0.05 ; table 1), but not statistically different among the 3 groups at any time point. HGI was lower than the target of 27 mg/dl in all cases. SF was significantly higher at any time point in the eMPC1 group, whereas the eMPC2 group showed the same pattern as the standard group (p < 0.05 ; table 1). HGI and SF remained low on day 4 and 5 of the eMPC2 study.

	Hyperglycemic index (mg/dl)			Sampling frequency (#/d)		
	Standard	eMPC1	eMPC2	Standard	eMPC1	eMPC2
day 1	11.4 (± 2.1)	14.4 (± 2.4)	11.0 (± 3.2)	12 (± 1)	18 (± 1)*	13 (± 1)
day 2	1.5 (± 1.0)*	1.4 (± 0.5)*	4.7 (± 1.1)*	8 (± 1)*	11 (± 1)£	8 (± 1)*
day 3	1.1 (± 0.6)*	3.4 (± 1.2)*	3.9 (± 1.2)*	8 (± 2)*	12 (± 2)§	7 (± 1)*

p < 0.05 vs. Standard day 1 ; £ p < 0.05 vs. Standard day 2 ; § p < 0.05 vs. Standard day 3.

### Conclusion

Use of eMPC in ICU patients with prolonged mechanical ventilation is safe and efficient. In contrast to the eMPC1 algorithm, the adapted eMPC2 algorithm resulted in a workload comparable to the use of our standard ICU insulin protocol. eMPC2 is a reliable instrument for the implementation of TGC in the ICU.

### References

1. Van den Berghe G., NEJM, **345**, 1359-67, 2001.
2. Van den Berghe G., NEJM, **354**, 449-61, 2006.
3. Vogelzang, CRIT. CARE, **8**, 122, 2004.

Grant acknowledgement. EC 6<sup>th</sup> Framework Program, ref 506965 (Clinicip).

## Nicardipine does not protect *ex vivo* perfused rat liver against ischaemia and reperfusion injury.

C. MIRLAND, V. NUYENS, Y. MEFIRE, M. STADLER. CHU of Charleroi, Boulevard Paul Janson 92, 6000 Charleroi, Belgium.

### Introduction

The mechanisms involved in liver injury during ischaemia-reperfusion (IR) include the liberation of calcium ( $\text{Ca}^{2+}$ ) from micro-organelles to the cytosol (1). Free  $\text{Ca}^{2+}$  ions activate intracellular enzymes such as phospholipases, resulting in membrane dysfunction and induce reactive oxygen species (ROS) generation (2). Theoretically,  $\text{Ca}^{2+}$  antagonists could protect the liver from anoxic injury by blocking the increase in cytosolic  $\text{Ca}^{2+}$ . The goal of this study was to investigate whether the  $\text{Ca}^{2+}$  blocker nicardipine could protect the rat liver from warm IR injury.

### Methods

After University Animal Care Committee approval, female Wistar rats were fasted for  $\pm 16$  h but were allowed to tap water *ad libidum*. After they were anaes-

thetized, the portal vein was cannulated, the liver removed and perfused at a flow rate of 5 ml/min ( $\pm 12$  cm  $\text{H}_2\text{O}$ ) at  $37^\circ\text{C}$  in a closed *ex vivo* system with HBSS supplemented with insulin, HEPES and  $\text{O}_2$ . The experiment consisted of three phases: perfusion for 15 min, warm ischaemia for 60 min, and reperfusion during 60 min. Animals were divided into 3 groups ( $n = 5$ ): control and nicardipine-treated livers at two concentrations, *i.e.* 4 and 40 mg/ml administered in the perfusate before ischaemia. Glucose and lactate (mg/dl), potassium (mEq/l), ALT, AST, LDH (IU/l), ROS, *i.e.* dienes and trienes (Oxidative Index ; OI) were analysed in perfusate samples at different time-points. Mean  $\pm$  SD. ANOVA.

### Results and discussion

Numbers in Table 1 correspond to final time-point, *i.e.* 135 min.

