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Anesthetics impair dendritic spine development in the postnatal mouse somatosensory cortex

Adrian Briner¹, Matthias De Roo², Paul Klausner², Jozsef Kiss², Dominique Muller², Laszlo Vutskits^{1,2}

¹Department of Anesthesiology, Pharmacology and Intensive Care, University Hospital of Geneva; ²Department of Fundamental Neuroscience, University of Geneva Medical School

Background: An important feature of the developing mammalian brain is the intense burst of synaptogenesis during the early postnatal period. In the mouse somatosensory cortex, the number of synaptic contacts increases several folds between the 2nd and 4th postnatal week. Whether exposure to anesthetics during this period affects development of neural circuitry remains to be determined. Transgenic mice, expressing the yellow fluorescent protein (YFP) in layer 5 pyramidal neurons of the somatosensory cortex (SSC) provide valuable tools to address this issue. Using this mouse strain, the present study was aimed to investigate whether anesthetics alter physiological developmental patterns of dendritic spines, representing the principal sites of excitatory synaptic contacts of neurons, in the SSC during the brain growth spurt period.

Methods: YFP mice (C57BL6 background) were exposed to a 5-hour-long sedation protocol using propofol, midazolam or ketamine at postnatal day (PND) 15, 20, 30 or 90. Animals were then sacrificed for histopathological evaluations of the brains either immediately at the end of the treatment or, in case of PND15 animals, also at later developmental stages including PND20, PND30 and PND90. Using laser scanning confocal microscopy, the effects of anesthetics on neural circuitry of layer 5 pyramidal neurons of the SSC were evaluated by quantifying the following morpho-functional parameters describing dendritic spines: (i) density; (ii) type (iii) length and (iv) head diameter.

Results: The 5-hour-long treatment paradigm did not induce any significant perturbations in blood-gas parameters or in blood glucose levels. Activated-caspase-3 immunohistochemistry revealed that neither propofol, nor midazolam or ketamine induce apoptotic response in the SSC at any ages tested (PND 15-90). In contrast, all drugs induced rapid remodeling of dendritic spines in PND15 and PND20, but not in older animals. As soon as 5 hours following anesthesia induction, a significant increase in the number of dendritic spines ($p < 0.01$) and filopodia ($p < 0.01$) as well as a significant decrease in dendritic spine head diameter ($p < 0.005$) was observed on apical dendrites of layer 5 pyramidal neurons of the SSC. In animals, receiving anesthesia at PND15, spine density was still significantly higher ($p < 0.05$) at PND20 compared to control groups, and significant differences ($p < 0.01$) in spine head diameter persisted up to PND30.

Conclusion: These data show that exposure to anesthetics during critical periods of synaptogenesis can induce long-lasting impairments in dendritic spine development. Given the essential role of dendritic spines in synaptic transmission, our results thus raise the intriguing possibility that administration of anesthetics during the brain growth spurt period might interfere with appropriate development of neural circuitry.

FM 1

volumes were: TA 0.40 (0.50), SOL 0.10 (0.14), BF 0.17 (0.19), VL 0.10 (0.17).

Conclusions: We could quantify receptive fields in all subjects. The areas are associated with much less variability than the volumes. This method is the first one that allowed a quantification of normal values of receptive fields in humans. The method has important potential applications in research to explore aspects of central plasticity in patients. Furthermore, it may be utilized as a diagnostic tool for central hypersensitivity.

Feasibility of gene therapy for the treatment of neuropathic pain: downregulation of GTP cyclohydrolase 1 expression via RNA interference

Sandy Jean, Chris Towne, Patrick Aebischer, Isabelle Decosterd CHUV, UNIL & EPFL

Background: Following peripheral nerve injury, changes in gene expression in dorsal root ganglia neurons contribute to neuropathic pain (NP). Among those modifications, the GTP cyclohydrolase 1 (GCH1) is upregulated in primary sensory neurons. GCH1, a rate limiting enzyme for tetrahydrobiopterin synthesis, is a key modulator of pain. This work concerns the downregulation of GCH1 expression *in vitro* using RNA interference, an effective tool to silence gene expression. Our goal is to modulate *in vivo* the expression of GCH1 using viral vectors, and explore the feasibility of a gene therapy treatment for NP.

Method: PC 12 cells, derived from pheochromocytoma of the adrenal medulla, express GCH1. Recombinant adeno-associated viral plasmids were generated that drive the expression of 6 different GCH1 silencers and 2 GCH1 mismatches together with an enhanced green fluorescent protein marker (eGFP). Control conditions consist of the 2 mismatches or the viral plasmid containing the GFP only. Plasmids are incorporated in PC12 by electroporation in triplicate. Three days later, transfected cells are separated using fluorescence-activated cell sorting (FACS) and analysed for GCH1 expression by Western blot.

Results: For each of the transfected plasmid, we obtained specific bands for GCH1 by Western blot analysis. After normalization of GCH1 by tubuline as loading control, we observed a significant decrease in GCH1 expression in 2 constructs out of the 9 plasmids. For the best plasmid, the decreased expression was $54\% \pm 12\%$ ($n = 3$), ($p < 0.05$).

Conclusion: We demonstrated that GCH1 gene expression is downregulated in PC12 cells. Our results suggest that RNA interference may be a tool for silencing genes of interest into the pain pathway.

Perspective: We plan to generate a recombinant adeno-associated virus vector with the most efficient plasmid we obtained. We need to confirm these preliminary results *in vivo* then test the efficacy in a model of NP.

FM 3

Nociceptive receptive fields: normal values in the pain-free population

Alban Y. Neziric^a, Ole K. Andersen^b, Antony Dickenson^c, Lars Arendt-Nielsen^b, Michele Curatolo^a

^aUniversity Dep. of Anaesthesiology and Pain Therapy, University Hospital of Bern; ^bCenter for Sensory-Motor Interaction, University of Aalborg, DK; ^cDep. of Pharmacology, University College London, UK

Aim of investigation: Expansion of the receptive fields of spinal neurones is an important manifestation of central plasticity leading to amplification of pain. No validated model for such an assessment in patients exists. The purpose of this study was to investigate a new method to assess receptive fields in humans based on reflex responses and set reference values of the normal population for future research and clinical applications.

Methods: We studied 300 healthy subjects (150 males and 150 females, 18–80 years old). Nociceptive withdrawal reflexes (NWR) were evoked by applying painful electrical stimulation at intensity of 1.5 times higher than the pain threshold at ten spots of the foot sole. The reflexes were measured as electromyographic response from the muscles tibialis anterior (TA), soleus (SOL), biceps femoris (BF) and quadriceps vastus lateralis (VL). The area of nociceptive reflex receptive field (RRF) was defined as the skin area from which a NWR could be evoked in a specific muscle, expressed as proportion of the total foot sole area. The volume of the RRF was defined as the integrated reflex size within the detected RRF area.

Results: The area and volume of the receptive fields were quantified in all cases. The mean values (standard deviations) of the areas were: TA 0.44 (0.28), SOL 0.66 (0.34), BF 0.68 (0.28), VL 0.63 (0.33). The

FM 2

Regulation of the voltage-gated sodium channel Nav1.7 current *in vitro*

Cédric Laedermann, Isabelle Decosterd, Hugues Abriel University of Lausanne

Background: Chronic pain, and especially neuropathic pain (NP), is a frequent and disabling disorder occurring as a consequence of lesion or dysfunction of the nervous system. The pathogenesis of NP involves multiple players; one of the prominent among them is the appearance of a positive shift in the excitability of the peripheral and central nervous system. This peripheral activity is mainly carried by voltage-gated sodium channels, where Nav1.7 isoform seems to be an important candidate since loss of function mutations reported in the corresponding gene was associated with congenital inability to experience pain. These channels contain an α -subunit (Nav1f), forming the pore of the channel, and β -subunit responsible for the regulation of channel density at the cell membrane. Ubiquitin ligases of the Nedd4 family are also known to regulate the channel density at the cell membrane. The aim of this study was to investigate the cellular mechanisms involved in the regulation of the membrane density of the Nav1.7 isoform that may be altered in NP.

Methods: *In vitro* experiments were carried out to investigate whether Nedd4-2 and different β -subunits are involved in modulating the amount of Nav1.7 channels at the cell surface. Whole cell patch clamp experiments using a cell line expressing Nav1.7 alone allowed the recording of sodium currents INa. We assumed that the recorded INa reflects the number of channels at the cell surface. If β -subunits or Nedd4-2 have any modulatory effects, co-transfection of these regulatory proteins should modify the amplitude of INa.

Results: Co-transfection experiments with Nedd4-2 decreased the current amplitude by $\sim 80\%$ ($n = 18$, *** $p < 0.001$). This effect was

FM 4

dependent on a known consensus motif since a mutation affecting this sequence abolished the down-regulatory effect of Nedd4-2. Co-transfection of β -subunits showed an opposite effect as they increased the INa: for $\beta 1$ by ~155% (n = 22, ***p < 0.001); for $\beta 2$ by ~ 55% (n = 22, ***p < 0.001).

Conclusion: Nedd4-2 and beta subunits have opposite effects in terms of regulating the amount of Nav1.7 at the cell surface thus modifying the excitability of these cells.

Perspectives: We need to confirm *in vivo* these preliminary results combining experimental pain animal models together with knock-out mice for these two genes in order to correlate the cell surface modulation of Nav1.7 with differences in pain sensitivity.

FM 5 Ultrasound imaging of the nerves supplying the cervical zygapophysial joints: a descriptive study

Siegenthaler A, Curatolo M, Eichenberger U
Universitätsklinik für Anästhesiologie und Schmerztherapie,
Inselspital Bern

Background: The cervical zygapophysial joints are a common source of chronic neck pain. Diagnostic blocks and radiofrequency neurotomy of the nerves that supply the joints are validated tools in the diagnosis and therapy of zygapophysial joint pain, respectively. These interventions are typically performed with fluoroscopic needle guidance. However, the actual target, i.e. the nerve, remains invisible. Ultrasound imaging could offer new opportunities, with this technique being increasingly used in regional anaesthesia and pain therapy. We previously described an excellent sonographic visualisation of the third occipital nerve that supplies the C2-3 joint in healthy volunteers (Eichenberger et al, *Anesthesiology* 2006). However the visibility of the remaining smaller nerves that supply the zygapophysial joints (medial branches of the dorsal rami of the spinal nerves) has so far not been described, especially in an ordinary patient population suffering from chronic neck pain.

Objectives: To describe the sonographic visibility of all the nerves supplying the cervical zygapophysial joints in a patient population suffering from chronic neck pain.

Methods: In this preliminary analysis, data from 27 consecutive patients with chronic neck pain who were treated in our pain clinic were included. Ultrasound imaging of the cervical zygapophysial joint region was performed in a longitudinal plane through the articular pillars. The ease of identification of each nerve (third occipital nerve and medial branches of the dorsal rami of the spinal nerves) was categorized as "good", "difficult but visible" or "impossible".

Results: Third occipital nerve: 21/27 good, 4/27 difficult, 2/27 impossible. Medial branch C3: 18/27 good, 4/27 difficult, 5/27 impossible. Medial branch C4: 20/27 good, 4/27 difficult, 3/27 impossible. Medial branch C5: 17/27 good, 6/27 difficult, 4/27 impossible. Medial branch C6: 16/27 good, 4/27 difficult, 7/27 impossible. Medial branch C7: 3/27 good, 2/27 difficult, 22/27 impossible.

Conclusions: With the exception of the medial branch C7, the nerves supplying the zygapophysial joints can be visualized in the vast majority of cases. Ultrasound imaging could provide an additional or an alternative tool in the performance of diagnostic or therapeutic interventions on these nerves in patients with cervical zygapophysial joint pain.

FM 6 The effect of magnesium sulphate on the time course of rocuronium induced neuromuscular block – a randomized electrophysiological study

C. Czarnetzki, C. Lysakowski, N. Elia, L. Dumont, E. Tassonyi,
M.R. Tramèr
Hôpitaux Universitaires de Genève

Background and goal: It has been claimed that pre-treatment with magnesium sulphate (Mg) has no impact on the speed of onset of rocuronium-induced neuromuscular block [1]. The aim of our study was to verify this assumption.

Methods: Patients ASA I to II were randomly allocated to one of two groups: (1) Pre-treatment with an IV infusion (15 min) of 60 mg kg⁻¹ of Mg; (2) An identical volume of saline. After induction (propofol, sufentanil), recording of neuromuscular transmission was commenced (TOF-watch SX acceleromyograph®) with TOF stimulation at the wrist every 15 seconds. After obtaining stable recordings, rocuronium 0.6 mg kg⁻¹ was administered and patients were intubated when fully curarized.

Results: Sixty adults were included.

Times	Mg	Plac	P
Onset of max. block (T1 5%) [sec]	77.0 ±17.3	122.2 ±49.5	<0.001
Injection to recovery 25% [min]	43.6 ±14.6	33.8 ±8.3	=0.003
Recovery 25–75% [min]	13.9 ±5.8	12.1 ±5.1	=0.223
Total recovery (to TOF ratio 0.9) [min]	70.5 ±22.6	58.5 ±14.8	<0.021

Data are means±SDs

Conclusion: Pre-treatment with Mg significantly shortens onset time and prolongs the early, but not late, recovery period of rocuronium-induced neuromuscular block.

References: 1 Kussmann B, et al. Administration of magnesium sulphate before rocuronium: effects on speed of onset and duration of neuromuscular block. *BJA*. 1997;79:122–4.

FM 7 Prospective randomized controlled multi-centre trial on cuffed versus uncuffed tracheal tubes in small children

Weiss M¹, Dullenkopf A¹, Fischer JE², Schmitz A¹, Keller C³, Gerber AC¹

¹Department of Anaesthesia, University Children's Hospital Zurich, Switzerland; ²Mannheim Institute of Public Health, University of Heidelberg, Germany and ³Department of Anaesthesia, Schulthess Clinic, Zurich, Switzerland

Background: Cuffed tubes have so far not been used routinely in children because of fear of airway damage (1). The aim of this study was to compare tube exchange rate and post-intubation morbidity when using cuffed versus uncuffed tubes in small children.

Methods: Patients aged from birth to <5 years requiring general anaesthesia and tracheal intubation were included in 24 European paediatric anaesthesia units. Cuffed tubes sizes (Microcuff PET®) were selected as follows: ID (mm) 3.0: 0 (>3 kg) – 8 months / ID 3.5: 8–18 months/ ID 4.0: 18–36 months/ ID 4.5: 36–60 months. Uncuffed tubes sizes (Mallinckrodt®, Portex®, Rüsch®, Sheridan®) were selected according to local institutional guidelines. The number of tube exchanges to find an appropriate tube with a small air leak at airway pressure of 20 cmH₂O allowing satisfactory ventilation, was noted. Minimal cuff pressure required to seal the airway was noted. Cuff pressure was monitored and limited with a pressure release valve at 20 cmH₂O. Post-extubation stridor was recorded by an independent assessor. Data are presented as mean±sd and were compared using T-Test and chi-squares analysis (p < 0.05).

Results: 2249 children were studied (1119/1130 cuffed/uncuffed tubes). Children age's was 1.93 ± 1.48 yrs in the cuffed and 1.86 ± 1.45 yrs in the uncuffed study group (p = 0.31). Tube exchange rate was 2.1 % in the cuffed and 29.9% in the uncuffed study group (p < 0.0001, risk ratio 0.07, 95% CI 0.045–0.10). Post-extubation stridor was noted in 4.38% in the cuffed and in 4.69% in the uncuffed study group (p = 0.16, risk ratio 0.93, 95% CI 0.64–1.36). Minimal cuff pressure to seal the trachea was 10.6 ± 4.3 cmH₂O.

Conclusion: This large prospective randomized controlled multi-centre trial demonstrates that the Microcuff PET® can be used in children without increased post-intubation morbidity. Minimal tube exchange rate and a reliable sealed airway at cuff pressures of ≤20 cmH₂O are the main benefits compared to uncuffed tracheal tubes.

References: 1) Orliaguet GA, et al. *Paediatr Anaesth*. 2001;11:277–81.

