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## *Epidural neostigmine administration during labor analgesia: Bolus dose and continuous infusion versus Patient-controlled epidural analgesia (PCEA).*

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*Introduction*

Epidural analgesia remains the best technique to provide pain relief during labor and combination with analgesic adjuvants is recommended to spare local anesthetic consumption. Available analgesic adjuvants involve opioids, clonidine and the cholinesterase inhibitor, neostigmine (N). In contrast with opioids and clonidine which have both demonstrated a significant local anesthetic sparing effect, epidural N administered as a bolus dose of 5-7 µg/kg at the beginning of labor (Roelants *et al.*, Anesthesiology 2005) or as a continuous infusion of 120 µg/h (Ross *et al.*, Anesthesiology 2006 ; 104: A-33) failed to reduce local anesthetic requirements. Because underlying mechanisms of action differ between these adjuvants, the formers being direct receptor agonists while the later (N) acts as an indirect agonist to increase locally spinal acetylcholine levels, the present study assessed the way of epidural neostigmine administration on ropivacaine (R ) needs during labor analgesia.

*Methods*

After Ethical Committee approval and informed consent, healthy parturients (singleton pregnancy, term > 37 weeks) in active labor and asking for epidural analgesia were included. After lumbar epidural catheter placement and negative test dose (3 mL lidocaine 2% with epinephrine), the parturients (n = 20 per group) were randomly allocated to receive analgesia by either continuous infusion (CI) or PCEA device :

| | CI R | CI RN | PCEA R | PCEA RN |
|---|---|---|---|---|
| Bolus dose | R 0.1% 10 mL | R 0.1% 10 mL with N 500 µg | R 0.1% 10 mL | R 0.1% 10 mL |
| Epidural analgesia | R 0.1% at 10 mL/h | R 0.1% + N 12.5 µg/mL at 10 mL/h | R 0.1% at 5 mL/15 min | R 0.1% + N 25 µg/mL at 5 mL/15 min |

Rescue analgesia was available at any time as epidural bolus of 10 mL R 0.1% (if VAS < 6/10) or R 0.2% (if VAS ≥ 6/10). Number and timing of rescue doses, total R needs and labor duration as well as fetal and maternal parameters were recorded. Statistical analysis used ANOVA one way or Kruskal-Wallis test with posthoc comparison, P < 0.05 was considered to be significant.

*Results*

Demographic data (age, weight, parity, induced labor, ocytocine use) and labor duration did not differ between the groups. In PCEA RN, N use was 160 ± 52 µg/h while in CI RN, the rate was fixed at 125 µg/h.

Results are expressed as median (IQR) or mean ± SD ; (*) P < 0.05 with CI R, CI RN and PCEA R groups ; (†) P < 0.05 with CI RN group

| | CI R | CI RN | PCEA R | PCEA RN |
|---|---|---|---|---|
| Rescue doses (n) | 2 (1-3) | 2 (1-2) | 2 (1-3) | 2 (1.5-2.5) |
| First rescue dose: | | | | |
| VAS (0-10) | 5.7 ± 2 | 5.5 ± 1.9 | 7.4 ± 1.8 † | 7.0 ± 1.4 † |
| Cervical dilatation (cm) | 5.5 (4-6) | 5 (5-6) | 6 (4.5-7) | 5.5 (4-7) |
| Time elapsed (min) | 125 (101-172) | 117.5 (90-170) | 125 (90-165) | 120 (100-207) |
| Ropivacaine use (mg/ h) | 19.6 ± 5 | 18.6 ± 4 | 18.3 ± 5 | 14.5 ± 4 * |

*Discussion*

Epidural neostigmine administered by PCEA mode and without an initial bolus dose affordes a significant local anesthetic sparing effect during labor. The present results correlate with previous observations in humans concerning both the pharmacokinetic and pharmacodynamic of spinal neostigmine : i.e. neostigmine, independently of the dose administered, rapidely provokes sustained plateau concentrations of acetylcholine in the CSF, during 4-6 h after N injection (Shafer et al, Anesthesiology 1998). Therefore, initiation of analgesia with a significant N bolus dose (e.g. 500-750 µg) certainly may prevent further analgesic effect from the following doses. In contrast with intermittent bolus doses (PCEA mode), continuous infusion might also yield to the saturation of the mechanism of cholinesterase inhibition.

*Combined spinal epidural analgesia in labour : effects on maternal glycaemia.* Marissa BRAES, Frederik DE BUCK, Eugéne VANDERMEERSCH, Marina KUYPERS, Marc VAN DE VELDE. Department of Anaesthesiology, UZ Leuven, Belgium.

*Introduction*

Two case reports of acute maternal hypoglycaemia following combined spinal epidural analgesia (CSE) for labour pain have been reported in the literature (1, 2). One case report occurred in a diabetic patient. We recently encountered a similar case of hypoglycaemia in our own practice. Hypoglycaemia most likely occurred as a result of decreased stress hormone levels. Hypoglycaemia may be a cause of foetal distress when it occurs after regional analgesia. The present prospective study was therefore undertaken to evaluate the effects of CSE on maternal glycaemia in healthy parturients.

*Methods*

Following institutional ethics committee approval, 50 ASA 1 and 2, singleton, vertex presenting pregnant patients were recruited to participate in this prospective un-blinded, single group trial. Standard obstetric parameters as well as obstetric, foetal and neonatal outcome were recorded. Maternal glycaemia was measured using venous blood collected 5 minutes before CSE and 15 and 30 minutes after spinal analgesic injection. The blood was collected from an intravenous line used only for blood sampling. Hypoglycaemia was defined as a glycaemia of < 80 mg/dl and a decrease in maternal glycaemia of > 20% of baseline. Hypoglycaemia was treated with 3 g of glucose if glycaemia was less then 50 mg/dl or if the patient had symptoms of hypoglycaemia.