Variable	Control (n = 5)	Nicardipine 4 mg/ml (n = 5)	Nicardipine 40 mg/ml (n = 5)
Glucose (mg/dl)	52 $\pm$ 35	93 $\pm$ 81	74 $\pm$ 61
Lactate (mg/dl)	0.2 $\pm$ 0.1	12.3 $\pm$ 8.6**	11.6 $\pm$ 7.1**
K <sup>+</sup> (mEq/l)	9 $\pm$ 1.1	10.0 $\pm$ 1.0	8.9 $\pm$ 1.0
AST (IU/l)	958 $\pm$ 721	782 $\pm$ 581	688 $\pm$ 443
ALT (IU/l)	1049 $\pm$ 880	609 $\pm$ 388	551 $\pm$ 317
LDH (IU/l)	4,808 $\pm$ 3,331	11,516 $\pm$ 10,510	10,535 $\pm$ 6,768
Dienes (% OI)	60 $\pm$ 3	63 $\pm$ 6	57 $\pm$ 5
Trienes (% OI)	30 $\pm$ 2	31 $\pm$ 3	29 $\pm$ 3

\*\* P  $\leq$  0.01 vs. control.

No difference was observed in glucose, potassium, ROS and enzymes release in the perfusate. Lactate was greater in the two nicardipine-treated groups when compared to control rats (P  $\leq$  0.01). In the present conditions, nicardipine did not protect rat hepatocytes from IR injury. Worse,  $\text{Ca}^{2+}$  antagonists appeared to be deleterious to hepatic parenchymal cells enhancing the release of lactate. These results are in line with a previous experiment showing that  $\text{Ca}^{2+}$  antagonists did not prevent release of LDH or the rise in intracytosolic  $\text{Ca}^{2+}$  during anoxia in isolated rat hepatocytes (3). The question remains if hepatocytes possess voltage-sensitive  $\text{Ca}^{2+}$  channels.

### Conclusion

Regarding the experimental condition of isolated perfused rat livers, nicardipine does not reveal a protective effect on livers exposed to IR injury.

### References

1. Thomas C. E., Reed D. J., HEPATOLOGY, **10**, 375-84, 1989.
2. Jaeschke H., *et al.*, J. CLIN. INVEST., 1988, **81**, 1240-6.
3. Gasbarrini A., *et al.*, BIOCHIM. BIOPHYS. ACTA, **1177**, 1-7, 1993.

*Neostigmine versus Sufentanil as epidural analgesic adjuvant to Ropivacaine during labor analgesia.* E. NARDELLA, M.D., F. ROELANTS, M.D., P. LAVAND'HOMME, M.D., Ph.D. St Luc Hospital, Université Catholique de Louvain, Brussels, Belgium.

### Introduction

Epidural analgesia remains the best technique to provide pain relief during labor. To date, local anesthetic and lipophilic opioid combination is commonly used for its synergistic efficacy (a local anesthetic sparing effect of 20-25%) (1). Among analgesic adjuvants used for epidural analgesia in parturients, cholinesterase inhibitor, neostigmine (N) presents with interesting properties (greater analgesic effect observed in females, no motor or sympathetic block, no particular side effect). To date, only bolus administration has been studied (2) and the potential benefit of N continuous infusion during labor deserves further attention. The present study is

aimed to compare the efficacy of epidural N with epidural sufentanil (S) for labor analgesia as well as their respective ropivacaine (R) sparing effect.

### Materials and methods

After Institutional Ethical Committee approval and Informed Consent, healthy parturients (ASA 1&2, singleton pregnancy, term > 37 weeks) in active labor and requesting epidural analgesia were included in the study. After lumbar epidural catheter placement and negative test dose (3 mL lidocaine 2% with epinephrine), the parturients were randomly assigned to one of the three following groups to receive :

	ROPI group (n = 24)	RS group (n = 25)	RN group (n = 26)
Bolus dose	R 0.1% 10 mL	R 0.1% 10 mL + S 10 µg	R 0.1% 10 mL + N 500 µg
Continuous Infusion 8 – 10 mL/h	R 0.1%	R 0.1% + S 0.25 µg/mL	R 0.1% + N 12.5 µg/mL

Rescue analgesia was available at any time as an epidural bolus of 10 mL R 0.1% or R 0.2% (if VAS > 60/100).