FM 8 In children undergoing tonsillectomy, dexamethasone decreases dose-dependently the risk of PONV but is associated with an increased risk of bleeding

C. Czarnetzki, N. Elia, C. Lysakowski, L. Dumont, B.N. Landis,
R. Giger, P. Dulguerov, J. Desmeules, M.R. Tramèr
Hôpitaux Universitaires de Genève

Background: Dexamethasone is widely used for the prevention of postoperative nausea and vomiting (PONV) in paediatric tonsillectomy. The aim of our study was to assess whether dexamethasone reduced the risk of PONV dose-dependently at 24 hours.

Methods: Children were randomized to receive dexamethasone (0.05, 0.15, or 0.5 mg/kg) or placebo intravenously after induction of anaesthesia. Postoperative analgesia was with paracetamol-codeine; ibuprofen was used as a rescue analgesic. Follow-up was until 10 days postoperatively.

Results: The trial was stopped early for safety reasons; we analysed 213 children. At 24 hours, 44% of those receiving placebo had

suffered from PONV as compared with 38%, 24%, and 12% receiving dexamethasone 0.05, 0.15, or 0.5 mg/kg, respectively (P for linear trend, <0.001). Children receiving any dose of dexamethasone received significantly less ibuprofen during the first 24 hours. Blood glucose and infection rates were not different among groups. There were 26 postoperative bleedings in 22 children; 15 children (68.2% of those bleeding) had the 1st episode diagnosed later than the 1st postoperative day. Four percent of the children receiving placebo had at least one bleeding episode as compared with 11%, 4%, and 24% receiving dexamethasone 0.05, 0.15, or 0.5 mg/kg, respectively (P for linear trend, 0.01). The highest dose of dexamethasone was associated with the highest risk of bleeding (adjusted OR, 7.06 [95% CI, 1.34 to 37.1]; P = 0.021). Eight children had to undergo emergency re-operation due to bleeding; all had received dexamethasone, and 4 of those had received the highest dose (compared with placebo, P = 0.052).

Conclusions: In children undergoing tonsillectomy, dexamethasone decreased the risk of PONV dose-dependently, but was associated with an increased risk of postoperative bleeding although these children received significantly less ibuprofen for postoperative analgesia.

FM 9

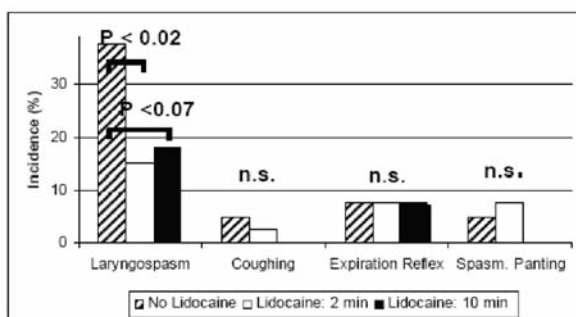
Effect of intravenous lidocaine on laryngeal responses in children anesthetized with sevoflurane

T.O. Erb, B. von Ungern-Sternberg, K. Keller, F.J. Frei
Division of Anaesthesia, University Children's Hospital, Basel, CH

Introduction: Laryngospasm (LS) is common and often more severe in children than in adults. In order to reduce the incidence of LS, the administration of lidocaine has been advocated [1]. However, its effectiveness in preventing LS is controversial [2]. The purpose of the study was to evaluate respiratory responses to laryngeal irritation in a clinical model after administration of lidocaine.

Methods: 40 children (3–7 years, 12–35 kg) scheduled for elective procedures. Premedication: Midazolam 0.3 mg/kg. Inhalational induction with sevoflurane 8%, insertion of LMA, maintenance of anaesthesia with 2.5% sevoflurane. Insertion of a fiberoptic bronchoscope via LMA, placing the tip above the glottic opening. Simultaneous recording of video images and respiratory parameters. The laryngeal mucosa of each patient was stimulated 3 times: i) before, ii) 2 min, and iii) 10 min after i.v. administration of 2 mg/kg lidocaine by spraying the vocal cords with 0.25 ml of distilled water. Evoked responses were classified into 4 categories [3] by a blinded reviewer: A) complete closure of the glottis lasting >10s on the video images, B) expiration reflex, C) cough reflex, D) spasmodic panting.

Results:



Conclusion: The results of the present study demonstrated that the intravenous administration of 2 mg/kg lidocaine resulted in a significant reduction of the incidence of laryngospasm. While this effect was traceable 2 min after the administration, this effect was already blunted after 10 min.

References: 1. A&A1978;57:506; 2. A&A1985;64:1193; 3. Anesthesiology 1998;88:45.

Comparison of prothrombin time values of standard laboratory test and two point-of-care devices

N. Urwyler, E. Staub, L. Staub, K. Dätwyler, S. Fluri, T. Sollberger, M. Deplaces, L. Theller, R. Greif
Universitätsklinik für Anästhesiologie und Schmerztherapie, Inselspital Bern

Background: Venous access may be challenging in children, and the required amount of blood might be large, especially with repeated studies in very small infants. The time needed to get results from standard laboratory methods is about 45 minutes but only three minutes using Point-of-Care devices. The aim of the study was to compare the standard laboratory prothrombin time test as “the gold standard” with two Point-of-Care methods for prothrombin time to assess the accuracy. That minimizes the difficulty in blood sampling and the amount of blood because the Point-of-Care tests can be performed from 10 µl of capillary blood.

Methods: We compared PT measured with CoaguChek XS Plus® (Roche Diagnostics, Basel, Switzerland), CoaLine® (DialLine, USA), and the standard laboratory test of plasma PT in pediatric ICU patients. Blood samples were drawn either from arterial or venous lines, or by direct venipuncture. The same blood sample was tested with all three methods in random order.

Results: from the first 28 pediatric ICU patients with a total of 71 measurements including 11 boys, 17 girls with median age of 4.2 months (range 0 days to 12 years), median height 53 cm (36–170 cm), median weight 4000 gr (1020 g to 57 kg). Direct comparison of the point-of-care devices to the standard laboratory test showed a correlation of $r = 0.82$ for CoaguChek and $r = 0.71$ for CoaLine. Bland-Altman analyses showed a mean difference of -0.65 ± 13.0 SD (CoaguChek) and 6.08 ± 22.8 (CoaLine) to the standard test. Standard laboratory test and CoaguChek failed each once to provide a result but CoaLine 7 times.

Conclusion: Capillary blood Prothrombin Time measurement with the Point-of-Care device CoaguChek XS Plus® is comparable to the gold standard laboratory measurements in pediatric ICU patients. The CoaLine was clinically not satisfying.

The Point-of-Care tool CoaguChek XS Plus® to measure capillary prothrombin time might reduce difficulties of venous blood sampling and the need for direct venipuncture substantially in children because capillary blood can be used for coagulation measurements.

FM 11

Postoperative troponin T release is associated with 12-month mortality after on-pump cardiac surgery in adults

G. Lurati Buse¹, C. Brüni¹, J. Kasper¹, M. Grapow², E. Seeberger¹, D. Bolliger¹, M. Seeberger¹, M. Filipovic¹

¹Anaesthesiology Department, University Hospital Basel; ²Division of cardiac surgery, University Hospital Basel

Introduction: Postoperative events are often neglected in risk stratification for patients undergoing cardiac surgery. We hypothesised that postoperative troponin T (TnT) release is associated with 12-month mortality after cardiac surgery.

Methods: After approval by the ethical committee and with patients' written informed consent, we prospectively assessed the 12-month outcome of consecutive patients undergoing cardiac surgery with cardiopulmonary bypass at our institution from January 2005 to September 2006. TnT values on the 1st and 2nd postoperative morning and baseline characteristics were documented and outcome information obtained by direct patient contact. All reported events were confirmed by the family physician or by hospitalisation charts. We calculated the TnT cut-off value by ROC-curve, and classified patients in 3 risk groups by Euroscore: low (Euroscore 0–2), moderate (Euroscore 3–5), and high risk (Euroscore ≥ 6).¹ The crude odds ratio (OR) between TnT release and 12-month mortality was adjusted for risk groups by logistic regression.

Results: We included 764 patients; mean age was 66 years (± 11.7); 73% were men. Isolated CABG was performed in 54%, valvular surgery in 29%, combined valvular and coronary surgery in 12%, and other procedures in 5%. Of the patients 21% were at low, 35% at moderate, and 44% at high risk. In the 723 patients (94.6%) with complete 12-month follow-up, we registered 56 deaths (7.7%). At the TnT cut-off level 0.80 µg/L, the crude OR (95% confidence interval) for the association between TnT and 12-month mortality was 3.75 (2.03–6.92). After adjustment for the Euroscore, the OR between postoperative TnT release and 12-month mortality was 3.55 (1.91–6.64).

Discussion: Troponin T release after cardiac surgery was a strong and independent predictor of 12-month mortality in adults undergoing cardiac surgery.

FM 12

Elevated BNP values does not allow for diagnosing cardiac dysfunction in young subjects

J. Kasper, D. Bolliger, M. Filipovic, M. Seeberger
Universitätsspital Basel

Introduction: Elevated brain natriuretic peptide (BNP) levels are used for the diagnosis of systolic and/or diastolic cardiac dysfunction in subjects ≥ 45 years [1]. Cut-off levels are established, however, few data are available in younger subjects. The purpose of this study was to evaluate the range of BNP values in healthy young subjects.

Methods: Sixty-one subjects (41 men and 20 women, aged 18–48 years) free from cardiovascular or relevant concomitant disease and medication were studied. BNP was measured in awake, unpremedicated subjects immediately before the transthoracic echocardiographic study was performed. Mean arterial pressure (MAP), heart rate (HR), and the following echocardiographic parameters were analysed: fractional area change (FAC), early diastolic mitral annulus velocities (E') obtained by pulsed-wave (PW) Doppler tissue imaging, transmitral early peak flow velocities (E) obtained by PW Doppler, and the E/E' ratio. BNP was reevaluated after one hour.

Results: BNP values ranged from <15 to 388 ng/l. Elevated BNP values (>50 ng/l) were found in 20 subjects (33%); BNP levels suggestive for heart failure (>100 ng/l) were found in four subjects (7%). Echocardiographic signs of impaired systolic (FAC $<45\%$) and diastolic left ventricular function ($E' <8.5$ cm/s or $E/E' >8$) were present in one and two subjects, respectively; all of them had BNP values <50 ng/l. There was no correlation between BNP levels and FAC ($R = 0.01$, $p = 0.93$), E' ($R = 0.19$, $p = 0.16$), or E/E' ($R = -0.06$, $p = 0.66$). There were no differences in echocardiographic parameters between the groups with normal and elevated BNP levels (Mann-Whitney U test). Variation of BNP before and after echocardiography ranged from 0.0 to 15.5 ng/l.

Discussion: A high percentage of healthy young subjects had elevated BNP levels if cut-off values previously defined in an older subject population are applied. Due to a low pretest probability, BNP cut-off levels found in older subjects are not useful for diagnosing heart failure in this young population without a history of cardiac disease.

Reference: [1] Dong JS, et al. JASE 2006; 19:1017–25.

FM 13

Effect of different HES preparations (HES 130/0.42; HES 200/0.5) on activated proximal tubular epithelial cells in vitro

Moritz Wittlinger^{1,2}, Elisena De Conno^{1,2}, Thomas Neff¹, Martin Schläpfer^{1,2}, Donat R. Spahn¹, Beatrice Beck-Schimmer^{1,2}
¹Institute of Anesthesiology, University Hospital Zurich; ²Institute of Physiology and Zurich Center for Integrative Human Physiology, University of Zurich

Background and goal of study: Acute renal failure is a frequent complication of sepsis. Hydroxyethyl starches (HES) are widely used in the treatment of such patients [1, 2]. However, the effect of HES on renal function during sepsis remains controversial. This *in vitro* study has been performed to assess possible effects of HES 130/0.42 and HES 200/0.5 on activated proximal tubular epithelial cells.

Materials and methods: HK-2 cells (human proximal tubular epithelial) were stimulated with tumor necrosis factor alpha (TNF- α) in the presence or absence of HES 130/0.42 or 200/0.5 (Braun, Germany) to mimic a septic condition requiring fluid replacement. After 4, 10, and 18 h of incubation monocyte chemoattractant protein-1 (MCP-1), a key chemoattractant for neutrophils and macrophages, was determined, and colorimetric viability- and cytotoxicity assays were performed.

Results: MCP-1 expression was enhanced by 100% upon TNF- α exposure. In the presence of 2% and 4% HES 200/0.5 during a stimulation time of 10 h and 18 h, MCP-1 concentration was decreased between 26% and 56% ($p < 0.05$). TNF- α stimulation resulted in a significant decrease of viability by 53–63%, while viability decreased by only 32–40% in co-incubation with HES 130/0.42 ($p < 0.005$), and remained even less affected by TNF- α in the presence of HES 200/0.5 ($p < 0.001$). TNF- α -induced cell death rate was attenuated in the presence of HES 200/0.5 ($p < 0.05$).

Discussion and conclusion: Data of this *in vitro* study show that both HES products attenuate cell injury upon inflammatory stimulation. Protective effect was more pronounced in the HES 200/0.5 group compared to HES 130/0.42, pointing to a biological difference between both HES types.

References: 1. Curr Opin Crit Care. 2007;13:541–8; 2. Crit Care Med. 2004;32(11 Suppl):S451–4.

FM 14

Anti-inflammatory effect of ropivacaine in endotoxin-injured alveolar epithelial cells: elucidation of cellular signalling

M. Schläpfer^{1,2}, B. Roth Z'Graggen², S. Blumenthal³, A. Borgeat³, D. R. Spahn¹, B. Beck-Schimmer^{1,2}

¹Department of Anaesthesiology, University Hospital Zurich;

²Institute of Physiology, University Zuerich Irchel; ³Department of Anaesthesiology, Orthopedic University Clinic Zurich Balgrist, Zurich, Switzerland

Introduction: Ropivacaine, a new local anaesthetic, exerts anti-inflammatory actions in the endotoxin-induced lung injury model. We investigated the intracellular signalling pathway leading to decreased inflammation after ropivacaine administration in an *in vitro* model of acute lung injury. We focused on protein kinase C (PKC) and the prosurvival kinases ERK and Akt, the latter two presumably being involved in the NFB-pathway leading to cytoprotection.

Methods: Monolayers of alveolar epithelial cells (AEC) were stimulated with 20 $\mu\text{g/ml}$ lipopolysaccharide (LPS) and co-incubated with ropivacaine in a final concentration of 1 μM (controls exposed to phosphate-buffered saline, PBS). Four different groups were designed: PBS/PBS, PBS/ropivacaine, LPS/PBS and LPS/ropivacaine. LPS and ropivacaine were added at the same time to the cells for 4 h. PKC activity was assessed using a PepTag assay for non-radioactive detection. Activation of ERK and Akt via phosphorylation was determined by Western blotting, using a monoclonal anti-phospho-ERK (pERK) and a polyclonal anti-phospho-Akt (pAkt) antibody. Densitometry was performed, using 3 different experimental setups.

Results: Assessing PKC showed that this intracellular signalling pathway does not seem to be involved into ropivacaine-induced AEC protection. pERK levels, however, were significantly increased by 40% in the LPS/ropivacaine group in comparison to the LPS/PBS group ($p < 0.05$). No conclusive data were found for pAkt.

Conclusion: Our study shows for the first time that the anti-inflammatory and cytoprotective effect of ropivacaine might be mediated through phosphorylation of ERK.

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FM 15

Postconditioning with the volatile anaesthetic sevoflurane in an *in vivo* model of LPS-induced lung injury

Stefanie Voigtsberger^{1,2}, Robert A. Lachmann^{1,2}, Anik C. Leutert^{1,2}, Donat R. Spahn¹, Beatrice Beck-Schimmer^{1,2}

¹Institute of Anesthesiology, University Hospital Zurich; ²Institute of Physiology and Zurich Center for Integrative Human Physiology, University of Zurich

Objective: Acute lung injury (ALI) is a common complication in critical ill patients. Several studies suggest that volatile anaesthetics such as sevoflurane provide immunomodulating effects. Prior we could show a significant reduction of inflammatory mediators by postconditioning with sevoflurane *in vitro*¹. The aim of the present study was to determine the immunomodulating effects of sevoflurane in an *in vivo* model of LPS-induced lung injury and to compare it to propofol which is a commonly used intravenous sedative in critical ill patients.