*Results*

Maternal glycaemia remained stable in the study population : baseline glycaemia levels were 88 ± 18, at 15' it was 93 ± 14 and at 30' it was 94 ± 16 mg/dl. In two patients hypoglycaemia occurred based on our definition. Glycaemia decreased to 56 and 62 mg/dl. Both these patients did not show any clinical signs of hypoglycaemia and did not need intravenous glucose. In none of the hypoglycaemic patients foetal distress was observed. Obstetric and neonatal outcome was good.

*Discussion and conclusion*

Based on the results of this small, prospective, unblinded trial, in a healthy patient population in active labour CSE does not lead to significant hypoglycaemia. However lowered levels of glycaemia may be observed. If unexpected foetal distress occurs after CSE analgesia control of the plasma glucose concentration and glucose substitution should be considered.

*References*

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*Clonidine improves post-hypoxic vasomotricity of isolated rats aorta.* B. Brée*, M. Gourdin**, J. Jamart***, M. De Kock*. *Department of Anesthesiology, Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, Brussels, Belgium ; **Department of Anesthesiology and ***Biostatistics, Université Catholique de Louvain, Cliniques Universitaires de Mont-Godinne, Yvoir, Belgium.

*Background and Goal of the Study*

Clonidine (CL), an α2-adrenoreceptor agonist, reduces perioperative myocardial ischemia in patients undergoing surgery (1). In an isolated heart model, administrated α2-adrenoreceptor agonists portect against ischemia. We investigated to demonstrate that the beneficial effect of Clonidine is due to a post-hypoxic vasomotricity improvement (2).

*Materials and Methods*

After animal ethic committee approval, 60 aorta rings (3 × 20) from 15 different rats were studied according to a validated methodology (3). Two aorta rings were put into two Krebs solution baths where Clonidine 10-4M was added (CL Group). Two other aorta rings bathing in Krebs solution only (free from Clonidine) were used as the control group (CTL Group). After 15 minutes, all baths were emptied and filled with Krebs solution 3 times. Then 25 minutes of hypoxia (PpO2 < 10 mmHg) was applied, followed by 40 minutes of reoxygenation (PpO2 > 400 mmHg). After hypoxia-reoxygenation, we evaluated post-hypoxic vasoconstriction by cumulative Phenylephrine (PE) concentrations (10-10M – 10-4M). Post-hypoxic endothelium-dependent and independent vasoldilatations were investigated respectively by cumulative Acetylcholine and Nitroprusside concentrations (10-10M – 10-4M) on pre-contracted aorta with Phenylephrine 10-4M. The statistical analysis used GEE regression, $p < 0,05$ was considered as significant.

*Results and Discussions*

In CL group, post-hypoxic endothelium-dependent vasodilatation and vasoconstriction were significantly different from the CTL group ($p < 0,002$ and $p < 0,018$, respectively fig. 1 and 2). When considering post-hypoxic endothelium-independent vasodilatation, no significant difference was found.

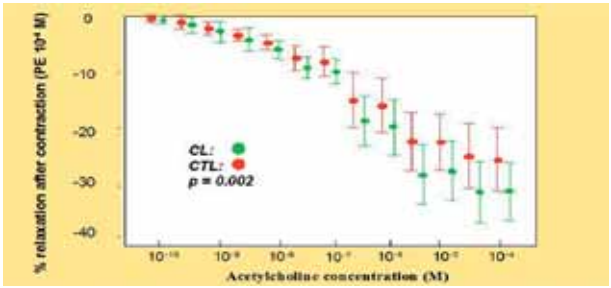


Fig. 1. — Dose response relationship of post hypoxic endothelium-dependent vasodilatation.

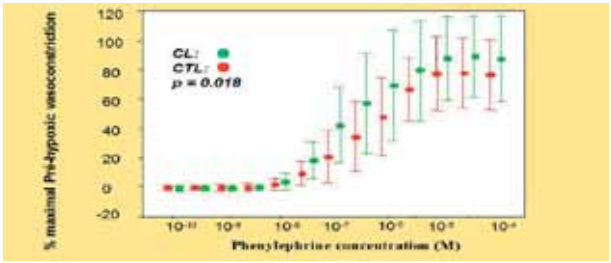


Fig. 2. — Dose response relationship of post hypoxic vasoconstriction with endothelium.

*Conclusion(s)*

CL enhances post-hypoxic endothelium-dependent vasodilatation and vasoconstriction, a phenomenon involved in myocardial ischemic protection. Then Clonidine could be used for ischemic protection in patient at risk.

*References*

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*The use of IV Tramadol (Contramal®) versus immediate release Tramadol (Tradonal odis® ) in the postoperative period after knee surgery in a day surgery setting.* R. DAKHEEL, M.D., A. TEUNKENS, M.D., E. VANDERMEERSCH, M.D., Ph.D., Anesth. Dept., C. Huygens, anesthesia research nurse. University Hospitals, Katholieke Universiteit Leuven, Herestraat 49, B-3000 Leuven, Belgium.

*Introduction*

Postoperative pain is a serious problem, requiring an appropriate response from the medical doctor.

In Orthopedics special attention is needed after knee surgery (1). Although Tramadol is available in different formulas (capsules, tablets, oral solutions, and injectable solutions), a new form has been developed to optimize and to simplify its use. The new formula is a tablet (Tradonal odis®) with chemical structure providing faster absorption due it's enhanced release (2). The aim of the study is to compare this formula type of tramadol (Tradonal odis®) with the intravenous route (Contramal®) for analgesia after knee surgery.

*Methods*

After Ethical Committee approval and following informed consent, 60 patients undergoing an elective knee arthroscopy in the surgical day clinic, participated to this open-label study, they were divided into 2 groups (30 received one dose of 100 mg Tradonal odis ® tablet and 30 received one dose of 100 mg IV (Contramal®) postoperatively in the PACU.

Both groups were premedicated with 0.5 mg alprazolam po and the general anesthesia was standardized with intravenous Sufenta®, propofol, ventilation with O2/air (30/70%) through a laryngeal mask and sevoflurane was used for maintenance anaesthesia. Peroperative all Patients received 2g IV Perfusalgan® and 30 mg of IV Taradyl®. Numerical Rating Scale (NRS) 1 to 10 was used to evaluate postoperative pain, and also patient satisfaction, adverse effects of the drugs were also evaluated every ten minutes for the first hour after administration of the study medication, then after an hour postoperatively.