Pain scores (VAS 0-100) were recorded hourly from test dose injection (T0) until delivery. Number and timing of rescue doses, total R needs and labor duration were noticed. Maternal and fetal parameters were closely monitored. Statistical analysis used ANOVA with posthoc test and Chi-square analysis, a  $P < 0.05$  was considered to be significant.

### Results

Demographic data did not differ among the groups (age, weight, parity, induced labor, oxytocine administration). Evolution of pain scores demonstrated lower VAS scores in RS group, significantly different from those in ROPI group at 2 h and 3 h after the beginning of CI. Pain scores in RN group did not differ from those in ROPI group throughout the labor course. Other results are in the Table (\*,  $P < 0.05$  with RS group).

	ROPI	RS	RN
Initial cervical dilatation (cm)	3.4 ± 1	3.2 ± 0.8	3.5 ± 0.8
Initial VAS (0-100)	39.5 ± 26	51 ± 24	46 ± 29
Rescue doses (n)	1.6 ± 1.1 *	0.76 ± 0.8	1.1 ± 0.8
First rescue dose			
- cervical dilatation (cm)	4.5 ± 1 *	6.4 ± 1.7	5.5 ± 1.5
- VAS (0-100)	58 ± 22	51 ± 19	56 ± 21
Labor duration (min)	308 ± 131	308 ± 123	265 ± 132
Ropivacaine use (mg/h)	18.8 ± 3.9 *	15.7 ± 2.7	17.6 ± 3.7
Instrumental delivery (n)	3	1	1
Cesarean section (n)	3	4	3

No particular side effects were recorded in parturients (hemodynamic problem, nausea vomiting, sedation) and in fetus. Rate of instrumental delivery and cesarean section were similar among the groups.

### Discussion

At the doses used in the study, neostigmine as epidural adjuvant does not improve labor analgesia. Addition of sufentanil allows a local anesthetic sparing effect as previously reported (1) (around 16% when

using CI and top up doses). In contrast, epidural neostigmine does not show a local anesthetic sparing effect either after CI or after single bolus dose (2).

### References

1. Boselli, *et al.*, ANESTH. ANALG., **96**, 1173-7, 2003.
2. Roelants & Lavand'homme, ANESTHESIOLOGY, **102**, 1205-10, 2005.
3. Roelants & Lavand'homme, ANESTHESIOLOGY, **101**, 439-44, 2004.

*Pharmacokinetic of bupivacaine associated with gelatine after epidural and plexic administration in the rabbit.* R. SAUVAGE, V. NUYENS, R. MULLER, M. DERNEDDE. CHU of Charleroi, Boulevard Paul Janson 92, 6000 Charleroi, Belgium.

### Introduction

Viscosity of a local anaesthetics (LA) solution is among other variables influencing vascular resorption of LA poorly studied (1-2). This increase of viscosity can reduce the cardiac and neurotoxicity of the LA and secondarily extend the length of action of this one. A previous *in vitro* experiment showed that gelatine decreases the speed of bupivacaine (BP) release during equilibrium dialysis (3). The aim of this study is to evaluate the effect of adding a gelatine to a plain bupivacaine solution and observe the pharmacokinetic profile of the obtained solution after epidural or plexic administration in the rabbit.