Methods: Rats were anaesthetized, tracheotomized and mechanically ventilated. Lipopolysaccharide (LPS) was administered intratracheally. Propofol was infused intravenously to maintain anaesthesia. Two hours after the onset of the ALI general anaesthesia was continued with either sevoflurane or propofol for further 4 hours. Arterial blood gases were measured every 2 hours. After six hours animals were sacrificed and bronchoalveolar lavage (BAL) was performed. Total cell count, cytokine-induced neutrophil chemoattractant-1 (CINC-1), and monocyte chemoattractant protein-1 (MCP-1) were analysed in BAL fluid. Experiments were repeated six times for every group.

Results: A significant improvement of $\text{PaO}_2/\text{FiO}_2$ was shown with sevoflurane postconditioning (275 ± 47) compared to a sedation with propofol (87 ± 12) [in mm Hg \pm SEM]. Total cell count as a measure of effector cell recruitment with lung destruction was significantly lower in the sevoflurane-LPS group (13.64 ± 2.33) compared to the propofol-LPS group (30.64 ± 3.16) [in $10^6 \text{ ml}^{-1} \pm$ SEM]. Furthermore expression of MCP-1 in BALF was decreased by 53% ($p < 0.05$) and of CINC-1 by 29% by postconditioning with sevoflurane.

Conclusions: Therefore we conclude that anaesthetic post-conditioning with sevoflurane has an immunomodulating organoprotective effect in the respiratory compartment in an *in vivo* model of ALI.

References: Yue T, et al. Eur. Respir J. 2008;31(1):118–25.

FM 16

In vitro investigation on the effect of sevoflurane on active transport of sodium, potassium-adenosine triphosphatase (Na⁺/K⁺-ATPase)

Anik C. Leuter^{1,2}, Stefanie Voigtsberger^{1,2}, Birgit V. Roth Z'graggen², Livia Reyes², Christa Booy², Donat R. Spahn¹, Beatrice Beck-Schimmer^{1,2}
¹Institute of Anesthesiology, University Hospital Zurich; ²Institute of Physiology and Zurich Center for Integrative Human Physiology, University of Zurich

Background: Pulmonary oedema is the hallmark of Adult Respiratory Distress Syndrome (ARDS). Alveolar epithelial type II cells (AECII) play a major role in maintaining the alveolar space fluid free by actively transporting sodium from the alveolar space to the interstitium. Sodium thereby enters alveolar cells through a variety of different pathways, including apical sodium channels, Na⁺-H⁺-antiport, and Na⁺-cotransporters and is extruded at the basolateral membrane by a sodium, potassium-adenosine triphosphatase (Na⁺/K⁺-ATPase) pump. Water follows to maintain isoosmolar conditions. There is significant evidence that fluid clearance is impaired in patients with lung injury [1]. Former studies have shown that volatile anaesthetics like halothane impair activity of Na⁺/K⁺-ATPase and sodium channels [2].

Objective: Aim of our study was to evaluate the activity of Na⁺/K⁺-ATPase in lipopolysaccharide (LPS)-exposed AECII and the effect of the nowadays commonly used volatile anaesthetic sevoflurane.

Methods: Monolayer of AECII were stimulated with 20 µg/ml LPS for 8 hours and co-exposed to either a CO₂/air mixture with sevoflurane 2.2 volume% or to CO₂/air mixture only. Activity of the Na⁺/K⁺-ATPase was assessed by ⁸⁶Rubidium influx studies [3].

Results: First results suggest that LPS decreases activity of the Na⁺/K⁺-ATPase. This effect was completely reversible in the presence of sevoflurane.

Conclusion: Our study disproves most likely the so far valid assumption that volatile anaesthetics have a repressing effect on Na⁺/K⁺-ATPase in AECII. Therefore, application of sevoflurane might be beneficial in the situation of ARDS, improving alveolar space fluid clearance.

References: 1 Garat C, et al. *J Appl Physiol.* 1995;79(6):2021–8. 2 Mollieux S, et al. *Anesthesiology.* 1998;88(6):1606–13. 3 Planes C, et al. *Am J Respir Cell Mol Biol.* 1997;17:508–18.

FM 17

Comparison of Laryngeal Mask Supreme™ and i-gel™ in simulated difficult airway in anesthetized patients

L. Theiler, M. Kleine-Brüggeney, N. Urwyler, C. Luyet, D. Kaiser, R. Greif
 Universitätsklinik für Anästhesie und Schmerztherapie, Inselspital, Bern

Background: The LMA Supreme™ (LMS) and the i-gel™ are both newly developed supraglottic single use airway devices. Both incorporate a drain tube, but the LMS does not enable insertion of a tracheal tube. We evaluated the performance of both devices in a prospective cross-over RCT in a simulated difficult airway scenario using an extrication collar to limit both mouth opening and neck movement.

Methods: With IRB approval and informed consent we studied 37 patients out of 60 patients undergoing elective surgery up to date. Outcomes were insertion time, overall success rate, manipulations required, tidal volume reached, airway leak pressure, ability to pass a gastric catheter, fiberoptic laryngeal view, epiglottic down folding and adverse events.

Results: The extrication collar reduced mouth opening from 46 ± 7 mm to 24 ± 3 mm (p < 0.001). Insertion time was 37.2 ± 9.4 sec. for the LMS vs. 49.7 ± 30.9 sec. for the i-gel (p = 0.019). Overall insertion success for the LMS was 35 and for the i-gel 33 (p = 0.674). The LMS required fewer minor airway manipulations (2 LMS vs. 4 i-gel, p = 0.421). They did not differ in tidal volume with 17cm H₂O pressure limited ventilation (650 ± 134 ml LMS vs. 671 ± 139 ml i-gel, p = 0.445), airway leak pressure (23.2 ± 7.7 cm H₂O LMS vs. 27.3 ± 7.9 cm H₂O i-gel, p = 0.604) and ability to pass a gastric catheter (one failure each). The i-gel enabled better fiberoptic laryngeal view (glottis totally visible 26 i-gel vs. 21 LMS, partially visible 4 i-gel vs. 6 LMS, only epiglottis visible 3 i-gel vs. 7 LMS, no laryngeal structure visible 0 i-gel vs. 1 LMS, p = 0.437) and showed less epiglottic down folding (9 of 35 LMS vs. 2 of 33 i-gel, p = 0.046). No major adverse effects (like severe hypoxemia, dental trauma, sustained sore throat) were encountered.

Conclusions: In our preliminary 37 patients both devices had similar insertion success and clinical performance except a faster insertion time of 12.4 ± 31.5 sec. for the LMS in this simulated difficult airway situation. The clinical significance of this difference remains unknown. The bulkier design of the i-gel made insertion more difficult when mouth opening was reduced by the tight extrication collars. However, once inserted the i-gel performed at least as good as the LMS – at approximately half the price.

FM 18

Role of small GPTases and v 5 Integrin in Pseudomonas aeruginosa-induced increase in lung endothelial permeability

Michael T. Ganter, Jérémie Roux, Jeanine P. Wiener-Kronish, Jean-François Pittet
 University of California, San Francisco, CA

Background, aim of the study: *Pseudomonas aeruginosa* (PA) is an opportunistic pathogen that can cause severe pneumonia associated with flooding of the airspaces with protein-rich edema in critically ill patients. The type III secretion system is a major virulence factor and contributes to dissemination of PA. However, it is still unknown which particular bacterial toxin and which cellular pathways are responsible for the increase in lung endothelial permeability induced by PA.

Methods: All studies were done in bovine pulmonary arterial endothelial cells (ATCC, CCL-209). Three different PA strains, PAO1, PAK and PA103 were used in the study. Single / combined deletion strains of PAK and PA103 permitted analysis of the contribution of each of the four known PA type III exotoxins to endothelial permeability. Transendothelial albumin flux was measured by standard techniques. Rac1 and RhoA activities of endothelial cells were determined using a luminescence-based G-LISA kit. β-catenin and actin stress fibers were visualized by immunofluorescence. Immunoprecipitation was used to detect phospho-β-catenin. Cell viability was measured by the Alamar Blue assay. Recombinant adenovirus expressing human Hsp72 was used to overexpress Hsp72.

Results: The results showed that ExoS and ExoT, two of the four known PA type III cytotoxins were primarily responsible for bacterium-induced increases in protein permeability across the lung endothelium via an inhibition of Rac1 and an activation of the RhoA signaling pathway. In addition, inhibition of the αvβ5 integrin, a central regulator of lung vascular permeability, prevented these PA-mediated increases in albumin flux due to endothelial permeability. Finally, prior activation of the stress protein response or adenoviral gene transfer of the inducible Hsp72 inhibited the damaging effects of PA on the barrier function of lung endothelium.

Conclusions: We specifically found that ExoS and ExoT, type III cytotoxins of PA, are responsible for the increase in protein permeability across the lung endothelium induced by this bacterium via RhoA- and αvβ5 integrin-dependent mechanisms. Furthermore, prior activation of the stress protein response blocked the effect of PA on the barrier function of lung endothelium by preventing the activation of the small GTPase RhoA.

FM 19

Real-time visualization of ultrasound-guided retrobulbar blockade: a CT-controlled cadaver study

C. Luyet, U. Eichenberger, B. Moriggl, R. Greif
 Universitätsklinik für Anästhesiologie und Schmerztherapie, Inselspital Bern

Introduction: Retrobulbar regional anesthesia, first described in 1961 enables eye surgery in awake patients. The standard blind technique introduces the needle laterally of the eye globe into the muscle cone behind the eye followed by injection of local anesthetic. Severe complications of this blind technique such as perforations of the globe, optic nerve damage and intravascular injection are described in the literature. Furthermore, more than 10% of all peripheral nerve blocks described in the American Society of Anesthesiologists Closed Claims Database are retrobulbar blocks. Ultrasound guided needle introduction and direct visualization of the spread of local anesthetic may improve quality and safety of retrobulbar anesthesia. Therefore we developed a new ultrasound guided technique using human cadavers.

Method: In total, 20 blocks in 10 embalmed human cadavers were performed. After restoring the normal intraocular pressure by injecting alcohol into the globe, a transverse sonogram showing the eyeball as well as the optic nerve was obtained. Using a small curved array transducer and a long axis approach a 22G short bevel needle was introduced with ultrasound guidance. Under vision the needle passed the equator of the eye globe and was introduced until the needle tip was seen 2 mm away from the optic nerve. At this point 2 mL of diluted contrast dye was injected as a substitute for local anesthetic. Immediately after the injection, the spread of the contrast dye was documented by means of CT-scans.

Results: The CT-scans showed the distribution of the contrast dye in the muscle cone and behind the posterior sclera in all except of one case which had a very difficult needle placement. No contrast dye was found inside the optic nerve or inside the eyeball. In one case there was an additional trace of contrast dye behind the orbit.

Conclusion: The CT controlled distribution of contrast showed that our new ultrasound guided technique for retrobulbar block using only 2 mL volume is accurate. Our ultrasound guided technique has the

potential to improve safety and efficacy of the procedure by direct visualization of the needle placement and the distribution of the injected fluid. Furthermore, the precise injection near the optical nerve could decrease the needed amount of local anesthetic reducing related local anesthetic complications.

FM 20

Randomized controlled comparison of volumes using an ED₉₅ nerve dimension based method for ultrasound-guided axillary plexus block

U. Eichenberger¹, G. Huber², P. Marhofer², S. Stöckli¹, P. Willmann¹, S. Kettner², M. Curatolo¹, S. Kapra²

¹Dep. of Anaesthesiology and Pain Therapy, University of Bern, Inselspital, Bern, Switzerland; ²Dep. of Anaesthesia and Intensive Care Medicine, Medical University of Vienna, Vienna, Austria

Introduction: Axillary plexus blockade is the most popular regional anaesthetic technique for the upper limb. Usually up to 50 ml of local anaesthetic (LA) are used. Previous studies showed a significant reduction of LA by using ultrasound-guidance. With this study we tested extreme low volumes of LA using ultrasound-guidance.

Methods: A prospective, randomized and double blinded crossover study was performed in 10 volunteers. Following ultrasound measurement and summation of the cross section areas of the radial, median and ulnar nerves in the axilla, two volumes of 1% mepivacaine were applied on two different days. Volume calculation: "high volume" (HV): 0.25 ml/mm²; "low volume" (LV): 0.11 ml/mm². HV reflects our daily clinical practice; LV reflects the ED₉₅ volume for a peripheral nerve evaluated in a preceding study¹. A Pinprick test in comparison with the contra lateral extremity was used to evaluate sensory onset time, block success (= anaesthesia within 20 min) and duration of sensory block for each targeted nerve.

Results: HV: 9.4–20.3 ml (mean: 14.8 ml); LV 2.7–5.5 ml (mean: 4.0 ml). Success rates for each of the single nerves were 97% (29/30) with HV and 80% (24/30) with LV, respectively. 4 of the 6 failures with LV were caused by insufficient block of the median nerve. There were no statistical significant differences between HV and LV for mean sensory onset times and mean duration of block except for the median nerve.

Conclusion: Successful ultrasound-guided axillary plexus block is possible using extreme low volumes of LA. Our LV success rate of 80% is comparable with results in the literature using none ultrasound-guided techniques and more than 10 times more volume of LA. Further studies are necessary to determine the minimal volume of LA needed to achieve a near 100% success rate using ultrasound-guidance.

Reference: 1. Eichenberger U, et al. Minimal local anaesthetic volume for peripheral nerve block: a new ultrasound-guided nerve dimension based method. *Reg Anesth Pain Med*; in press.

FM 21

Ultrasound guided popliteal lateral sciatic nerve block. A study on cadavers comparing three different injection techniques

Faust A¹, Benkhadra M², Fournier R¹, Feigl G³

¹Département APSI; Service of Anesthésiologie; Hôpitaux Universitaires de Genève; ²Département d'Anesthésiologie et Soins Intensifs, Centre Hospitalier Universitaire, le Bocage, Dijon, France; ³Anatomisches Institut der Karl-Franzens-Universität, Graz, Austria

Introduction: Ultrasound imaging has been shown to be a valuable technique to localize the sciatic nerve (SN) in the popliteal fossa (1) and to guide block needle placement (2). This study compares the distribution of a colored solution on nerves structures in the popliteal fossa, following three different injection techniques.

Materials and methods: 40 cadavers preserved according to Thiel's embalming method have been used. Using lateral approach, 80 popliteal regions were randomly assigned to 3 groups. Under ultrasonic imaging control, 20 mL of a mixture of ropivacaine and methylene was injected at a point proximal to the bifurcation of the tibialis and peroneal components either on the anterior aspect of SN (group AI) or on the posterior aspect of the SN (group PI) or 10 mL on the anterior and 10 mL on the posterior aspect of the SN (A/PI). Quality of images was defined as 1 for bad, 2 for acceptable and 3 for good visibility. Fine dissection of each injected popliteal region was then performed and colorations the SN, the common peroneal nerve (CPN) and the tibialis nerve (TN) were noted.

Results: Injection success rate was not different between the 3 groups (65% vs 63% vs 69%; p = 0.4 for AI, PI and A/PI respectively). There was a trend for a better injection success rate when the visibility was better (56% vs 65% vs 76%; for visibility = 1, 2 and 3 respectively).

Discussion: All the three techniques were equivalent in terms of success. The mean success block rate for the three techniques is 68%. This rate seems to be dependent on the quality of the nervous

structures visibility. It could be probably enhanced if we consider that in clinical practice local anesthetic distribution around the nerve can be influenced on real time by needle readjustments, which was not the case in this study. Thiel's embalming technique is known to provide spectacular colors and flexibility like living conditions (3). We describe an original application of this method for teaching ultrasound guided nerve block.

References: 1) Sites, et al. *Reg Anesth Pain Med* 2004;29:413–6. 2) Sinha, et al. *Reg Anesth Pain Med* 2004;29:130–4. 3) Benkhadra, et al. *Anesth Analg* 2008;106:182–5.

FM 22

Ultrasound-guided paravertebral puncture and catheter insertion: an imaging study in human cadavers

C. Luyet, U. Eichenberger, R. Greif, B. Moriggl
Universitätsklinik für Anästhesiologie und Schmerztherapie, Inselspital Bern

Introduction: Paravertebral regional anesthesia used to treat pain after thoracic, cardiac, breast and upper abdominal surgery avoids epidural space puncture to reduce possible thoracic medulla injury. In 1979 Eason and Wyatt¹ described the still used technically challenging landmark approach. The loss of resistance by passing through the very small superior costo-transverse ligament is often missed while the risk of pleural puncture remains. To avoid these difficulties we intended to develop an ultrasound-guided puncture and catheter placement technique to access the paravertebral space.