The patient was received extra opioids (IV piritramide), when pain relief proved to be insufficient 30 minutes after administration of the study medication.

The Chi-Square Tests and t-test were used to evaluate statistical relevancy. A value of $p < 0.05$ was considered as statistically significant.

*Results*

20 pateints were excluded from the study because they did not match the preoperative standardized conditions. In the participated patients the NRS revealed that mild or absent pain(NRS < 4) was present in 18 out of 21 of patients that were treated with contramal®, and 10 out of 19 of patients that were treated with Tradonal odis® ($p < 0.05$). Furthermore, 9 out of 19 patients in the Tradonal odis® group requested extra piritramide as opposed to 3 out of 21 in the Contramal® group (P = 0,02). The incidence of nausea and vomiting was equal between the two groups, nausea was present in 4 out of 21 patients that were treated with contramal®, and 2 out of 19 patients that were treated with Tradonal odis®.

Table

NRS 30 minutes after administration of the study medication

| TYPE | TIME (minutes) | Cases | | | | | |
|---|---|---|---|---|---|---|---|
| | | NRS < 4 | | NRS ≥ 4 | | Total | |
| | | N | Percent | N | Percent | N | Percent |
| T Odis® | 30 m | 10 | 52,4% | 9 | 47,6% | 19 | 100,0% |
| Contramal® | 30 m | 18 | 85,7% | 3 | 14,3% | 21 | 100,0% |

*Discussion*

The efficacy of intravenous tramadol (Contramal®) has already been demonstrated in many trials investigating pain relief after knee surgery (3), there is however no literature made to compare the efficacy of Tardonal odis® in the postoperative setting with the IV Contramal®. In this study we found that patients treated with Contramal® had pain of lower intensity in the first hour after administration compared to those treated with Tradonal odis ®, and less patients required piritramide as supplementary treatment. Furthermore, no significant difference was found in the incidence of nausea and vomiting between the two group.

*Conclusion*

We concluded that Contramal® is more effective compared to Tradonal odis ® to treat immediate postoperative pain following knee surgery, and with the same incidence of nausea and vomiting.

*References*

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3. Bamigbade T. A., Langford R. M., *The clinical use of tramadol hydrochloride*, PAIN REV., **5**, 155, 1998.

# Accuracy and clinical feasibility of a new Bayesian-based closed-loop control system for propofol administration using the BIS as a controlled variable.

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*Background*

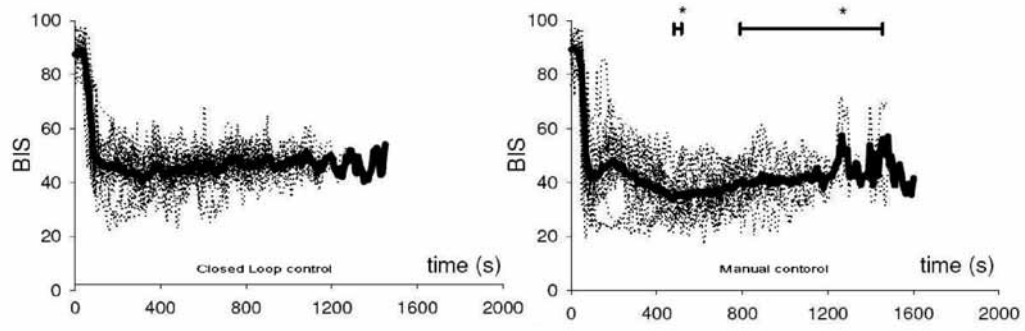
Closed-loop control of the hypnotic component of anesthesia has been proposed in an attempt to optimize drug delivery. Here, we introduce a newly developed Bayesian-based, patient-individualized, model-based, adaptive control method for BIS guided propofol infusion into clinical practice and compare its accuracy and clinical feasibility under direct observation of an anesthesiologist versus BIS guided, effect compartment controlled propofol administration titrated by the anesthesiologist during ambulatory gynecological procedures.

*Methods*

After Institutional Ethics Committee approval, informed consent was obtained from 40 ASA I and II female patients, aged 18-45 years. All patients were randomly allocated to the closed-loop or manual control group. All patients received midazolam 1 mg iv and alfentanil 0.5 mg iv prior to induction. In the closed-loop control group, propofol was administered using the previously described closed-loop control system (1, 2) to reach and maintain a target BIS of 50. In the manual control group, the propofol effect-site concentration was adapted at the discretion of the anesthesiologist to reach and maintain a BIS as close as possible to 50. Induction characteristics, performance and robustness during maintenance and recovery times were compared. Hemodynamic and respiratory stability were calculated as clinical feasibility parameters. Statistical analysis was performed using SPSS. All data were checked for Gaussian distribution by the method of Kolmogorov and Smirnov. Differences between groups were analyzed by a Student-T-test or Mann-Withney test, depending on their distribution. Categorical data (movement) were analyzed by a Chi-squared test.

*Results*

The closed-loop control system titrated propofol administration accurately resulting in BIS values close to the set point (figure, * = $p < 0.05$ between groups). The closed-loop control system was able to induce the patients within clinically accepted time limits and with less overshoot than the manual control group (Induction time (s) 66 ± 25 versus 49 ± 9 ; $BIS_{peak}$ 40 ± 7 versus 33± 10, $P < 0.05$). Automated control resulted in beneficial recovery times (time between stop propofol and opening eyes (s) 215 ± 133 versus 316 ± 125, $P < 0.05$). Our closed-loop control group showed similar acceptable clinical performance specified by similar hemodynamic, respiratory stability, comparable movement rates and quality scores than the manual control group.




*Conclusions*

The Bayesian-based closed loop control system for propofol administration using the BIS as a controlled variable performed accurate during anesthesia for ambulatory gynecological procedures. This control system is clinical feasible and can be further validated in clinical practice.