### Materials and methods

Plain BP 0.5% or associated with gelatine (Haemacel®) is administered in the epidural space (sacral injection S2-3) (0.5 ml) or in the brachial plexus

(1 ml) of albino rabbits (2.5 kg) (n = 4 for each group). The rabbits are anaesthetized by a mixing of fentanyl and dehydrobenzperidol. The viscosity of the two solutions was measured and expressed in centipoise (cP). Arterial blood samples (2 ml) were withdrawn at different times during 180 min. The plasmatic concentration of BP was measured by High Performance Liquid Chromatography (HPLC). The calculated pharmacokinetic parameters are : distribution ( $T^{1/2} \alpha$ ), elimination ( $T^{1/2} \beta$ ), the maximum plasma concentration (Cmax), the time to reach C max (Tmax), area under the time-concentration curve (AUC) and clearance (Cl). Mean  $\pm$  SD. Students' *t* test with  $P < 0.05$  significant.

### Results

The viscosity of plain BP is 0.827 cP and 0.856 cP for BP associated with gelatine. The pharmacokinetic parameters are displayed in the table.

Variables	BP	BP + gelatin
	Epidural	
$T^{1/2} \alpha$ (min <sup>-1</sup> )	11.8 $\pm$ 1.9	9.1 $\pm$ 0.5*
$T^{1/2} \beta$ (min <sup>-1</sup> )	111.9 $\pm$ 15.0	90.0 $\pm$ 23.4
C max (ng.ml <sup>-1</sup> )	874 $\pm$ 410	935 $\pm$ 84
T max (min)	6.7 $\pm$ 2.5	5.0 $\pm$ 0.0
ASC (ng.min)	60249 $\pm$ 39771	43271 $\pm$ 19189
Cl (ml.min <sup>-1</sup> )	55.25 $\pm$ 30.80	66.27 $\pm$ 20.01
	Brachial Plexus	
$T^{1/2} \alpha$ (min <sup>-1</sup> )	19.2 $\pm$ 4.0	17.6 $\pm$ 7.0
$T^{1/2} \beta$ (min <sup>-1</sup> )	130.6 $\pm$ 32.9	149.2 $\pm$ 71.4
C max (ng.ml <sup>-1</sup> )	974 $\pm$ 177	951 $\pm$ 229
T max (min)	13.7 $\pm$ 10.2	5.0 $\pm$ 0.0
ASC (ng.min)	303643 $\pm$ 75654	241619 $\pm$ 25232
Cl (ml.min <sup>-1</sup> )	22.85 $\pm$ 5.12	20.92 $\pm$ 2.28

\*  $P < 0.05$ .

### Discussion

In the present experimental conditions, adjunction of gelatin does not modify the pharmacokinetic profile of BP after epidural and plexic administration in the rabbit. Our results were not in accordance with the studies using other viscous formulations as hyaluronic acid which show that the plasmatic peak of the LA is significantly delayed in the group associating hyaluronic acid.

### References

1. Hassan H. G., *et al.*, ACTA ANAESTHESIOLOGICA SCAND., **29**, 380-3, 1985.
2. Renck H., *et al.*, CURRENT OPINION IN ANAESTHESIOLOGY, **9**, 399-403, 1996.
3. Kanku J. P., *et al.*, ACTA ANAESTHESIOLOGICA BELG., **52**, 307, 2001.

*Haemodynamic effect of three different effect-site concentrations of sufentanil during induction, laryngoscopy and intubation.* M. TURLOT, T. SCHMITZ, C. VANLERSBERGHE, C. VERBORGH, F. CAMU. Department of Anesthesiology, UZ-Brussel, Vrije Universiteit Brussel, Belgium.

*Background and goal of the study*

Propofol and sufentanil are often combined during induction of anesthesia (1). Recent developments in pharmacokinetics and technology have allowed the development of target effect-site controlled infusion (TECI) systems for the administration of both drugs (2, 3). In this study, we assessed the effect of 3 different predicted effect-site concentrations (EC) of sufentanil on the induction characteristics of propofol at a target effect-site concentration of 4 µg/ml and on the haemodynamic response to laryngoscopy and intubation.