Methods: We performed 20 punctures and catheter placements on both sides of the vertebral column in 10 embalmed human cadavers. After anatomical studies in cadavers we aimed for a sonographic view showing the pleura as well as the superior costotransverse ligament. This could be obtained using a curved array transducer placed obliquely between TH4 and TH8. A 18G Tuohy needle was inserted in the long axis related to the transducer. The needle tip was advanced under view through the superior costotransverse ligament into the paravertebral space. Injection of 10 ml normal saline distended the space and enabled 5 cm of catheter insertion. After injection of 10 mL of contrast dye through the catheter, the spread of the dye was documented by means of 5 mm transverse CT scans.

Results: The CT-scan revealed a correct paravertebral spread of contrast in 11 of the 20 cases (55%). Out of the remaining 9 cases 1 catheter was found in the pleural space (5%), 6 catheters were found epidural (30%) and in 2 cases (10%) we detected prevertebral spread of contrast dye.

Conclusion: Ultrasound guidance kept the needle tip away from the pleura and the epidural space and allowed to reach the paravertebral space without problems, but the insertion of the catheter remained technically difficult. Furthermore in 45% of the cases, if advanced more than 5 cm, the catheter migrated not to the expected place (to the epidural space, pleural or anterior towards the mediastinum). Further studies are needed to optimize that approach and to observe the final placement of catheters introduced with the standard technique.

Reference: 1 Eason, M.J. and R. Wyatt. Paravertebral thoracic block-a reappraisal. *Anaesthesia*. 1979;34(7):638–42.

FM 23

High incidence of non-routine events during standard anesthesia inductions: A prospective analysis of synchronized video and vital parameter recordings.

J. Wacker¹, B. Kleeb¹, B. Künzle², E. Leisinger¹, A. Kobler¹, M. Kolbe², T. Manser², M. Burtcher², D.R. Spahn¹, G. Grote²
¹Institute of Anesthesiology, University Hospital Zurich; ²Work and Organizational Psychology, Swiss Federal Institute of Technology ETH, Zurich

Background: Non-routine events (NRE) are defined as "any event that is perceived by clinicians or skilled observers to deviate from ideal care" for a specific patient in a specific clinical situation [1]. In contrast to investigation of adverse events, NRE analysis is thought to be less affected by biases and more likely to identify latent conditions promoting active errors and patient injury [2]. NREs occurred in approximately 30% of cases in retrospective studies with mixed complexity [1–3]. To estimate the value of advanced NRE analysis, we aimed at prospectively determining incidence and types of NRE in routine anesthesia inductions in a tertiary teaching hospital operating suite.

Methods: We recorded teams during general anesthesia inductions with tracheal intubation (ASA I/II) for minor to intermediate surgical

procedures. Combined cases with additional nerve block were excluded. Synchronized recordings of the anesthesia team (video), vital parameter, and ventilator data were obtained using a mobile setup. NREs were identified by experienced staff anesthesiologists using all three synchronized data sets in DVD format.

Results: In 25 anesthesia inductions, we found overall 238 NRE (minimum 3, maximum 16, mean 9.4, SD 3.8 per case). A basic typology was derived from main characteristic of events: Cardiovascular response 57 events (24%); ventilation 37 (16%), drug administration 36 (15%); airway management 23 (10%); infection control 15 (6%); patient comfort 15 (6%), depth of anesthesia 10 (4%), others 43 (19%).

Conclusions: Unlike results from retrospective studies, our prospective analysis detected high incidence of NREs even in low risk cases. NRE analysis may facilitate process analysis and improve patient safety in anesthesia practice.

References: 1. Weinger MB et al, J Biomed Inform. 2003;36:106–19. 2. Oken, et al. Anesthesiology. 2007;107:909–22. 3. Boelle PY, et al. Qual Health Care. 2000;9:203–9.

FM 24

Evaluation of the blood-saving Kaolin i-STAT ACT technique in paediatric cardiac anaesthesia

Ulmer F², Bettex D¹, Baulig W¹, Bürki C¹, Weiss M¹
¹Department of Paediatrics and ²Anaesthesia, University Children's Hospital Zurich, Switzerland

Objective: To compare activated clotting time (ACT) values measured by the blood-saving Kaolin i-STAT ACT technique (2 x 45 µl) with those obtained from the widely used Medtronic ACT II device (2 x 0.5 ml) in children undergoing cardiac surgery (1).

Methods: In a prospective, observational clinical study, ACT values obtained from the i-STAT device (Kaolin) were compared with the Medtronic ACT II device in paediatric cardiac surgical patients. Samples were taken from the central venous catheter according to the clinical protocol and were pair-analyzed in both techniques before, during and after heparinisation for cardiopulmonary bypass. Data were compared using simple regression analysis, Bland-Altman analysis and student T-Test (p <0.05).

Results: 26 children aged from 0.01 to 10.2 yrs (median 0.6 yrs) undergoing cardiac surgery were studied. Values are Pearson's r (n paired values), Bias/Precision.

Conclusion: Our preliminary data demonstrates that intra-rater reliability was similar in both techniques. However activated clotting time values obtained from the Kaolin i-STAT ACT did not agree with those obtained with the Medtronic ACT II. Further data are required to elucidate factors explaining the disagreement between the two techniques.

References: 1) Hug MI, et al. Acta Anaesthesiol Scand. 2004;48: 211–7.

	Medtronic Channel 1 vs 2	i-STAT Analyzer Device 1 vs 2	Medtronic versus i-STAT (mean values)
All Measurements	0.997 (113) –2.0/53.1 sec	0.998 (108) 0.8/49.4 sec	0.924 (134) 10.7/259.0 sec
Before CPB	0.995 (42) 0/44.9 sec	0.994 (41) 4.8/60.3 sec	0.873 (50) –25.4/257.4 sec
During CPB	0.982 (41) –5.9/73.6 sec	0.993 (40) 2.9/52.5 sec	0.711 (52) –19.0/325.2 sec
After CPB	0.951 (30) 0.7/15.0 sec	0.990 (27) 0.3/4.7 sec	0.782 (33) 24.4/30.0 sec**

** p <0.01

Monocyte chemoattractant protein 1 (MCP-1) induces pain related behavior and microglial activation in mice

M.R. Suter^{1,2}, Gao Y.J.¹, R.R. Ji¹

¹Pain Research Center, Department of Anesthesiology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115; ²Anesthesiology Pain Research Group, Anesthesiology Department, University Hospital Center and University of Lausanne, CH-1011 Lausanne, Switzerland

Background: Monocyte chemoattractant protein 1 (MCP1 or CCL2) is one of the most studied chemokines in the pain field. Microglia is activated after nerve injury and expresses the receptor for MCP1 (CCR2).

Methods: We studied the effect of intrathecal MCP1 injection (100 ng/day over 3 days) on pain related behavior (paw withdrawal to heat and mechanical stimulus) and on microglial activation (immunofluorescence) in mice. We measured MCP1 expression in the spinal cord after spinal nerve ligation (SNL) with ELISA and immunofluorescence.

Results: MCP1 injection induced pain related behavior, mechanical allodynia and heat hyperalgesia from day 1 to 3. It also produced mild but significant ($p < 0.05$) microglial activation as shown by increase in Iba1 staining (microglial marker). We observed an upregulation of MCP1 after nerve injury peaking at day 3 post SNL. MCP1 colocalizes with an astrocytic marker.

Conclusion: MCP1 is upregulated after nerve injury in spinal cord astrocytes. MCP1 injection activates microglia and induces pain related behavior. Whether this is an example of astrocyte-microglia interaction after nerve injury still need to be examined.

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Furthermore, vector-mediated transduction is a promising gene therapy for intractable pain. We have characterized gene transfer in the DRG using recombinant adeno-associated adenovirus type 6 (rAAV2/6) through five different routes of delivery. rAAV2/6 were generated that drive expression of green fluorescent protein (GFP) under control of the cytomegalovirus immediate-early promoter. The vector was injected into six-week-old C57Bl/6 mice in i) the triceps surae muscle, ii) the sciatic nerve, iii) subcutaneously in the hindpaw, iv) intravenously via the tail vein and v) intrathecally. GFP expression was characterized in DRG and spinal cord three weeks following injection using anatomical and molecular markers. We observed GFP-positive cells in the DRG following all administration routes. Highest GFP expression was achieved by injection into the sciatic nerve ($28.1 \pm 3.1\%$ of the total number of L4 DRG neurons) compared to subcutaneous ($3.5 \pm 1.7\%$) and intramuscular injections ($1.6 \pm 0.64\%$). More than ninety percent of GFP positive cells were less than $500 \mu\text{m}^2$ (corresponding to nociceptors) with only three percent larger than $500 \mu\text{m}^2$ (corresponding to mechano- and proprioceptive sensory neurons). These small cells colocalized with transient receptor potential vanilloid type 1 (TRPV1), Substance P and isolectin B4. This transduction pattern was consistent in the spinal cord with GFP afferent fibers predominantly in lamina I and II. Interestingly, intravenous delivery of rAAV2/6 resulted in transduction of predominantly large non-nociceptive neurons ($>500 \mu\text{m}^2$) with corresponding projections into the deeper lamina of the spinal cord dorsal horn. We demonstrate that delivery route is a major factor influencing efficacy and specificity of nociceptive cell transduction. We are currently analyzing rAAV2/6 delivery into the subarachnoid space via intrathecal administration.

Continuous epicapsular ropivacaine 0.3% infusion after minimal invasive hip replacement. A prospective, randomised, double-blind study comparing the PAINfusor with morphine-PCA

J. Aguirre¹, C. Neudoerfer¹, H. Jutzi¹, C. Schultz¹, F. Kalberer², C. Dora², A. Borgeat¹

¹Department of Anesthesiology, University Clinic Balgrist, Zürich; ²Department of Orthopedics, University Clinic Balgrist, Zürich

Background and aims: The analgesic efficacy of continuous wound infiltration with ropivacaine after minimal invasive hip surgery and its safety are unknown.

Methods: After approval by the ethics committee and written informed consent 72 consecutive patients (ASA I-III) for elective minimal invasive hip replacement were prospectively randomized to both groups. Anesthesia management (spinal anesthesia and sedation) were standardized. The epicapsular placement of the 15 cm PAINfusor fenestrated catheter (Baxter) was performed by the surgeon. 20 ml ropivacaine 0.3% (R-group) or NaCl 0.9% (P-group) were applied into the wound as bolus before its closing. Thereafter, continuous infusion of ropivacaine 0.3% or placebo according to the study group were continuously infused at 8 ml/h for 48 hours after surgery by the elastomeric membrane balloon of 2 infusor pumps (Baxter LV10, 300 ml). A morphine PCA and standardized rescue pain medication were offered to all patients. Morphine consumption, pain at rest and with motion, total and unbound ropivacaine plasma concentration, PONV, sedation, mental status and hospitalization time were recorded. A follow up was performed 12 weeks postoperatively.

Results (preliminary data with 30 patients): Demographic and surgical data were similar in both groups. The total morphine consumption and the pain scores with motion were lower in the R-group ($p < 0.05$). No difference was found in the other parameters. After 12 weeks there was no difference in hip pain but a slight reduction of wound pain in the R-group ($p < 0.05$). Total and unbound ropivacaine plasma concentrations were below toxic levels in the R-group.

Conclusions: Continuous wound infusion is a save and effective technique for postoperative analgesia after minimal invasive hip replacement.

P 2

Peripheral nerve injury is associated with a reorganization of the central terminals of primary sensory neurons expressing parvalbumin

A. Axis, A.T. Beggah, T. Berta, A. Friese, M. Pertin, S. Arber, C.J. Woolf, I. Decosterd

CHUV, UNIL, Biozentrum, Harvard Medical School

Background: Peripheral nerve injury is associated with structural reorganization of sensory afferent fibers in the central nervous system that may explain the development of allodynia in neuropathic pain syndromes. The dorsal horn of the spinal cord (DH) receives central axons of the primary afferents and usually myelinated fibers are absent of the lamina II, the major site of projection of nociceptors. The aim of this study was to investigate the remodeling of the central terminals of Parvalbumin (PV) expressing sensory neurons (myelinated A fibers) in superficial lamina of DH after peripheral nerve injury.

Methods: PV central fibers in the spinal cord are visualized in double transgenic mice ($Tau^{mGFP/+}PV^{Cre/+}$) because they are engineered to express a fluorescent membrane-linked-eGFP protein (mGFP) restricted to PV⁺ neurons. Central fibers were quantified in $Tau^{mGFP/+}PV^{Cre/+}$ mice spinal sections 1, 3 and 6 weeks after sciatic nerve axotomy and compared to sham operated animals. GFP positive fibers were traced in Lamina I + IIouter (distinguished by PKC gamma staining) and using NeuroLucida software by an observer unaware of the treatment (axotomy or sham). RESULTS: The number of GFP positive fibers was significantly increased in Lamina I+IIo 3 and 6 weeks after axotomy compared to the sham operated group or contralateral side ($p < 0.01$, $n = 4$ in each group). Similarly, total fiber length, number of varicosities, endings and nodes were different between axotomy and sham/contralateral injury side ($p < 0.01$).

Conclusion: Our data confirm the sprouting of large myelinated afferent terminals into the area (lamina I and IIo) normally occupied by nociceptor terminals. Taken together with previous anatomical and electrophysiological studies, our results demonstrate a structural rewiring in the spinal cord that may contribute to allodynia in neuropathic pain.

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Neuropathic pain: Gene therapy as a tool to transduce nociceptors

Marie Pertin¹, Chris Towne², Temugin Berta¹, Ahmed Beggah¹, Patrick Aebischer², Isabelle Decosterd¹

¹University Hospital Center (CHUV) and University of Lausanne (UNIL); ²Brain Mind Institut, EPFL

Manipulating gene expression using viral vectors in dorsal root ganglion (DRG) is an alternative to pharmacological and transgenic animal approaches for the investigation of gene function in pain.

P 3

Nerve conduction blockade differentially affects microglial activation after peripheral nerve injury

M.R. Suter^{1,2}, I. Decosterd^{2,3}, R.R. Ji¹

¹Pain Research Center, Department of Anesthesiology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115; ²Anesthesiology Pain Research Group, Anesthesiology Department, University Hospital Center and University of Lausanne CH-1011 Lausanne, Switzerland; ³Department of Cell Biology and Morphology (DBCM), Faculty of Biology and Medicine, Lausanne University, CH-1005 Lausanne, Switzerland

Background: Microglial activation participates in the development of chronic pain following nerve injury. This could explain why our current

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therapies targeting neurons often fail. Microglial activation encompasses upregulation of cellular markers, change in intracellular pathways, altered morphology, or cell proliferation. We hypothesized that some of these changes are dependant on peripheral nerve injury induced activity and could be prevented by a peripheral blockade with local anesthetics

Method: In the rat spared nerve injury (SNI) model, we used bupivacaine-loaded microspheres to induce a proximal long term conduction blockade of the sciatic nerve. We then analyzed different features of microglial activation at 1 or 3 days after SNI.

Result: After SNI, we could see an upregulation of Iba1 (microglial marker) and phosphorylation of ERK mitogen activated kinase (pERK) as well as microglial proliferation. Nerve conduction blockade prevented the early (1 day), but not the late (3 day) Iba1 and pERK increase ($p < 0.05$). Post injury microglial proliferation was not influenced by the block.

Conclusion: We here show that blocking peripheral nerve activity can modify some features of microglial activation, but other triggers need also to be targeted to completely prevent it.

The analgesic properties of propofol and its solvent: a double-blind, randomized crossover trial

Bandschapp O¹, Filitz J², Urwyler A¹, Koppert W², Ruppen W¹
¹Anästhesie, Universitätsspital Basel, Schweiz; ²Anästhesie, Universitätsspital Erlangen, Deutschland

Introduction: Propofol has long been considered a non-analgesic. However, previous work of one of the authors (unpublished results) found anesthesia with propofol to be associated with less postoperative pain and morphine consumption, when compared to anesthesia with isoflurane; while the group treated with a combination of isoflurane and intralipid showed the highest pain scores. Due to different endpoints of the former study and therefore inadequate design, the current study was required to determine possible modulatory effects of propofol on pain perception and the potential role of its solvent.