*References*

1. De Smet T., Struys M. M. R. F., Greenwald S., Mortier E. P., Shafer S. L., *Estimation of optimal modeling weights for a Bayesian-based closed loop system for propofol administration using the BIS as a controlled variable : A simulation study*, Anesth. Analg., **105**, 1629-38, 2007.
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*Usefulness of Coagulation Screening before Labour Epidural Analgesia.* H. Ismael-Aguirre, A. Pregaldien, P. Y. Dewandre, M. Lamy, J. F. Brichant. Department of Anesthesia & ICM, Liege University Hospital, 4000 Liege, Belgium.

*Background*

The incidence of epidural haematoma is a very rare phenomenon (1/168 000) complication of epidural anaesthesia (1). It is usually associated with an altered coagulopathy profile. Guidelines recommend coagulation tests on an individual basis, according to history and physical examination (2). But many anaesthesiologists opt for systematic coagulation screening before performing an epidural analgesia out of fear of a neurologic complication.

Studies have demonstrated that such a policy is useless in general surgical procedures (3).

The aim of this study was evaluate the usefulness of such a systematic coagulation screening in obstetric anaesthesia.

*Methods*

In this retrospective study, we have reviewed the charts of 1500 women who delivered between September 2005 and April 2007 and in whom coagulation had been screened during the last month of pregnancy.

*Results*

A platelet count was performed in 1101 patients. All of them were > 100 000/mm$^3$. PT and APTT or TCA were performed in 996 patients. Only 3 patients presented abnormalities for these tests. In one patient the PT was 69% and this patient received an uneventful epidural analgesia. In the second patient, the APTT was 40 sec. The patient underwent a caesarean section under general anaesthesia for eclampsia. Postoperative evolution was favourable and coagulation was normal at day 3.

In a third patient the PT was 61% and the TCA 43.6 sec. These abnormalities were ignored. The patient received an epidural analgesia for labour followed by an uneventful caesarean section under epidural anaesthesia for mechanical dystocia.

No coagulation tests were performed during the postpartum period.

The three patients with coagulation abnormalities presented a history suggesting possible coagulation disorder.

*Discussion*

Among the 1500 patient records we reviewed, 3 patients had abnormal coagulation tests. In these 3 patients, a coagulation disorder would have been suspected by an oriented questionnaire that would have prompted the anaesthesiologist to order coagulation tests.

We conclude that coagulation disorders are rare and can be suspected by a well designed questionnaire.

*References*

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2. Anesthesia : An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia, Anesthesiology, **106**, 843-863.
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*The Efficacy Of The Semi-Automated Closed-Loop propofol-remifentanil effect-site versus Manual TCI Anaesthesia.* F. KANDIL*, G. BEJJANI*, O. CAELEN**, G. BONTEMPI**, E. ENGELMAN*, L. BARVAIS*. Erasmus Hospital Anaesthesia Department and **Machine Learning Group, Computer Science, Free University of Brussels, Belgium.

*Introduction*

The primary aim of this study was to compare the preliminary results of a semi automated closed-loop (SACL) TCI system allowing the anaesthesiologist to build predefined algorithms to titrate simultaneously the propofol and remifentanil effect site concentrations (Ce), with a manually controlled effect site model.

The secondary aim was to investigate if the (SACL) refocused the anaesthetist attention to patient care.

*Material and Methods*

After institutional review board approval and written informed consent,eighteen patients undergoing abdominal surgery lasting more than 2 hours were anaesthetized using the TOOLBOX System (1) with a SACL proportional propofol and remifentanil effect-site Target Controlled Infusion (eTCI). Propofol Ce was titrated according to a predefined range of BIS or entropy values using the population PK/PD set of Schnider (2). Remifentanil Ce was based on a range of heart rate and systolic blood pressure limits represented in a matrix using the PK/PD set of Minto (3). For both drugs, minimum and maximal Ce values which cannot be overtaken by the SACL system were preprogrammed. The eTCI induction phase was manually titrated by the anaesthetist in charge of the patient and the SACL control was activated from the tracheal intubation until end of surgery. During surgery, the anaesthetist could adapt the BIS or Entropy and haemodynamic range values of the controller and could change the proposed Ce limit targets of the SACL pilot. At any time, the anaesthesiologist was the final decider. The haemodynamic data and Ce target concentrations were saved every 5 seconds. A group of 23 patients undergoing the same type of surgical procedure and anaesthetized by the same team of anaesthetists served as the control group. These patients were anaesthetized using remifentanil and propofol eTCI controlled manually according to the EEG and haemodynamic patients' responses. Results were analyzed using a 2-tailed Student t-test for continuous data after verification for normal distribution otherwise the Mann-Whitney U test was used. A p value $< 0.05$ was considered statistically significant. Data are reported as mean ± SD. Analyses were performed using SPSS version 15.0 (SPSS Science Inc., Chicago IL).

*Results*

| * : $p < 0.05$ | SACL Control | Manual Control |
|---|---|---|
| Mean Propofol Ce (µg/ml) | 2.4 ± 0.9 | 2.7 ± 0.8 |
| N = Ce Propofol changes/hour | 30.9* | 2.3* |
| Mean Remifentanil Ce (ng/ml) | 5.2 ± 2.4 | 6.1 ± 2.4 |
| N = Ce Remifentanil changes/hour | 18.5* | 4.4* |
| % of time BIS in the range 40 to 60 | 68.5* | 49.1* |
| % of time BIS less than 40 | 27.9* | 43.4* |
| % of time BIS more than 70 | 3.6* | 7.5* |

*Discussion*

The number of interventions of the SACL controller during the maintenance phase of anaesthesia is much higher than the anaesthetist eTCI responsiveness as measured by the number of target changes. The use of such a SACL eTCI system decreases the number of episodes of BIS or Entropy values out of the proposed range (40-60) and the likelihood of BIS or Entropy values greater than 70 which could be associated with awareness. The SACL eTCI system also shows a trend of a decrease of the mean propofol and remifentanil Ce. In conclusion, the combined use of semi-automated algorithms of propofol Ce according to frontal EEG values and remifentanil Ce according to a matrix of heart rate and systolic blood pressure bound limits must be tested in the future on a larger scale to evaluate its pharmacoeconomic interest, its safety for the patient and its acceptance by the anaesthetist.