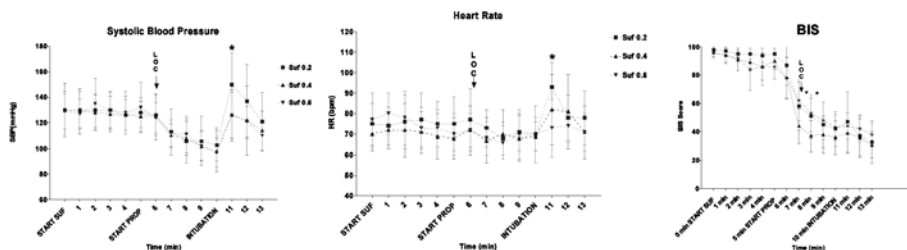
*Methods*

After approval by the Ethics Committee and informed consent, 24 patients ASA physical status I-II, scheduled for elective surgery were randomly allocated to receive a predicted sufentanil effect-site concentration of either 0.2, 0.4 or 0.6 ng/ml. All patients were premedicated with midazolam 5 mg IM and glycopyrrolate 0.2 mg IM. After preoxygenation by facemask with 100% oxygen for 3 min, the sufentanil TECI was started at the randomized target EC, using the Gepts model integrated in an Asena PK pump (Alaris). Once the chosen sufentanil EC was reached (after 5 min), a propofol TCI was started at a fixed predicted EC of 4 µg/ml using the Schnider model, integrated in the Asena PK pump (Alaris). Tracheal intubation was facilitated with cis-atracurium (0.15 mg kg<sup>-1</sup>). Standard haemodynamic

parameters (SBP, DBP, MAP and HR) and BIS index (Aspect A-1000, USA) were recorded every minute. We assessed time to loss of consciousness (LOC), corresponding predicted propofol EC and the haemodynamic effects of laryngoscopy and intubation. Data were analysed using ANOVA and P < 0.05 was considered significant (Graph Pad Prism® Statistical software package).

*Results and discussion*

The patients characteristics did not differ significantly among the three groups. Time to LOC was significantly shorter in SUF 0.4 and SUF 0.6 groups compared to the SUF 0.2 group (57.2 ± 10.6 sec and 50.9 ± 5.3 sec vs 75.6 ± 18 sec) and the predicted EC of propofol at LOC was also lower with increasing sufentanil ECs (3.6 ± 0.4 µg ml<sup>-1</sup>, 3.4 ± 0.3 µg ml<sup>-1</sup> and 3.2 ± 0.2 µg ml<sup>-1</sup> respectively). During the first 5 min, when the sufentanil TECI was build up, no significant haemodynamic changes occurred. Subsequent administration of propofol, irrespective of the sufentanil concentration, reduced BP, HR and BIS value. Laryngoscopy and intubation was associated with an increase in SBP, DBP, MAP and HR compared to values at LOC in all groups, while the BIS values only increased slightly in the SUF 0.2 ng ml<sup>-1</sup>. The total dose of sufentanil administered at the time of intubation was 10 µg, 20 µg and 30 µg for the SUF 0.2, SUF 0.4 and SUF 0.6 groups respectively.



*Conclusion*

Our results demonstrate a concentration-dependent effect of sufentanil on decreasing haemodynamic response to intubation. The combination of a predicted EC of propofol of 4 µg ml<sup>-1</sup> with a predicted EC of at least 0.4 ng ml<sup>-1</sup> seemed necessary to blunt cardiovascular response and prevent an increase in BIS value associated with laryngoscopy and intubation.

*References*

1. Los G. J., Lauwers M. H., Vanlersberghe C., Camu F., ACTA ANAESTESIOLOGICA BELGICA, **46**, 153-159, 1995.
2. Gepts E., Shafer S. L., Camu F., Stanski D. R., *et al.*, ANESTHESIOLOGY, **83**, 1194-204, 1995.
3. Schnider T. W., Minto C. F., Shafer S. L., *et al.*, ANESTHESIOLOGY, **90**, 1502-16, 1999.