Methods: Fourteen healthy volunteers were included in this randomized, double-blind, placebo-controlled crossover study. Transcutaneous electrical stimulation (48.2 ± 26.3 mA) induced spontaneous acute pain (numerical rating scale (NRS) = 6 on a scale of 0 to 10) and stable areas of hyperalgesia and allodynia. Pain intensities and areas of hyperalgesia were assessed regularly before, during, and after a 45 min target-controlled infusion ($2 \mu\text{g/ml}$) of propofol, its solvent intralipid 10%, and saline, respectively.

Results: Propofol significantly decreased pain scores and areas of hyperalgesia and allodynia, during administration, as compared to intralipid 10% and saline ($p < 0.01$). These differences became negligible as soon as the infusion was halted. There were no differences between the three groups in the evolution of NRS scores, or areas of hyperalgesia or allodynia during the period following infusion.

Conclusion: Propofol showed analgesic properties during its administration. This effect, however, was not extended to the period following its infusion in our pain model. Intralipid was free of pain-modulatory action and pro-algic effects in our experiments.

Effects of low-dose lidocaine on peripheral nerve excitability measured with threshold tracking in human and rat

Konrad Maurer¹, Hugh Bostock², Paul Nand³, Martin Koltzenburg^{1,2}
¹UCL Institute of Child Health; ²UCL Institute of Neurology, UCL, London, United Kingdom; ³Pain Management Centre, National Hospital

Aim of investigation: To investigate the excitability changes induced by low-dose lidocaine on peripheral sensory nerve in humans and in a rat in-vitro model of the saphenous nerve.

Methods: 11 patients who received an intravenous bolus of lidocaine (3 mg/kg body weight over 1 hour) as a therapy for a variety of pain conditions were enrolled in the study. We used a computerized threshold tracking program (QTRAC, ©Institute of Neurology, London, UK) to investigate multiple nerve excitability parameters. Strength-duration time constant, recovery cycle and threshold electrotonus were recorded from the median nerve. Using the same threshold tracking protocol, the effects of lidocaine at concentrations ranging between 5 and 150 μM were measured in a rat in-vitro model of the saphenous nerve.

Results: In patients, intravenous lidocaine induced a significantly increased rheobase, a significantly longer relative refractory period and a shift of the stimulus-response relationship to higher currents. In the rat in-vitro model, lidocaine had a significant impact on all

measured parameters in a dose-dependent manner. This effect was strongest on increasing the thresholds during depolarizing electrotonus, followed by reducing superexcitability, increasing relative refractory period, increasing subexcitability and shortening strength-duration time constant.

Conclusions: The method of threshold tracking provides a tool to measure the effects of low-dose lidocaine in humans. In the rat in-vitro model, the same method reveals blocking of persistent sodium channels as well as transient sodium channels induced by lidocaine concentrations as low as 10 μM .

Is it possible to identify muscles as primary source of pain by intramuscular injection of ropivacaine?

R. Herren Gerber¹, Hongling Nie², Th. Graven-Nielsen², L. Arendt-Nielsen², M. Curatolo¹
¹Universitätsklinik für Anästhesiologie und Schmerztherapie, Inselspital Bern; ²Center for Sensory-Motor Interaction, Aalborg University, Denmark

Background: Muscle pain is commonly observed in patients with cervical and low back pain. However, it is unknown whether muscles are the primary source of pain or if they represent a referred pain area. The origin of pain in a referred pain area is not that area itself, but another anatomic structure such as a joint. To date, there is no validated test for the diagnosis of primary muscle pain.

Objectives: In order to explore the potential usefulness of local anesthetic injections for the diagnosis of primary muscle pain, we tested the hypothesis that muscle pain, as induced experimentally in healthy volunteers by Nerve Growth Factor (NGF), can be abolished by intramuscular injection of ropivacaine.

Methods: NGF was infiltrated in the left and right supraspinatus muscle of 11 healthy subjects. 24 hours after injection of NGF pain was measured on a visual analog scale (VAS) for each side separately. The VAS measurements were repeated 30 min after ultrasound-guided injection of ropivacaine 0.25% or saline into the left or right supraspinatus muscle in a randomized double-blind manner. In a preliminary analysis, VAS changes after saline and ropivacaine injections were evaluated.

Results: Mean (SD) of VAS before and after injection of saline was 2.9 (2.1) and 4.1 (2.3) respectively. Mean (SD) of VAS before and after injection of ropivacaine was 3.0 (2.1) and 3.0 (1.9), respectively.

Conclusions: Muscle pain induced by injection of NGF is not abolished by local anesthetic infiltration of the muscle. This finding questions the validity of intramuscular injections of local anesthetics for the diagnosis of primary muscle pain.

Tolerance of laryngoscopy isoboles as reference for alfentanil and propofol dosing in gynecologic surgery

M. Luginbuehl, D. Kaiser, V. Hartwich and. P.M. Schumacher, M.Sc., Ph.D
 Universitätsklinik für Anästhesiologie Inselspital, Bern

Background: In a two-dimensional anesthesia drug display (ADD) relating the predicted effect site concentrations (Ce) of hypnotics and opioids, isoboles representing the probability of tolerating laryngoscopy (pTOL) and of tolerating shake and shout (pTOSS) [1, 2] are used as reference. The pTOL and pTOSS have been computed for propofol and remifentanyl [2]. We determined the pTOL values at skin incision and during surgery from data of a previous study [3].

Methods: We re-evaluated the dosing history of 69 patients anesthetized with propofol and fentanyl for gynecologic surgery. For each patient the plasma propofol and fentanyl concentrations at skin incision and the median plasma concentrations during surgery and the corresponding pTOL values were computed assuming a fentanyl/remifentanyl potency ratio of 6/10 [4]. The mean (SD) plasma concentrations and pTOL values during surgery were compared between patients with laparotomies, breast and endoscopic gynecologic surgery using one-way ANOVA. Numbers are mean (SD)

Results:

		Laparotomy	Breast surgery	Laparoscopy	P
Incision	Propofol Cp $\mu\text{g/ml}$	3.2(1.0)	2.7(0.9)	3.0(0.6)	0.17
	Fentanyl Cp ng/ml	1.9(0.9)	1.5(0.5)	1.7(0.5)	0.16
	pTOL	0.63(0.3)	0.42(0.3)	0.6(0.23)	0.33
Surgery	Propofol Cp $\mu\text{g/ml}$	3.1(0.2)	2.7(0.6)	3.0(0.7)	0.15
	Fentanyl Cp ng/ml	1.6(0.3)	1.2(0.2)	1.4(0.3)	0.01
	pTOL	0.5(0.1)	0.3(0.2)	0.4(0.2)	0.01

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Conclusion: The pTOL values computed from combinations of propofol and fentanyl in gynaecologic surgery were between 0.3 and 0.7.

References: [1] Schumacher et al. *Anesthesiology*. 2004;101:A504, [2] Bouillon et al. *Anesthesiology* 2004;100:1353–72, [3] Luginbühl et al. *Acta anaesth scand* 2003;47:167–73, [4] Gambus et al. *Anesthesiology*, 1995;83:747–56.

Tolerance of laryngoscopy isoboles as reference for alfentanil and propofol dosing in orthopedic surgery

M. Luginbuehl, M. Baechtold, V. Hartwich, T.W. Bouillon and P.M. Schumacher, M.Sc., Ph.D.

Background: In a two-dimensional anesthesia drug display (ADD) relating the predicted effect site concentrations (Ce) of hypnotics and opioids, isoboles representing the probability of tolerating laryngoscopy (pTOL) and of tolerating shake and shout (pTOSS) [1, 2] are used as reference. We determined the pTOL values at intubation, incision and during surgery.

Methods: After IRB approval and written informed consent 40 patients scheduled for major hip or low back surgery were anesthetized with a Propofol TCI and Alfentanil (boli of 0.5–1.0 mg) aiming at minimizing hemodynamic variability. From the predicted drug concentrations pTOL values were calculated. The values were compared between subjects with MAP increase after intubation and incision < or ≥15%.

Results: The mean (SD) pTOL computed from the predicted Ce of propofol and alfentanil at intubation, skin incision and during surgery were 0.91 (0.12), 0.74 (0.2) and 0.75 (0.15) respectively.

	MAP <15%	MAP 015%	P
Intubation, pTOL, mean(SD)	0.94(0.06)	0.86(0.16)	0.055
Intubation, Ce Alfent. ng/ml	226(62)	166(51)	0.003
Intubation CePropofol µg/ml	4.9 (1.0)	4.8 (1.3)	0.796
Incision, pTOL, mean(SD)	0.80 (0.18)	0.55(0.18)	<0.001
Incision, CeAlfent ng/ml	205(70)	145(47)	0.029
Incision, CePropofol mg/ml	3.3(0.9)	2.7(0.4)	0.031

Conclusion: To avoid hemodynamic responses to intubation and incision propofol and alfentanil need to be titrated to a pTol of 95% and 80% respectively.

References: [1] Schumacher et al. *Anesthesiology*. 2004;101:A504, [2] Bouillon et al. *Anesthesiology* 2004;100:1353–72.

Renal function during the perioperative period of liver transplantation: study in 30 consecutive patients

Eduardo Schiffer, Marc Beaussier, Claude-Eric Klopfenstein, Catherine Pastor
Division d'Anesthésiologie, University Hospitals of Geneva, Geneva, Switzerland

Renal dysfunction is an important complication of end-stage liver disease and is characterized by sodium retention and impaired free-water excretion. During liver transplantation (LT), the anhepatic phase is the key event for anesthesiologist as neurohumoral and hemodynamic homeostasis are modified with possible consequences on renal function. To evaluate the consequences of LT on renal function during the perioperative period in 30 consecutive patients who had LT at our institution.

The study protocol was approved by our institutional ethics committee and 30 patients (25 males; 5 females), median age 56 [23–65] were prospectively included after written informed consent. Hemodynamic assessment and blood sampling were performed one hour after anesthesia induction, during the anhepatic phase, and 2 and 24 hours after liver reperfusion. Six months later, patients were reassessed for liver and renal function.

Hemodynamic parameters and renal function are shown in table.

	Pre anhepatic phase	Anhepatic phase	2H after reperfusion	24H after reperfusion	Follow-up at 6 months	P-value
Cardiac Index	4.0 ± 1.2	2.5 ± 0.8	4.6 ± 1.4	4.2 ± 0.7		0.02
SVRI	1577 ± 666	2400 ± 954	1145 ± 437	1548 ± 378		0.03
PVRI	123 ± 59	182 ± 90	141 ± 71	144 ± 82		0.04
SvO ₂	89 ± 12	82 ± 10	88 ± 13	81 ± 15		NS
Serum lactate	1.4 ± 0.7	2.7 ± 1.1	2.6 ± 1.8	0.9 ± 0.4		0.02
Renin (PRA)	6.9 ± 10.3	18.9 ± 22	9.0 ± 15.0	6.0 ± 10.2		0.03

	Pre anhepatic phase	Anhepatic phase	2H after reperfusion	24H after reperfusion	Follow-up at 6 months	P-value
Adrenalin	1.3 ± 1.1	4.0 ± 3.0	2.3 ± 2.8	0.6 ± 0.6		0.01
Noradrenalin	4.3 ± 2.9	7.9 ± 6.3	5.3 ± 2.8	4.4 ± 3.8		0.04
GFR	96 ± 80	44 ± 47	51 ± 49	84 ± 72	84 ± 40	0.03
Cystatin C	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	1.4 ± 0.5		NS
Fe Na	1.1 ± 1.4	1.1 ± 1.8	1.5 ± 1.5	1.3 ± 1.7	1.0 ± 0.6	NS
Urinary output	62 ± 54	28 ± 33	72 ± 79	65 ± 80	73 ± 16	0.04

Conclusion: The anhepatic phase of LT is characterized by increases in plasma renin activity and sympathetic humoral response resulting in significant decrease of glomerular filtration rate. However, these events did not alter long term renal function.

Course of base excess, lactate concentration and ScvO₂ during repeated prolonged deep propofol sedation in children undergoing proton radiation therapy

Bührer S¹, Frei M¹, Frühauf M¹, Mauch J¹, Feurer R¹, Immoos S¹, Timmermann B², Hug E², Weiss M¹

¹Department of Anaesthesia, University Children's Hospital Zurich, Switzerland, and ²Proton Radiation Center, Paul Scherrer Institut, Villigen, Switzerland

Background: Long-term administration of propofol in children is considered to evoke propofol-infusion syndrome with severe metabolic acidosis, increased level of serum lactate and fall in cardiac output [1–3]. The aim of this study was to evaluate the course of acid base state, serum lactate concentration and SvO₂ in paediatric patients undergoing repeated prolonged deep propofol sedation for proton radiation therapy.

Methods: Sedation was induced with small boluses of propofol until sufficient sedation was obtained for positioning. Deep sedation was maintained for the whole course of CT scanning and proton radiation therapy using continuous propofol infusion (10 mg/kg/h) four to five times a week. Central venous blood was taken weekly immediately after cessation of propofol infusion at the end of the radiation procedure. Blood samples were analysed for base excess, lactate concentration and SO₂. Data are mean ± SD and are analysed using unpaired, two-sided student T-test (p < 0.05).

Results: 36 children aged 2.9 ± 1.0 years and weighing 13.7 ± 2.9 kg were enrolled. They had 29.4 ± 3.3 radiation procedures within 6 to 8 weeks. Mean duration of the 1058 sedation procedures was 59.2 ± 20.8 minutes and total amount of propofol administered per session was 13.4 ± 2.5 mg/kg. No significant changes in individual base excess, lactate concentration and ScvO₂ were observed during the period studied. Weekly summarized base excess, lactate concentration and ScvO₂ did not reveal statistically significant differences between the first and the following assessments.

Conclusion: Based on our data, repeated prolonged deep sedation over several weeks using propofol for induction and maintenance does not cause metabolic acidosis, elevation of lactate concentration or decrease in cardiac output and seems to be safe.

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Detection of oesophageal intubation in children using low-frequency forced oscillation technique

Weiss M¹, Basek P², Straub D², Wildhaber J²

¹Department of Anaesthesia and ²Pulmonology, University Children's Hospital Zurich, Switzerland

Objective: The aim of the present study was to evaluate the ability of low-frequency Forced Oscillation Technique (FOT), allowing for rapid and precise assessment of airway mechanic, to discriminate between tracheal and oesophageal intubation [1, 2].

Methods: In children undergoing general anaesthesia the trachea was intubated first, the high-volume low-pressure tube cuff inflated to 20 cmH₂O cuff pressure and the tube secured by tapes. Oesophageal intubation was performed afterwards with a tracheal tube of the same size and the cuff was also inflated to 20 cmH₂O cuff pressure. Four FOT measurements were performed first at the tracheal tube followed at the oesophageal tube (P_{airway} = 0 mbar). The analysis of complete impedance-spectra (reflection pattern using frequencies in range 0,4–12 Hz) for each mentioned condition was done. Based on resistance, inertance, tissue damping and elastance the mechanic

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properties of trachea versus oesophagus were compared using paired T-test ($p < 0.05$). Data are presented as range (median) or mean \pm SD as appropriate.

Results: 10 children aged from 0.4 to 15.4 years (8.1 years) were investigated.

Parameters	Units	Trachea	Oesophagus	T-test
Resistance	cmH ₂ O \times s \times L ⁻¹	3.4 \pm 2.3	-262.5 \pm 87.7	$p < 0.00001$
Inertance	cmH ₂ O \times s ² \times L ⁻¹	0.06 \pm 0.02	-2.6 \pm 1.2	$p < 0.0001$
Tissue damping	cmH ₂ O \times L ⁻¹	4.3 \pm 6.3	-266.6 \pm 418.2	$p = 0.001$
Elastance	cmH ₂ O \times L ⁻¹	33.1 \pm 21.5	-1375.0 \pm 979.5	$p = 0.07$

Conclusions: Preliminary data demonstrates that low-frequency Forced Oscillation Technique based measurement of resistance and inertance at the tracheal tube has the potential to reliably discriminate between tracheal and oesophageal intubation.