*References*

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3. Minto C. F., ANESTHESIOLOGY, **86**, 24-33, 1997.

*Ropivacaine sparing effect of epidural neostigmine administered for labor analgesia.* V. LAMBEAUX, F. ROELANTS, P. LAVAND'HOMME. Cliniques Universitaires St Luc, Université Catholique de Louvain, Bruxelles.

*Introduction*

Epidural analgesia remains the best technique to provide pain relief during labor and the combination of local anesthetic with analgesic adjuvant is recommended to spare the local anesthetic consumption (Practice guidelines, Anesthesiology 2007). Currently available adjuvants involve lipophilic opioids, clonidine and the cholinesterase inhibitor, neostigmine (N). Epidural opioids and clonidine have both demonstrated reproducible significant local anesthetic sparing effect (25-30%) during labor analgesia. In contrast, N administered as a bolus dose or as a continuous infusion failed to demonstrate any local anesthetic sparing effect (Ross *et al.*, Anesthesiology 2006, 104 : A33 ; Belhadj *et al.*, ASA 2007 : A1774 ; Roelants *et al.*, Anesthesiology 2005). The underlying mechanisms of action differ between these classes of adjuvants, opioid agonists and clonidine being direct receptor agonists while N acts as an indirect agonist which inhibits cholinesterase enzyme and thereby increases locally spinal acetylcholine concentrations (Shafer *et al.*, Anesthesiology 1998). Taking that into account, the present study evaluated analgesic efficacy and eventual local anesthetic sparing effect of N added to ropivacaine 0.1% and administered by patient-controlled epidural analgesia (PCEA) without an initial bolus dose.

*Methods*

After Ethical Committee approval and informed consent, healthy parturients (singleton pregnancy, term > 37 weeks) in active labor and asking for epidural analgesia were included. After lumbar epidural catheter placement and negative test dose (3 mL lidocaine 2% with epinephrine), all the parturients received a bolus dose of 10 mL ropivacaine 0.1% before being allowed to use a PCEA device set as a 5 mL bolus dose per 15 min, with no background infusion. The parturients were randomly allocated to the following groups according to the analgesic solution : ropivacaine (R) 0.1% (R group, n = 20), ropivacaine 0.1% with sufentanil 0.5 µg/mL (RS group, n = 21) and ropivacaine 0.1% with neostigmine 25 µg/mL (RN group, n = 19). Rescue analgesia was available at any time as an epidural bolus of 10 mL R 0.1% (if VAS < 6/10) or R 0.2% (if VAS ≥ 6/10). Number and timing of rescue doses, total ropivacaine needs and labor duration were recorded. Fetal and maternal parameters were continuously monitored and maternal side effects were noted. Statistical analysis used ANOVA one way or Kruskal-Wallis test with posthoc comparison, $P < 0.05$ was considered to be significant.

*Results*

Demographic data (age, weight, parity, induced labor, ocytocine use) and labor duration did not differ between the groups. Results are expressed as median (IQR) or mean ± SD ; (*) $P < 0.05$ with R group.

Epidural sufentanil use was 3.4 ± 2 µg/h and neostigmine use was 160 ± 52 µg/h.

| | R group | RS group | RN group |
|---|---|---|---|
| Rescue doses (n) | 2 (1-3) | 1 (1-2) | 2 (1.5-2.5) |
| First rescue dose: | | | |
| VAS (0-10) | 7.4 ± 1.8 | 6.3 ± 1.9 | 7.0 ± 1.5 |
| Cervical dilatation (cm) | 6 (4.5-7) | 5.5 (4-9) | 5.5 (4-7) |
| Time elapsed (min) | 125 (90-165) | 177 (110-230) | 120 (100-207) |
| Labor R use (mg/ h) | 18.3 ± 5 | 13.6 ± 6 * | 14.5 ± 4 * |
| Side effects : nausea (n) | 1 | 1 | 4 |
| Cesarean delivery (n) | 2 | 4 | 2 |

*Discussion*

Epidural neostigmine administered by PCEA mode and without an initial bolus dose affordes similar analgesia than epidural sufentanil and shows a significant local anesthetic sparing effect during labor. The present results correlate with previous observations in humans concerning both the pharmacokinetic and pharmacodynamic of spinal neostigmine : i.e. neostigmine, independently of the dose administered, rapidely provokes sustained plateau concentrations of acetylcholine in the CSF, during 4-6 h after N injection (Shafer *et al.*, Anesthesiology 1998). Therefore, initiation of analgesia with a significant bolus dose of neostigmine (e.g. 500-750 µg) certainly may prevent further analgesic effect from the following doses. Continuous administration might also yield to similar effect with a saturation of the mechanism of cholinesterase inhibition.

*Efficacy of a single dose epidural neostigmine for postpartum pain.* A. Pospiech, F. Roelants, AL Richard, A. Payen, P. Lavand'homme. St Luc Hospital, Université Catholique de Louvain, Brussels.

*Background and Goal of the study*

Severe perineal pain is a common problem after vaginal delivery (1). Single dose epidural morphine decreases postpartum use of oral pain medication (2). Epidural neostigmine produces analgesia devoid of side effects during labor (3). The study evaluates the benefit of a single dose epidural neostigmine on postpartum pain and analgesics requirements.