References:

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Effect of late sevoflurane postconditioning on myocardial enzyme kinetics after on pump cardiac surgery – preliminary data

Marc P. Steurer, M.D., Milo Puhan, M.D., Edith R. Schmid, M.D., Donat R. Spahn, M.D., Beatrice Beck-Schimmer, M.D

Institute of Anesthesiology, University Hospital of Zurich, Switzerland

Introduction: Cardiac surgery with the use of extracorporeal circulation is frequently associated with a postoperative elevation of myocardial enzymes as an expression of myocardial injury or even myocardial infarction. The protective effect of preconditioning with volatile anesthetics on preservation of myocardium has been well studied. However, there are very limited data on postconditioning in intensive care units (ICU) after cardiac surgery.

Objectives: The following question was addressed: Does postoperative sedation with Sevoflurane have a positive effect on myocardial enzyme kinetics after on pump cardiac surgery?

Material and method: 38 Patients undergoing on pump cardiac surgery were analyzed: all patients received Propofol as anesthetic during surgery. In the ICU, patients were randomized to be sedated with either Sevoflurane ($n = 17$) or Propofol ($n = 21$). Creatinine kinase (CK and CK-MB), Myoglobin (Mb) and Troponin T (TT) were measured on admission to the ICU (T0), after 4 hours (T1) and in the following morning (T2).

Results: The myocardial enzymes showed no statistically significant difference in the two groups at baseline (T0). Afterwards (T1 and T2) there was a clear trend towards all myocardial markers being lower in the Sevoflurane group. Statistical significance ($p < 0.05$) between the two groups was reached for CK at T2, and for Mb at T1 and T2.

Conclusion: There is emerging evidence that a late postconditioning setting with Sevoflurane results in a better profile of myocardial injury marker kinetics after on pump cardiac surgery.

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Impact of different probe types and probe positions on cardiac output measurement by electrical velocimetry

Woitzek K^{1,2}, Schmitz A¹, Tomaske M², Knirsch W², Kretschmar O², Balmer C², Bauersfeld U², Weiss M²

¹Department of Anaesthesia and ²Cardiology, University Children's Hospital Zurich, Switzerland

Background and purpose: To evaluate whether probe type and probe placement influences cardiac output measurement by electrical velocimetry with the Aesculon® Monitor (Osypka Medical GmbH, Berlin, Germany) in anaesthetized children (1).

Methods: Cardiac output (CO) values measured with two different probe types in 20 children in randomised order on the thoracic (standard position) under steady state haemodynamic conditions. In second group CO values were recorded with the electrodes applied to 3 different positions on the patients' surface (neck versus thoracic (standard), femoral or tibial artery position). A special switch box, built by the manufacturer, allowed changing the measured probe position in quick succession without any manipulations of the probes. Data are compared with linear regression analysis, T-Test and Bland-Altman analysis. Values are median (range) or mean \pm SD.

Results: Data are median (range) or mean \pm SD; * $p < 0.01$; ** $p < 0.005$; *** $p < 0.001$.

	Probe I	Probe II	Standard position	Femoral position	Tibial position
n/Age (yrs)	25 / 9.9 (1.5-16.6)		25 / 11.0 (0.1-20)		
CO-Value [l/min]	4.3 \pm 1.6	3.7 \pm 1.4***	3.9 \pm 1.7	4.5 \pm 1.9*	4.4 \pm 1.8**
R	0.91		-	0.87	0.91
Bias/Precision [l/min]	0.6 l/1.35		-	0.54/1.83	0.49/1.48

Conclusion: Type of probe and position of probe has considerable impact on CO-values determined by electrical velocimetry. Further evaluation of ideal type and placement of probe is required with reference to cardiac output measurement techniques.

References:

- 1 Osypka MJ, Bernstein DP. *AACN Clin Issues.* 1999;10:385–99.
- 2 Tomaske M et al. *Br J Anaesth.* 2008;100:517–20.

P 16

Percutaneous transarterial aortic valve replacement for symptomatic severe aortic stenosis in high-risk patients

Basciani RM¹, Trachsel S¹, Zobrist C¹, Wenaweser P², Windecker S², Eberle B¹

¹University Department of Anesthesiology and Pain Therapy, and ²Cardiology, University Hospital Bern

Background: Percutaneous aortic valve replacement (PAVR) is an alternative therapy option for severe, symptomatic aortic valvular stenosis in selected high-risk patients. We report the anesthesiological management and procedural outcome of our first PAVR series.

Methods: 27 patients (mean age \pm SD: 84 \pm 5; 13 m/14f) presenting with symptomatic (mean NYHA class: 2.7 \pm 1), severe (aortic valve area: 0.6 \pm 0.2 cm²) aortic stenosis at high-risk for surgical valve replacement (logistic EuroSCORE: 27 \pm 16%, STS score 12 \pm 8) underwent PAVR ($n = 23$ CoreValve Revalving™ System; $n = 4$ Edwards-SAPIEN™ valve) between 08.07 and 03.08. Pre-procedural evaluation revealed significant coronary artery disease in 52%, a mean left ventricular ejection fraction of 52 \pm 12%, systolic pulmonary hypertension >60 mm Hg in 33%, previous cardiac surgery in 20%, peripheral arteriopathy in 44%, and renal failure (creatinine >200 μ mol/l) in 11%.

Results: PAVR was performed under general anesthesia in 11/27 (GA), and under local anesthesia with mild systemic sedative/analgesic treatment (MAC) in 16/27. All patients received a radial artery and a pulmonary artery catheter, and 2 transvenous pacers (rapid pacing). Edwards valves were placed under TEE control. Vasopressors were used in 11/11 patients under GA (100%), and 8/16 under MAC (50%). Immediately after PAVR, 23/27 patients were awake, extubated and neurologically normal. One patient (conversion of MAC in GA during CPR) was extubated at postop. day 1 (POD), another at POD 2 (preop. mechanical ventilation). 2/27 patients died during PAVR (LV perforation, severe aortic insufficiency), 1/27 died at POD 13 (RV failure). Mortality at 30 days was 11%. In 25/27 (93%) patients, PAVR was successful (mean transvalvular gradient: pre 50 \pm 12 mm Hg; post 7 \pm 6 mm Hg). Three patients required minor vascular repair. No periprocedural stroke, coronary artery occlusion or pericardial tamponade were observed.

Conclusions: Our first experience of PAVR in selected high-risk elderly patients with severe symptomatic aortic stenosis demonstrates good device success, good hemodynamic results and a very rapid recovery. MAC was associated with stable hemodynamic conditions.

P 17

A combination of propofol and ketamin for patient sedation in percutaneous aortic valve replacement

S. Trachsel, R. Basciani, S. Henle, M. Neumann, C. Zobrist, B. Eberle
Universitätsklinik für Anästhesiologie und Schmerztherapie

Introduction: An increasing number of interventional cardiac procedures are performed faster with less physiologic strain. Therefore monitored anesthesia care (MAC) is getting increasingly popular. Adequate and safe sedation in octogenarians with severe aortic stenosis and high surgical risk is mandatory. Sedation with benzodiazepine – opioid combination is prone for respiratory depression, insufficient control of administration, and effects on hemodynamics may be detrimental in view of, e.g. severe aortic valve stenosis. A mixture of ketamine and propofol anesthesia was used in pediatric patients undergoing cardiac catheterization (1). We report a case series of 12 patients sedated with a combination of ketamin in propofol for PAVR.

Methods: 12 patients scheduled for elective PAVR (Corevalve), without indication for transesophageal echocardiography for valve placement, were equipped with two peripheral venous canulas, an arterial line, two jugular introducer sheaths for temporary transvenous pacing electrodes and pulmonary artery catheter placement. The sedative mixture was prepared as ketamin 0.3% in propofol 1%. The mixture was infused intravenously by a continuous, manually controlled perfusion pump regimen and set from 5 to 10 ml/h. Vital signs, BIS and procedure-related parameters were continuously monitored.

Results: 4 women and 8 men with a mean age of 84 ± 4 years were sedated with the combination of ketamin and propofol. One patient died due to an interventional complication. The median intervention time was 98 (60–210) min. During that time the patients received a mean dose of 3.3 ± 1.3 mcg/kg/min ketamine and 11 ± 4.3 mcg/kg/min propofol. In 6 cases vasoactive support was necessary. Cardiac index did not change before and shortly after valve placement (2.8 vs. 2.8 l/min/m²). Intubation was necessary in one case and ICU admission planned in 5 of the 12 cases.

Conclusion: A combination of ketamine and propofol is useful for sedation of elderly patients for PAVR presenting high surgical and anesthetic risk. BIS is not reliable for sedation depth monitoring because of the ketamine compound.

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P 18

Evaluation of the Glidescope®, the McGrath® and the Airtraq® laryngoscopes in simulated difficult airways: a randomized controlled comparison

Savoldelli GL, Waeber JL, Abegg C, Baeriswyl V, Clergue F, Schiffer E Service d'Anesthésiologie, HUG

Background and goal of study: Few studies have compared the efficacy of recently developed video and optical laryngoscopes. Using a manikin, we compared the Glidescope (GVL), the McGrath (MVL), the Airtraq (AOL) and the Macintosh (MI) laryngoscopes in 3 difficult airway scenarios.

Materials and methods: Sixty anaesthetists were enrolled. After standardized training, they intubated the Laerdal SimMan® with each laryngoscope in 3 different scenarios: 1) Pharyngeal obstruction, 2) Pharyngeal obstruction and cervical rigidity, 3) Tongue Oedema. The sequence of use of the devices was randomized. Outcome measures were: time to intubate (TTI), Modified Cormack-Lehane grades (MCL) and failure rate. Friedmann and Wilcoxon signed rank test were used as appropriate.

Results and discussion: In scenario 1 and 2, TTI for MI and AOL did not differ. Both were faster than MGL and GVL ($p < 0.01$). In scenario 3, TTI were highly different (all $p < 0.001$): Intubation was the fastest with AOL, followed by MGL, GVL, and the MI. Intubation failures occurred with the MI (37%), the GVL (2%) and the AOL (2%). MCL distributions for each scenario and each device are shown in the Table.

	Macintosh MCL (%) I/IIa/ IIb/III/IV	Glidescope MCL (%) I/IIa/IIb	McGrath MCL (%) I/IIa/IIb	Airtraq MCL (%) I/IIa
Scenario 1	25/57/18/0/0	72/28/0 *	95/5/0* #	97/3* #
Scenario 2	23/50/27/0/0	70/28/2 *	90/8/2* #	97/7* #
Scenario 3	3/8/27/58/3	43/48/8 *	93/7/0* #	90/10* #

(* $p < 0.001$ vs. MI; # $p < 0.001$ vs GVL)

Conclusion(s): Our study demonstrates that, in comparison to the MI blade, indirect laryngoscopes provide better laryngeal exposure and facilitate tracheal intubation, in simulated difficult airway scenarios. These advantages increased with the level of difficulty of the scenario and were more pronounced in the "tongue oedema scenario".

P 19

Automated cuff pressure regulators worsen tracheal sealing in HVLP tracheal tube cuffs

Weiss M¹, Doell C², Madjdpour C¹, Woitzek K¹, Bernet V²
¹Department of Anaesthesia and ²Intensive Care, University Children's Hospital Zurich, Switzerland

Objective: To investigate the effect of automated cuff pressure regulators on tracheal self-sealing mechanism [1, 2] during cyclic respiratory pressures changes in high volume – low pressure (HVLP) tracheal tube cuffs.

Methods: In vitro tracheal sealing was studied in HVLP tracheal tube cuffs (Microcuff ID 8.0 mm, Microcuff GmbH, Weinheim, Germany) in combination with a conventional cuff manometer (Cuff Pressure Manometer, Microcuff GmbH, Weinheim, Germany) and two different automated cuff pressure regulators (Cuff Controller, VBM Medizintechnik GmbH, Sulz a.N., Germany and Cuff Pressure Control, Tracoe™, TRACOE medical GmbH, Frankfurt, Germany). Experiments were performed at cuff pressures of 10, 15, 20 and 25 cmH₂O during intermittent positive pressure ventilation with peak inspiratory pressures of 20 and 25 cmH₂O. Air leakage was spirometrically assessed. Experiments were performed four times using two tracheal tubes with two exemplars of each cuff pressure controller type.

Results: The Tracoe™ automated cuff pressure regulators revealed rapid pressure compensation whereas the VBM cuff pressure controller demonstrated delayed pressure regulation. With the conventional cuff pressure manometer and the slow-reacting VBM cuff pressure controller sufficient sealing (air leakage ≤ 20 ml/tidal volume) was obtained at all cuff pressures tested in both ventilation settings. With the fast-reacting Tracoe™ cuff pressure controller sufficient sealing was only achieved at cuff pressures of 20 and 25 cmH₂O. This was because of immediate compensation of any respiratory induced cuff pressure changes with even cyclic excessive deflation of the tube cuff below initially set cuff pressure level.

Conclusions: Automated cuff pressure regulators with rapid pressure correction characteristics interfere with the self-inflating mechanism of HVLP tube cuffs and impair the improved tracheal sealing characteristics of HVLP tube cuffs.

References: 1) Carroll RG, et al. Int Anesthesiol Clin. 1974;12: 111–41. 2) Guyton D et al. Chest. 1991;100:1076–81.

P 20

Simultaneous modeling of drug induced hypercarbia and hypoventilation in the nonsteady state

Antonello LG Caruso¹, Peter M Schumacher², Manfred Morari¹, Thomas W Bouillon²
¹Automatic Control Laboratory, ETH Zurich;
²Department of Anesthesiology, Inselspital Bern

Background: An integrated description of drug induced respiratory depression with parameters identifiable from clinically available data is not available so far. Several studies describe the effect of respiratory depressant drugs on isolated endpoints (minute ventilation (MV) under isohypercapnic and pseudo steady state conditions, MV under isohypercapnic conditions, PaCO₂ or PetCO₂ under pseudo and nonsteady state conditions). Concomitant modeling of MV and PCO₂ changes under nonsteady state conditions has not been undertaken. We propose a model describing simultaneously measured MV and PaCO₂ changes after bolus administration of a fast onset opioid (alfentanil, 1 mg) and describing changes of PaCO₂ following changes of MV from a physiological model of human ventilation [1].

Methods: The following conditions were defined prior to model building: i) Any parameter, including CO₂ sensitivity had to be identifiable from measured PaCO₂ and MV values after bolus administration of a fast acting mu agonist; ii) Simulations with these parameter values must reproduce changes of PCO₂ for different input patterns of MV into a physiological model [1]. After IRB approval and written informed consent had been obtained, 10 volunteers received 1 mg alfentanil i.v. bolus; PaCO₂ was sampled at 0, 1, 2, 3, 4, 5, 7.5, 10, 12.5, 15, 20, 30, 45 minutes, MV was averaged per minute from single breath values obtained via a face mask. Dead space was assumed 30% of MV. The structure of the respiratory controller of the model was taken from our previous work [2]. Model building, fits and simulations were done with MATLAB using SIMULINK.

Results: CO₂ turnover was well described with a 1-compartment model, drug dependent production and elimination (common C50, different ke0). CO₂ sensitivity could be estimated without performing drug naive CO₂ response curves. In simulation case studies using a complex metabolic model as benchmark, it was demonstrated that this very simple structure is sufficient to describe PCO₂ time courses generated from the complex model given varying MV.

Discussion: This modeling approach extracts both drug and CO₂ sensitivity from the time course of MV and PaCO₂ after administration of a mu agonist while remaining compatible with more complex physiological models.

References: [1] Clin Physiol 2001; 21:447–64; [2] Anesthesiology 2007;107:A20.

P 21

Comparison of sealing quality of the Super Seal Guard versus the Standard Seal Guard tracheal tube cuff

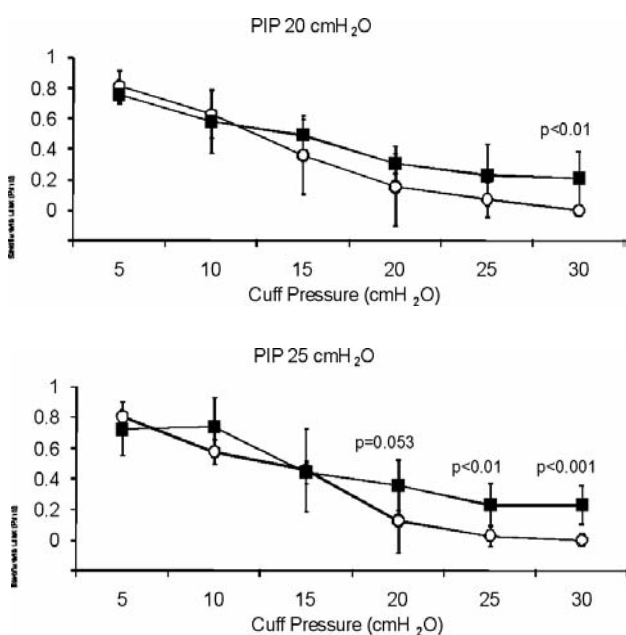
Madjdpour C¹, Mauch J¹, Bernet V², Doell C², Kutter A³, Bettschart R³, Weiss M¹

¹Department of Anaesthesia and Department of Intensive Care and Neonatology, University Children's Hospital Zurich, Switzerland; ²Equine Department Vetsuisse Faculty, Zurich, Switzerland

Background: This study compared sealing characteristics of the recently introduced cone-shaped Super Seal Guard (SSG) tracheal tube cuff with the standard cylindrical-shaped Seal Guard (SG) tracheal tube cuff (Covidien, Athlone, Ireland) (1).

Methods: ID 7.5 mm SSG and SG tracheal tube cuffs were compared in an *in vitro* set up. A PVC tracheal model (ID 25 mm) attached to a test lung was intubated and tube cuffs were inflated to 5, 10, 15, 20, 25 and 30 cmH₂O. The test lungs were ventilated with IPPV as followed: fresh gas flow of 4 lt/min air with 1% sevoflurane, PEEP 5 cmH₂O, respiratory rate 12/min, peak inspiratory pressure (PIP) of 20 and 25 cmH₂O. Sevoflurane passing the tube cuff was measured at the upper cuff border using an anaesthetic gas analyser. Experiments were repeated six times with new tubes for each run. Data are presented as mean/SD and were compared using t-Test ($p < 0.05$).

Results: (■ = SG; ○ = SSG)



Conclusion: The new Super Seal Guard tracheal tube cuff was superior to the Standard Seal Guard tracheal tube cuff regarding prevention of air leakage in an *in vitro* tracheal model.

References: 1) Lorente L, et al. Am J Respir Crit Care Med. 2007;176:1079-83.

P 22

Learning curves for the Glidescope®, the McGrath® and the Airtraq® laryngoscopes in normal airways: a manikin study.

Savoldelli GL, Waeber JL, Abegg C, Baeriswyl V, Clergue F, Schiffer E.

Service d'Anesthésiologie, HUG

Background and goal of study: Several Video and optical laryngoscopes have been developed but few have been compared in terms of their learning curves and efficacy. Using a manikin with normal airways we compared the Glidescope® (GVL), the McGrath® (MVL), the Airtraq® (AOL) and the Macintosh (MI) laryngoscopes.

Materials and methods: Sixty anaesthetists participated in this randomized study. All subjects were novices with the new devices. They intubated a Laerdal SimMan® (with normal airway) 5 times in a row with all laryngoscopes. The sequence of use of the GVL, MGL and AOL was randomized. Before using a device, a presentation and a demonstration were provided. Outcome measures were: time to intubate, Modified Cormack grades (MCL), dental trauma (0 to 3) and difficulty of use (0 easy to 100 difficult). Data were analysed using the Friedman (overall) and the Wilcoxon signed rank (post-hoc) tests as appropriate.

Results and discussion: The AOL had the most favourable learning curve and mirrored the MI after 2 intubation attempts. The GVL and MGL had steep learning curves but, after 5 attempts, differences

persisted in TTI when compared to MI and AOL. Other outcome measures are shown in the Table ($P =$ overall).

	MI	GVL	MGL	AOL	P
MCL I/IIa/IIb/III (%)	62/35/2/1	79/21/0/0	97/3/0/0	99/1/0/0	<0.001
Dental trauma (Mean±SD)	1.8 ± 0.6	1.7 ± 0.5	0.7 ± 0.6	0.7 ± 0.5	<0.001
Difficulty of use (Mean±SD)	16 ± 17	27 ± 18	22 ± 17	19 ± 15	= 0.014

Conclusion(s): In a normal airway model, the three devices provided better laryngeal exposures in comparison with the MI blade. Intubation skills with new devices were rapidly acquired. The AOL displayed a more favourable learning curve than the GVL and the MGL.

P 23

Urinary retention after spinal anesthesia with hyperbaric prilocaine 2% in the ambulatory setting

J. Kreuziger, B. Frankenberger, S. Zbinden
Klinik für Anästhesie und Intensivbehandlung, Luzerner Kantonsspital, Departement Wolhusen

Introduction: Hyperbaric prilocaine 2% has gained popularity as a medium-long acting spinal anesthetic in the ambulatory setting. Successful micturition is still the critical discharge criterium in many centers. Data is sparse on the time to recovery and the rate of urinary retention after spinal hyperbaric prilocaine. This prospective observational study was undertaken to evaluate the time to spontaneous micturition and to quantify the rate of bladder catheterization after spinal anesthesia with hyperbaric prilocaine 2%.

Patients and methods: Adult, ASA I or II patients (16-80 years) scheduled for ambulatory surgery of the knee or lower leg were enrolled. Patients were urged to micturate preoperatively. After standard monitoring they received 60 mg of hyperbaric prilocaine 2% intrathecally Ringer's lactate (RL) was administered for volume replacement. After the operation patients were allowed to drink freely. Bladder scan was performed before spinal anesthesia and hourly until spontaneous micturition or catheterization. Patients were catheterized when bladder filling reached 600 ml. Descriptive analysis of data, Student's *t*-test and Fisher's exact test were performed to detect significant differences due to age or gender. Correlation among different outcome parameters and potential factors influencing micturition was performed by Pearson's correlation test.

Results: Of 93 enrolled patients, 85 were included ($m = 49$, $f = 36$, exclusion due to incomplete data). Patients received on average 550 ml RL intraoperatively and a total of 870 ml until micturition or catheterization. They drank an average of 280 ml. 36.1% of women and 12.1% of men were catheterized. Mean time between spinal puncture and catheterization was 190 min. 65 patients (76.5%) were able to micturate spontaneously after an average time of 275 min. Patients under 40 years or older than 60 years had a significantly higher incidence of catheterization than patients between 40 and 60 years. Overall women had a significantly higher incidence of catheterization ($p = 0.016$).

Conclusion: 24.5% of patients receiving 60 mg of hyperbaric prilocaine 2% had to be catheterized. Patients under 40 years or older than 60 years, especially women, have a significantly higher incidence of urinary retention. Spontaneous micturition should remain a discharge criterium after spinal hyperbaric prilocaine 2%.

P 24

Key performance indicators for management of severe traumatic brain injury by emergency medical services

P. Schoettker¹, M. Rebetz², G. Haller², B. Walder²

for the PEBITA research network

¹Dpt of Anaesthesiology, CHUV, Lausanne;

²Division of Anaesthesiology, HUG, Geneva

Introduction: The prehospital period for traumatic brain injured patients is critical due to the incidence of secondary brain injuries. Key performance indicators for the management of these patients have been identified and we aimed to report performance of out-of-hospital emergency medical services (OHEMS) and mortality in western Switzerland.

Methods: Patients having sustained traumatic brain injury with an Abbreviated Injury Score of Head (HAIS) >3 brought to the University Hospitals of Geneva (HUG), Lausanne (CHUV) and the Hospital of Sion between June 2007 and March 2008 were prospectively included. Demographics, timing, OHEMS skill level, hypoxia and hyperventilation were analyzed. Key performance indicators were defined (table). Outcome indicator was mortality until 3 months. We used standard descriptive statistics.

Results: 229 patients were identified by OHEMS; 158 fulfilled inclusion criteria and were included consecutively.

Key performance indicators	HUG	CHUV	Sion
Indirect admission (<10%)	11/53 (20.75%)	14/72 (19.4%)	3/20 (15%)
Time from call to 1 st CT <90 min*	25/37 (67.6%)	28/54 (51.9%)	5/15 (33.3%)
Hypoxia* (SpO ₂ <90%)	1/42 (2.4%)	3/55 (5.5%)	0/16 (0%)
Hyperventilation* (PaCO ₂ <30 mm Hg)	0/28 (0%)	8/45 (17.8%)	0/12 (0%)

* direct admission, parameters at hospital admission

Conclusion: A number of modifiable key performance indicators were not met in the western part of Switzerland. Differences in management and timing were noted between centres. Further training is necessary to improve our trauma system and to influence mortality.

P 25

Anesthesiologic management and severity of injury of the first 100 patients of the Lausanne Trauma Registry

C. Heim, P. Schoettker, N. Gilliard
Service d'Anesthésiologie, CHUV, Lausanne

Introduction: In Switzerland, anesthesiologists are trauma team members and are systematically involved in the management of the severely injured patients.

Based on our newly developed trauma registry, we aimed at analyzing the demographics, injury patterns, anesthesiology procedures and outcome of our trauma patients.

Method: Data from pre-hospital, shock room and operating room settings as well as procedures, treatment and outcome were prospectively collected with the help of dedicated trauma registry software. The first 100 adult trauma patient brought to the shock room and included in the registry beginning on the 1st of January 2008 were analyzed.

Results 79 patients were male with a median age of 41.7 years (IQR 24.5–53.6). Trauma was related to road accidents (40%), falls (38%), self-inflicted violence (10%), burns (5%), criminal intention (5%) and unknown (9%). Median ISS Score was 16.5 (IQR 9–29) and 29% of patients had ISS >15. 21% of patients were admitted intubated and further 16% required intubation in the shock room (7% within the first 10 minutes after arrival). Arterial catheters were inserted in 26%, and central line catheters in 5%. 71% had a shock-room CT-Scan. Cardiopulmonary resuscitation was required in 5% of which 2% survived. After shock-room management, 53% of patients were transferred to the emergency department, 29% to the operating room and 16% to the intensive care. The median time in the shock room was 51 minutes (IQR 35–72), with extremes of 10 and 185 minutes. Of the 100 patients, 8 died (2 deaths in the shock-room, 3 in theater, 2 in ICU and 1 in the ward).

Discussion: Trauma patients require a dedicated team to manage life-threatening injuries in which the anesthesiologists play an integral role. Although Switzerland offers a high level of care in the pre-hospital setting, specialized care is needed in a number of cases in the trauma shock room. Time consuming procedures are necessary which mandates a constant anesthesiology team presence.

P 26

Feasibility of an Anaesthesiology based trauma registry in a swiss university hospital

C. Heim, P. Schoettker, I. Demiéville, N. Gilliard
Service d'Anesthésiologie, CHUV, Lausanne

Introduction: In organized trauma care, a registry is an integral part of a modern comprehensive trauma system and is the primary source of data for resource allocation, quality improvement efforts and hypothesis-generating research in trauma care. In Switzerland, anaesthesiologists are essential team members in trauma care as they manage severely injured patients throughout their hospital stay from shock-room arrival through operating room procedures until arrival in the intensive care unit. During operating room management, mandatory data collection by anaesthesiologists is standard level of care.

Aim: To develop a tool for collaborative and prospective survey on epidemiologic characteristics, treatment and outcome of severely injured trauma patients managed by anaesthesiologists in the university hospital of Lausanne, CHUV and to validate the quality of data collection.

Method: Dedicated software based on ACCESS 2000 was developed and 262 items were prospectively collected for every adult trauma patient brought to the shock-room. Parameters about pre-hospital, shock-room and operating room management as well as timing,

demographics, severity of injury, adverse events and outcome were analyzed. Scores and codes used are AIS/ISS 2005, CHOP, ICD-10, RTS, TRISS and MTOS.

Results: From the 1st of January to 31 May 2008, data of 120 patients were entered by a trauma data manager supervised by an anaesthesiologist. An average of 59 minutes were necessary to collect all data for one patient. Missing values were mainly respiratory rate, temperature and Visual Analog Scale(VAS) on scene of the accident as well as in the shock-room. Glasgow Coma Scale recording and data about fluid quantity were insufficient by the shock-room-team.

Discussion: Trauma registries are essential tools for quality assurance, teaching and research. Most trauma registries are created and managed by surgeons. In our institution, anaesthesiologists provide emergency care from site of the accident throughout the shock and operating room until arrival to intensive care. Despite some quality issues about missing data, the establishment of an anaesthesiology based trauma registry has proven to be an achievable goal.

P 27

A Web-based knowledge database (Wiki platform) is a powerful, widely accessible tool for learning and documentation of SOPs in cardiac anesthesia

Sebastian Trachsel, Jörg Breitenstein, Balthasar Eberle
Universitätsklinik für Anästhesiologie und Schmerztherapie

Introduction: A clinicians infrastructure aims to improve communication, learning and facilitate access to knowledge [1]. Manuals and quality management systems are commonly used in order to guarantee quality and consistency of workflow. Maintenance of these documents is laborious and access to information can be difficult. A "collaborative hypermedium" is a medium that consists of nodes representing content and arcs between contents. A wiki is collaborative software that enables documents to be authored collectively using a web browser. Performing anesthesia for highly innovative fields, as cardiac surgery or cardiology, requires exact and current SOPs for daily practice. Wiki platforms are used for educational purposes [2, 3] and are interesting tools for research networks [4]. The aim of this project was to develop a wiki platform that allows availability, continuous documentation and development of anesthetic SOPs for teaching and information in cardiac anesthesia.

Method: The wiki server software was configured online and access restricted by password. Registered users can freely create and edit web page content using any web browser without extensive IT knowledge.

Results: The new tool enables the clinicians to access and share knowledge simply, fast and worldwide. Wikis support hyperlinks and have text syntax for creating new pages and links between pages. It is possible to efficiently manage, navigate, and enhance SOPs and improve collective knowledge. Additional templates can be added as extensions that allow videos (TEE), pictures or PDF files to be uploaded and viewed. Of course, no confidential patient data are to be introduced in the database and all illustrations are to be anonymized carefully before upload. A calendar extension allows scheduling in the database lacking confidential information.

Conclusion: A wiki knowledge database is well suited for medical SOPs documentation, learning and access, and is easily edited for up-to-date information.

References: 1. Schüpfer G. *Der Anästhesist* 2007;56:983–91; 2. Stahmer T. *Technology and Learning* 2006;26(6):28; 3. Harris ST. *Perspect Inf Manag.* 2008 Jan. 30;5:1. 4. Sauer IM. *Artif Organs.* 2005; 12(Pt 1):157–61.

P 28

Utility assessment of an anesthesia drug display for anesthesia care in a pilot study setting

Peter M. Schumacher, Matthias Baechtold, Volker Hartwich,
Thomas W. Bouillon, Martin Luginbuehl
Universitätsklinik für Anästhesie, Bern

A system visualizing anesthetic drug concentrations and relating them to an effect could help to dose in a more rational manner. Two such display systems have been proposed [1, 2]. We have evaluated the utility of one of them [2] in a clinical pilot study.

Methods: After local ethics committee approval 40 patients were enrolled with their informed written consent. Twenty anesthesiologists performed a control and display case in randomized sequence. In both groups propofol was administered with TCI and alfentanil in boli of 0.5–1 mg. In the display group the anesthesiologists additionally had a PK/PD display as described in [2]. A standardized briefing of 45

minutes including hands-on training on the prototype display system was given to each anesthesiologist. The goal was to provide adequate anesthesia with minimal hemodynamic variability and rapid and pain free emergence. To assess the utility of the display subjective task load and performance ratings were collected with 3 anonymized NASA task load index (TLX) questionnaires [3]: one immediately after each case and one as an explicit comparison of the two cases a few days later. The NASA-TLX evaluates mental, physical and temporal demand and rates performance, effort and frustration levels. Furthermore the anesthesiologists were asked if the display simplified the task and if it should be added to standard monitoring.

Results: Of the twenty residents and staff members with 1 to >10 years experience 18 returned all 3 questionnaires. From the six NASA TLX questions 2 showed relevant differences between the groups: In comparison to the control case the performance in achieving the task was rated worse by 4, similar by 6 and better by 8. This came at a cost of a higher mental demand, however. The task simplification of the display was considered high or very high by 7, moderate by 7 and low to none by 4. Having the display in standard monitoring was rated high to very high by 7, moderate by 7 and low to none by 4.