*Material and Methods*

After Institutional Ethical Committee approval and Informed Consent, 41 healthy parturients (ASA 1&2, singleton pregnancy) with epidural analgesia for labor were included in the study. All parturients received epidural ropivacaine combined with sufentanil during labor. After delivery, patients were randomly allocated to receive 5 mL saline (Group S ; n = 20) or neostigmine 500 µg in 5 mL saline (Group N ; n = 21). All parturients were allowed to receive diclofenac (max 150 mg/d, with oral paracetamol (max 3 g/d) at their discretion as rescue analgesia. Postpartum pain scores (VAS : 0-10) and analgesics consumption were recorded for 72 hours. Side effects (nausea, vomiting and sedation) were recorded until 2 hours after delivery. Pain and VAS score were evaluated by phone call, at day 10. Statistical analysis used one way ANOVA, $P < 0.05$ was considered significant (*).

*Results*

Demographic data, including duration of first and second stage of labor, neonatal weight, episiotomy, perineal lacerations and instrumentation rate, did not differ between both groups. Postpartum VAS were similar between the groups during hospitalization (72 hours). Results are expressed as median (IQR) or mean ± SD.

| | Group S<br>n = 20 | Group N<br>n = 21 |
|---|---|---|
| Diclofenac (mg) | 325 (200-450) | 300 (139-412) |
| Paracetamol J2<br>J3<br>Total (mg) | 1500 (0-3000)<br>1000 (0-3000)<br>3500 (1000-9000) | 750 (0-1000) *<br>5000 (0-1750) *<br>2500 (1000-5000) |
| Pain at day 10<br>VAS at day 10 | 41%<br>3.7 ± 1.9 | 30%<br>4.5 ± 2.3 |

*Discussion and Conclusions*

Single dose epidural neostigmine 500 µg administered after delivery allowed a reduction of postpartum paracetamol consumption, but did not affect pain scores as previously observed with epidural morphine (1). In contrast with epidural morphine administration which is associated with nausea, pruritus and urinary retention, epidural neostigmine administration was devoid of side effects.

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*Shortterm effect of lidocaine 1% and depo-medrol 80 mg administered epidurally for acute back pain with sciatica.* L. TEUGELS*, M.D., M. VERCAUTEREN**, M.D., Ph.D., D. HIMPE*, M.D., Ph.D. ZNA Middelheim General Hospital (*) and University Hospital (**), Lindendreef 1, B-2020 Antwerp, Belgium.

*Background and Goals*

Acute back pain with sciatica (ABPWS) may originate form different causes (1). The effect on its relief by invasive treatments like epidural injection with corticoids is currently still controversial (2, 3). This retrospective cohort study of patients treated with 80 mg Depo-Medrol® and 3 ml Linisol 1%® for ABPWS tests the hypothesis that pain relief after 3 weeks is more pronounced if radiculopathy is the aetiologic factor.

*Material and Methods*

Following institutional guidelines, 19 patients treated for ABPWS with an epidural injection were screened for 3 weeks after the intervention. Examination and aetiological investigations included MRI and/or CT imaging results, pain drawing, and quadruple VAS scores for pain. These VAS scores regarded pain experienced over the past week : pain at its worst level (worse pain), at its least intense level (lowest pain), pain at the moment of the investigation, and average pain over the week. The cohort was dichotomized in a subgroup ABPWS with radiculopathy due to herniated intervertebral disc (n = 11) and a subgroup with ABPWS from other origins (n = 8). Non-parametric statistics were applied. A Wilcoxon matched-pair ranked sign test was used on both the subgroups to test whether changes in VAS-score over time were significant. This was followed by a Mann-Whitney-U test to compare the VAS scores at the moment of intake and three weeks later to test the hypothesis that the epidural injection affected pain relief differently in these two subgroups. Statistical significance was fixed at 0.05.

*Results*

The 19 patients were clinically comparable. Patients with a neuropathy restricted to just one dermatome (radiculopathy) had better VAS scores over time. Moreover, their most intense and lowest pain profile differed significantly from the other group. Data are shown in figure 1.

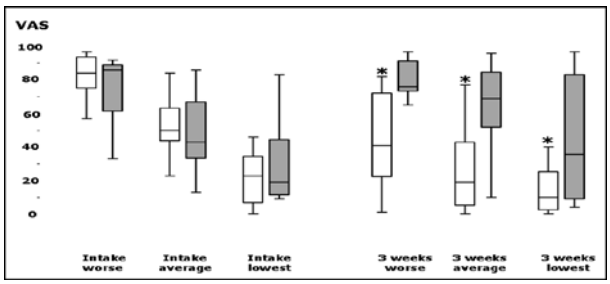


Fig. 1. — Visual Analog Pain scores (worse, average & lowest pain) at intake and 3 weeks after the epidural injection, presented as boxplots with median (line), box (25-75 percentiles) and whiskers (95% CI). The radiculopathy group (white) had statistically significant (* $p < 0.05$) lower pain scores than the other group (grey).

*Discussion and conclusion*

Treatment of ABPWS with epidural steroids should be scrutinized and preceded by thorough investigation of its aetiology. From this study steroid infiltration could be recommended in case of radiculopathy. However, a cohort of only 19 patients might be considered too small and therefore we suggest that more conclusive investigations are required in larger cohorts.

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*Characteristics, obstetric and anaesthetic outcome of the syndrome of Hemolysis, Elevated Liver enzymes, Low Platelets (HELLP) in a tertiary referral center.* Pascale WELTER, Frederik DE BUCK, Eugéne VANDERMEERSCH, Marina KUYPERS, Marc VAN DE VELDE. Department of Anaesthesiology, UZ Leuven, Belgium.

*Introduction*

Preeclampsia complicated with HELLP syndrome leads to increased maternal and foetal morbidity and mortality. The anaesthetic management is related to maternal and/or foetal parameters. The goal of the present retrospective chart analysis was to identify common traits in HELLP patients presenting in our obstetric department and describe the anaesthetic and obstetric outcome.

*Methods*

Following institutional approval, the obstetric and anaesthesia database was searched to identify patients that were diagnosed with the HELLP syndrome between Jan 1st 2000 and Dec 31st 2005. Obstetric and anaesthetic parameters were gathered. Data were analysed using Chi-square analysis and Student's t-test whenever appropriate.