Conclusion: We found promising utility results from first time users of an anesthesia drug display in this pilot study setting. The first time clinical use after a limited training may have caused the conflicting judgments on task simplification.

References: [1] Syroid et al. *Anesthesiology*. 2002;96(3):565–75. [2] Schumacher et al. *Anesthesiology*. 2004;101:A504. [3] Hart S, et al. *Human Mental Workd.* 1988;139–83.

Results: 486 catheters in 330 patients (199 male / 131 female) were identified. Jugular and sub-clavian insertions were observed in 422 CVCs (86%) (table), femoral insertion in 60 CVCs (12%); 5 insertions could not be identified. One pneumothorax (0.2%) and no haematothorax were observed.

Location	Number of CVCs (%)	Male / female	Pneumothorax/ Haematothorax	"wrong" [female]	"too high" [female]	"too low" [female]
Right jugular	281(58%)	176/105	0	3 (1%)	11 (4%)	50 (18%)
Left jugular	31 (6%)	14/17	0	[1 (1%)]	[3 (3%)]	[22 (21%)]
Right subclavian	84 (17%)	43/41	1 (1%)	4 (4%)	2 (2%)	32 (38%)
Left subclavian	20 (3%)	9/11	0	[2 (5%)]	[1(2%)]	[19 (46%)]
			0	0	0	2 (10%)
			0			[2 (18%)]

Conclusions: Intracardiac tip placement was frequently observed which may increase the risk of arrhythmia or cardiac perforation. Few pneumo- and no haematothorax were found in this short study duration. The high rate of CVCs femorally inserted may increase the risk for CVC-related bloodstream infection and thrombosis. A quality improvement program seems indicated for safe CVC tip placement and choice of vein access. More data are needed to adjust for patient-, operator- and catheter-related factors.

P 29

Knowledge of Glasgow Coma Scale by Swiss Air-Rescue Physicians

C. Heim¹, P. Schoettker¹, D.R. Spahn²

¹Service d'Anesthésiologie, CHUV, Lausanne;

²Universitätsspital Zürich, Institut für Anästhesiologie

Objective: To assess the theoretical and practical knowledge of the Glasgow Coma Scale (GCS) by trained Air-rescue physicians in Switzerland.

Methods: Prospective anonymous observational study with a specially designed questionnaire. General knowledge of the GCS and its use in a clinical case were assessed.

Results: From 130 questionnaires sent out, 103 were returned (response rate of 79.2%) and analyzed. Theoretical knowledge of the GCS was consistent for registrars, fellows, consultants and private practitioners active in physician-staffed helicopters. The clinical case was wrongly assessed by 38 participants (36.9%). Wrong evaluation of the motor component occurred in 28 questionnaires (27.2%), and 19 errors were made for the verbal score (18.5%). Errors were made most frequently by registrars (47.5%, $p = 0.06$), followed by fellows (31.6%, $p = 0.52$) and private practitioners (18.4%, $p = 1.00$). Consultants made significantly less errors than the rest of the participating physicians (0%, $p < 0.05$). No statistically significant differences were shown between anesthesiologists, general practitioners, internal medicine trainees or others.

Conclusions: Although the theoretical knowledge of the GCS by out-of-hospital physicians is correct, significant errors were made in assessing the clinical case. Less experienced physicians had a higher rate of errors. Further emphasis on teaching the GCS is mandatory.

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Incidence of mechanical complications after central venous catheter insertion in a university hospital

V. Cartier Faessler¹, C. Inan¹, S. Touveneau², W. Zingg², D. Pittet²,

A. Platon³, P.A. Poletti³, F. Clergue¹, B. Walder¹

¹Division of Anesthesiology; ²Infection Control Program;

³Radiology Department, HUG, Switzerland

Background: Mechanical complications after central venous catheter (CVC) insertion are related to insertion and to CVC tip placement. Few prospective collected data are available on mechanical complications and no published data are available for Switzerland.

Aim: of this investigation was to estimate mechanical complications on institutional level of a large university hospital.

Methods: During a 3 months period every CVC insertion in adults hospitalized in the University Hospital of Geneva was prospectively and consecutively identified. All post-insertion chest radiographies (CR) were reviewed. CRs with identified mechanical complications and/or inaccurate tip placement were secondary reviewed by radiologists. CVC tip placement was "too low" if located below the carina, "too high" if located more than 2 cm above the carina. CVC tip placement was in a "wrong placement" if located in a vein other than vena cava superior.

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Vermeidung von Eingriffsverwechslungen in der Chirurgie (Wrong Site Surgery)

Dr. med. Marc-Anton Hochreutener

Stiftung für Patientensicherheit

Objective: Entwicklung und Verbreitung von Empfehlungen zur Prävention von Wrong Site Surgery (Eingriffsverwechslungen).

Methods: In Zusammenarbeit mit dem deutschen Aktionsbündnis für Patientensicherheit, der deutschen Gesellschaft für Chirurgie, den Trägern der Stiftung für Patientensicherheit und mit Unterstützung durch die fmch entwickelte die Stiftung für Patientensicherheit knappe, handlungsrelevante Empfehlungen zur Prävention von Wrong Site Surgery. Diese wurden in einem mehrstufigen Delphiprozess und unter Berücksichtigung international sehr gut etablierter Vorlagen (USA: VA-Spitäler, Joint Commission/Australien: Australische Chirurgengesellschaft/UK: National patient Safety Agency des NHS) in einem Expertenprozess definiert. Nach der Formulierung wurden von der Stiftung Piktogramme entwickelt, um die Empfehlungen graphisch zu untermauern.

Results: Auf der Basis der breit abgestützten Entwicklungsarbeiten und den international bewährten Vorlagen wurde ein Pocketflyer und eine Plakatvorlage entwickelt, welche in Deutschland und in der Schweiz (hier mit Unterstützung durch die fmch) in der Fachwelt breit gestreut werden. Der Flyer spricht die folgenden Stationen des interventionellen Behandlungsprozesses an und formuliert konkrete Handlungsempfehlungen (checks), welche die Prävention von Wrong Site Surgery unterstützen: 1) Identifikation des Patienten und der Operation und Operationsstelle vor / bei Aufnahme; 2) Markierung des Eingriffsortes; 3) Zuweisung zum richtigen OP-Saal; 4) Team Time Out vor Schnitt.

Conclusion: Wrong Site Surgery ist zwar selten, wenn Eingriffsverwechslungen aber stattfinden, sind sie in der Regel für Patienten und den Operateur katastrophal und für beide Seiten traumatisierend. Zahlreiche Chirurgen berichten von Beinahe-Fällen oder von effektiv erlebten solchen Ereignissen. In der Handchirurgie geht man z.B. davon aus, dass im Durchschnitt eine Eingriffsverwechslung pro Berufsleben stattfinden wird. Nach der Risk Management Regel, dass auch seltene Ereignisse aktiv verhindert werden sollen, sofern sie ein grosses Schadenspotential haben, greifen alle patient safety Institute auf der Welt dieses Thema auf. Die Prävention von Wrong Site Surgery lässt sich mit relativ einfachen prozeduralen Elementen realisieren.

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Evaluation of the PediaSat continuous central venous oxygenation monitoring system in paediatric anaesthesia

Bettex D^{1,3}, Woitzek K¹, Bürki C¹, Baulig W^{1,3}, Schmitz A¹, Prêtre R², Weiss M¹

¹Department of Anaesthesia and ²Cardiac Surgery, University Children's Hospital Zurich and ³Division of Cardiac Anaesthesia, University Hospital Zurich

Objectives: This study was designed to compare the accuracy of a new continuous venous oxygenation monitoring system (PediaSat Oximetry Catheter; Edwards Life-sciences, Irvine, CA) with laboratory blood oximetry in paediatric surgical patients [1, 2].

Methods: Paediatric patients undergoing cardiac surgery under pulmonary bypass, orthopaedic or cranio-facial surgery with major blood loss were included into a prospective, non-randomized observational study. The central venous oximetry catheters ($S_{cv}O_2$) (2-lumen 4.5 Fr or 3 Lumen 5.5 Fr) were inserted preoperatively into the superior vena cava. Thereafter, the system was calibrated in vivo to S_vO_2 and haemoglobin measurements by laboratory co-oximeter (GEM OPL, Instrumentation Laboratory, Lexington, MA). Repeated blood samples were obtained from the distal port of the venous catheter according to the clinical protocol and were oximetrically analysed for haemoglobin and central venous oxygen saturation ($S_{v}O_2$). Data are compared with linear regression analysis and Bland-Altman analysis.

Results: So far 10 children, aged from 0.9 to 15.3 yrs (median 9.3 yrs) and weighing from 8.3 to 43.3 kg (24.4 kg) were studied. A total of 41 data pairs were recorded. SO_2 values from the PediaSat Oximetry Catheter ranged from 52 to 89% (median 79%) and those measured by oximetry from 57.2 to 84.7 (median 78.7). Correlation between $S_{cv}O_2$ and S_vO_2 was moderate with $r^2 = 0.550$ ($p < 0.001$). $S_{cv}O_2$ was only slightly higher than S_vO_2 (bias + 0.09%) but precision was poor (limits of agreement: -10.1/ 10.2%).

Conclusions: Based on our preliminary data, the tested PediaSat continuous central venous oxygenation monitoring system does not reliably reflect absolute S_vO_2 values and should be used with precaution.

References:

- 1 Spenceley N, et al. *Pediatr Crit Care Med.* 2008;9:e13-6.
- 2 Liakopoulos O, et al. *Anesth Analg.* 2007;105:1598-604.

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In-vitro evaluation of the new PediaSat continuous central venous oxygenation monitoring system

Baulig W¹, Woitzek K², Zaiter H³, LiJovic T³, Bettex D², Bürki Ch², Weiss M²

¹Division of Cardiac Anaesthesia, University Hospital Zurich;

²Department of Anaesthesia and ³Cardiac Surgery, University Children's Hospital Zurich

Background and objectives: This study was designed to investigate the accuracy of a new spectrophotometric based continuous venous oxygenation monitoring system (PediSat) in an in-vitro model.

Methods: A continuous fiberoptic oximetry catheter (PediSat Oximetry Catheter; Edwards Lifesciences, Irvine, CA) was inserted in a black testing chamber, connected with an extracorporeal circuit and filled with human whole blood. Flow was set at 1000 ml.min⁻¹. After calibration of the PediSat system, blood samples were taken for co-oximetric assessment of oxygen saturation (SO_2) at different PediSat oxygen saturation ($S_{PediSat}O_2$) levels under steady state conditions. Experiments were repeated with two different continuous fiberoptic oximetry catheters at a blood temperature of 37 °C. Data are compared with linear regression analysis, Bland-Altman analysis and Whitney-U-Test.

Results: Thirty-two data pairs were recorded: $S_{PediSat}O_2$ and SO_2 ranged from 28 to 98 % and from 24.9 to 99.5% respectively. Correlation between $S_{PediSat}O_2$ and SO_2 was high with $r^2 = 0.966$ ($p < 0.0001$). Bias between $S_{PediSat}O_2$ and SO_2 values was - 1.3% and precision was 3.4% (limits of agreement: - 4.7 / +2.2%). The disagreement between $S_{PediSat}O_2$ and SO_2 values was not different between SO_2 values above or below 70% ($p = 0.516$). Sensitivity and specificity of the first differences of $S_{PediSat}O_2$ and SO_2 were 1.0 and 0.91 respectively.

Conclusions: Based on the preliminary data, the tested PediSat Oximetry Catheter system reliably reflects oximetric assessed SO_2 values in this in-vitro setup and was without drift over a large range of measured SO_2 . In-vivo studies are required to confirm these results.

References:

- 1 Baulig W, et al. *J Clin Monit Comput.* 2008 April [Epub ahead of print].
- 2 Baulig W, et al. *Anaesthesia.* 2008;63:412-7.

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Validation of multi frequency phase fluorimetry for blood oxygen measurement in a porcine model

Andreas Vogt¹, Stefan Böhme², Bastian Dünge², Marc Bodenstern², Bernd Röhrig³, Klaus Markstaller²

¹University Department of Anaesthesiology and Pain Therapy, University Hospital Bern; ²Department of Anesthesiology and ³Institute of Medical Biostatistics, Johannes Gutenberg-University, Mainz, Germany

Background: Multi Frequency Phase Fluorimetry (MFPF, TauTheta, USA) was re-cently presented for the measurement of oxygen partial

pressure in gas or liquids by assessment of luminescence lifetime, phase and intensity. We determined precision out of replicated blood oxygen measurements and agreement with Clark type based analysis.

Method: In 10 anesthetized pigs (20.1 ± 1.9 kg) F_{IO_2} was set to 0.21, 0.4, 0.6, 0.8 and 1.0 to get readings over the whole measurement range. Single and replicated blood samples were taken and PaO_2 (mmHg) was determined simultaneously by two MFPF-100 (MF1 and MF2) and by Clark type (CT) sensor analysis at 37 °C and ambient pressure.

Results: PaO_2 readings mean±SD (range) were 296 ± 170 (67, 749) for MF1, 300 ± 180 (63, 749) for MF2 and 373 ± 212 (43, 712) for CT. Precision: coefficients of variation for replicated PaO_2 were 3.8% in MF1, 3.8% in MF2 and 1.8% in CT. Linear regression analysis yielded: MF2 = -7.9 + 1.04*MF1 ($r = 0.98$); CT = 4.05 + 1.22* MF1 ($r = 0.97$); CT = 25.6+1.14*MF2 ($r = 0.96$). Intraclass correlation coefficients were 0.980 for MF1 vs. MF2, 0.883 for CT vs. MF1 and 0.889 for CT vs. MF2. Agreement: for Bland Altman analysis of differences and averages the regression formulas were given as: MF2-MF1 = -13.40 + 0.06 * [(MF2+MF1)/2] ($r = 0.29$); CT-MF1 = -6.82+0.23 * [(CT+MF1)/2] ($r = 0.70$); CT-MF2 = 7.68 + 0.18 * [(CT+MF2)/2] ($r = 0.51$).

Conclusions: MFPF provides accurate reproducibility for oxygen partial pressure measurements and the readings are highly correlated. Agreement with CT is acceptable, however MF values were lower compared to CT in general (differences of means).

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Suicidal yew needles ingestion – a case report

H. Mattes, P. Berthold, A. Stürer, M. Neuhaus, T. Plattner, J. Beike, H.J. Beer, H.R. Brunner

Institut of perioperative medicin, Department of Medicine, Baden

A 44-years old patient was hospitalized because of attempted suicide. She ate a fistful of yew needles. After 2 hours she had dizziness, and progressive clouding of consciousness and circulation instability. In the course changing vigilance, blurred vision and hypotonia occurred, in the ECG a polymorph wide complex tachycardia was seen rapidly changing with extreme bradycardia. After the insertion of a stomach tube, to administer active coal, a bradycardia followed by a ventricular fibrillation (VF) arrived via stimulation of the nervous vagus. The VF was successfully defibrillated. After intubation, circulation was stabilized by magnesium and norepinephrine. Clinically extreme mydriasis with fixed pupils. After gastric lavage again bradycardia, than circulatory effective ventricular tachycardia witch persisted despite cardiopulmonary resuscitation (CPR), defibrillation and external pacing. After interruption of the CPR a spontaneous marginal sufficient rhythmus occurred. The echocardiographia shows a complete asynchronic heart activity. 2 hours later despite fluid resuscitation and catecholamines a progressive hypotension, another VF and finally asystolia occurred. External and internal pacing was unsuccessfully. CPR was stopped. 50-100 grams yew needles are lethal. Fundamental is the elimination of the poison, a specific therapy is not known. Some cases were reported with high digoxine levels , anecdotic successful therapy with digoxine-specific antibodies (Digoxine level in our case <0.26 nml/l). Another case with successful therapy with lidocaine. After the ingestion of hackled yew needles, the symptoms appear much faster. The Taxin level was 47 ng/g in blood. The group of J. Beike found taxin levels in lethal intoxication between 39 and 197 ng/g. A yew needles intoxication is mostly lethal, a specific therapy is missing and the elimination of the poison is often too late. Since this case two patients were admitted from the same psychiatric clinic with yew needles ingestion. The needles were successfully eliminated by gastroscopy.

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