*Results*

We found that 108 out of 13580 patients were diagnosed with preeclampsia and HELLP (incidence 0.8%). During the study period, 2912 patients were delivered by caesarean section (CS) (21.4%). In the HELLP patients the incidence of caesarean section was 78.7%. Vaginal delivery was scheduled for 45 patients but failed in 22. Gestational age at delivery was 31 weeks and 4 days. Gestational age at the diagnosis of HELLP was on average 3.5 days earlier. Thrombocyte count was 54 ± 25 [9-124]. Systolic and diastolic pressures were 180 ± 22 and 111 ± 12 mmHg respectively. De novo combined spinal epidural anaesthesia (CSE) was used in 39 patients undergoing caeserean section (46%), topped up epidural anaesthesia was used in 22 patients (26%) and general anaesthesia was used in 24 patients (28%). A higher incidence of general anaesthesia was found in patients with the HELLP syndrome compared to only 5% in the total population undergoing caesarean section.

*Discussion*

The high incidence of HELLP is explained by the referral function of our hospital. Delivery can usually be postponed with 3-4 days. General anaesthesia occurs frequently. Early epidural catheter placement must be stimulated to maximize the use of regional anaesthesia for delivery.

*Conclusion*

To avoid general anaesthesia whenever possible, early epidural catheter insertion is advised upon diagnosis.

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# Comparing methylprednisolone to dexamethasone-treatments for PONV : a prospective, randomised, double-blind, placebo-controlled trial.

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*Introduction*

The incidence of postoperative nausea and vomiting (PONV) is estimated to be 20 to 30%, but it may increase up to 70% in high risk patients. Dexamethasone (DXM) and methylprednisolone (MPS) have been proven effective in the prevention of nausea after chemotherapy. Prophylaxis of PONV with dexamethasone is effective(1), while literature about methylprednisolone is scarce (2).

*Methods*

After approval of our institutional ethical committee we therefore randomized 118 patients in a double blind way to receive either DXM 8 mg (38 patients), MPS 40 mg (40 patients) or placebo (40 patients) as a prophylactic agent. Inclusion criteria were female gender, adult age, elective abdominal or gynaecological surgery and informed consent of all subjects. Exclusion criteria were pregnancy or lactation, the intake of anti-emetic drugs within 24 hours preceding the surgery and emergency procedures. A standardized general anaesthesia regimen was performed. If normally distributed, results of continuous data were expressed as means (with SDs) and analyzed with Student's *t* test. Variables that did not show normal distribution were expressed as medians (with interquartile ranges) and compared with the Mann-Whitney *U* test. Categorical data were analyzed with Fisher's exact test. *P* values of $< 0.05$ were considered statistically significant.

*Results*

There were no significant differences between our 3 groups with regard to age, type of surgery, body mass index (BMI), history of PONV, smoking status, use of $N_2O$ or use of clonidine.

*Table I*

Incidence of PONV

| | DXM (n = 38) | MPS (n = 40) | Placebo (n = 40) | p value MPS vs. placebo | p value MPS vs. DXM |
|---|---|---|---|---|---|
| *Early nausea* | 7 (18, 8-34) | 4 (10, 3-24) | 7 (18, 7-33) | 0.289 | 0,35 |
| *Early retch* | 5 (13, 4-12) | 1 (3, 0-13) | 5 (13, 4-27) | 0.1 | 0,1 |
| *Early vomiting* | 4 (11, 3-25) | 2 (5, 1-17) | 6 (15, 6-30) | 0.132 | 0,43 |
| *Early PONV* | 7 (18, 8-34) | 4 (10, 3-24) | 7 (18, 7-33) | 0.259 | 0,35 |
| *Late nausea* | 11 (29, 15-46) | 5 (13, 4-27) | 14 (35, 21-52) | 0.017 | 0,09 |
| *Late retch* | 8 (21, 10-37) | 3 (8, 2-20) | 11 (28, 15-44) | 0.018 | 0,19 |
| *Late vomiting* | 5 (13, 4-12) | 3 (8, 2-20) | 8 (20, 9-36) | 0.096 | 0,5 |
| *Late PONV* | 11 (29, 15-46) | 6 (15, 6-30) | 14 (35, 21-52) | 0.045 | 0,1 |

All data are presented as number of patients (% of the total and 95% CI).

Late PONV was seen in 6 patients (15%, 95% CI 6-30) treated after MPS vs. 11 patients treated after DXM (29%, 95% CI 15-46) and 14 patients after placebo (35%, 95% CI 21-52). MPS was superior to placebo (p 0.045). No significant differences were shown between MPS and DXM, nor between DXM and placebo.

The relative risk reduction for late PONV for MPS is 57% (95% CI 40-82%), the number needed to threat is 5 (95% CI 3-97). The relative risk reduction for late PONV for DXM is 21% (95% CI -57-57%), the number needed to threat is 17 (95% CI 4-∞). The difference between MPS and DXM was not significant.

A longer duration of surgery contributed to a higher PONV appearance. (90 (+/- 44) vs. 75 (+/- 55), p 0.0024). Duration of anaesthesia was significantly longer in MPS group compared to placebo (127.5 (+/- 87.5 vs. 105.0 (+/- 43.7), p 0.044). More sufentanil was used in MPS group vs. placebo (27.9 (+/-10.3) vs. 23.9 (+/- 6.8), p 0.032).

The use of $N_2O$ was not significantly different between the 3 groups studied. Administration of $N_2O$ resulted in a higher incidence of PONV (19/42 (45%, 95% CI 30-61%) vs. 23/88 (26%, 95% CI 17-37%, p = 0.044).

*Discussion*

Although duration of anaesthesia was significantly longer and significantly more sufentanil was used in the MPS group, MPS was significantly better than placebo in the prevention of late nausea, retching and PONV. As stated in literature, steroids are mostly effective in the prevention of late PONV.

There was a beneficial clinical effect of DXM in this population, although not significant. Apfel found a relative risk reduction for DXM of 26% (1), which is consistent with the 21% relative risk reduction we found, although not significant.

A possible explanation for not finding a significant beneficial effect for DXM could be that our population is a population at risk according to risk scores of Apfel and Sinclair. In a population at risk a combination of anti emetic drugs is recommended (3).

In the majority of reports on DXM in the prevention of PONV, 8 mg of DXM was used, although Apfel *et al.* proved 4 mg of DXM to be as effective as higher doses in his 2004 article (1). While our data were collected in 2003 and 2004, we used 8 mg of DXM. We compared 8 mg of DXM to 40 mg of MPS to rule out a difference in potency for the prevention of PONV. MPS was used in much higher doses in the scarce other trials that found a beneficial effect on PONV (125 mg in one report, 15 mg/kg 1 hour prior to surgery and 0.3 mg/kg/6 hours, 4 times postoperatively in another (2)).

In our population the duration of surgery and use of nitrous oxide were risk factors for the occurrence of PONV. Duration of surgery was longer in the MPS group, there was no significant difference in the use of N2O between groups.

*Conclusion*

This study confirms that steroids are effective in the prevention of late PONV, less effective in early PONV. We showed a positive trend for DXM 8 mg vs. placebo with a NNT of 17 to prevent late PONV, although not statistically significant. MPS 40 mg is significantly better than placebo with a NNT of 4 to prevent late PONV. The difference between DXM and MPS is not significant in our study.

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*The Effects of rapid increases in desflurane and sevoflurane concentrations on spirometry in humans during balanced anesthesia with remifentanil.*

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*Introduction*

High concentrations of desflurane may irritate the airway and consequently increase airway resistance (1). The aim of this study was to assess the effects of rapid increases of desflurane and sevoflurane concentrations during bolus administration on spirometry parameters in humans during balanced anesthesia with remifentanil.

*Methods*

After Institutional Ethics Committee approval, written informed consent was obtained from 30 ASA I patients scheduled for minor non-laparoscopic surgery. Induction was with TCI remifentanil, propofol and rocuronium (0.9 mg.kg$^{-1}$ IBW). TCI remifentanil was initiated at 4 ng/ml and increased by 25% or decreased by 25% in order to maintain mean arterial pressure and heart rate within 20% of baseline during anesthesia. Patients were randomized into 2 groups (n = 15) to receive BIS-guided desflurane or sevoflurane targeted to maintain a BIS-value between 45 and 55. When BIS $\geq$ 55 for more than 30 s, an inhalation bolus was administered. The bolus administration of desflurane and sevoflurane was performed by setting the vaporizer to maximum output in a fresh gas flow of 4 L/min during 15 s. Afterwards, fresh gas flow was returned to baseline 2 L/min with a 25% increased vaporizer setting. This resulted in 45 boli desflurane and 58 boli sevoflurane. To assess the differences between spirometric data in a period 30 s before and 300 s afterwards, all data were synchronized on the start of the inhalation bolus. At every second the difference between the mean value and the 95% confidence intervals (CI) were calculated (group desflurane – group sevoflurane). Significance is reached when zero is not included in the 95% confidence intervals.

*Results*

Patient characteristics were comparable for the two groups. Mean end-tidal concentrations before bolus were 0.5 (0.12) MAC desflurane and 0.49 (0.18) MAC sevoflurane($p = 0.46$). Bolus administration resulted in mean peak inspiratory concentrations of 10.8 (1.6) vol% desflurane and 5.4 (1.2) vol% sevoflurane ($p < 0.05$). Pplateau was significantly lower during the 15 s bolus administration of desflurane. Airway resistance was lower in the desflurane group and did not differ significantly from the sevoflurane group (Fig. 1).

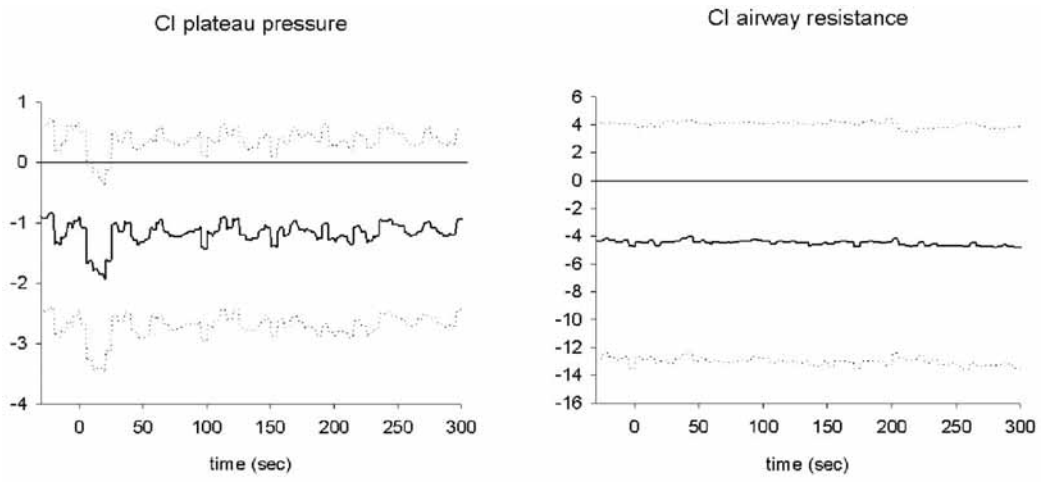


Fig. 1. — Time synchronised analysis of the differences in plateau pressure and airway resistance between groups. The difference of the means is plotted as continous line; the differnce in upper and lower 95% CI as dotted lines.
Significance is reached when zero is not included between the dotted lines.

*Discussion*

Our results are in conflict with the work of Goff and colleagues (1). When combined with remifentanil, high inspired concentration of desflurane did not provoke bronchoconstriction. Compared to sevoflurane, desflurane does have bronchodilating properties (2). Repetitive increases in desflurane concentrations might blunt airway responses (3).

*Conclusions*

Repetitive increases in inspiratory and end-tidal concentrations during inhalation boli of desflurane and sevoflurane did not result in increased airway resistance.

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