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FM 1

Hip fracture accelerated surgical treatment and care track (HIP ATTACK) trial-feasibility pilot

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Objective: Hip fractures lead to hypercoagulability, stress, and immobility that result in postoperative complications. The 30-day mortality is 5–9%. Recent studies hypothesized that early surgery improves outcomes by reducing the exposure to these harmful states.

Observational data (1) suggest a mortality reduction after early surgery. Medical clearance and limited operation room (OR) access are considered the main factors for delay. We designed the HIP ATTACK pilot to assess the feasibility of a randomized controlled trial (RCT) comparing surgery within 6 hours of diagnosis versus standard care.

Methods: We randomized patients with a hip fracture requiring surgery during working hours. We excluded patients with open hip fractures, and with intake of non-reversible anticoagulants. Patients were randomized to accelerated care or standard care. Accelerated care consisted in accelerated medical clearance by a dedicated medical team and accelerated operation room access (i.e. the accelerated patients gained priority over elective orthopedic cases).

The primary endpoint of the pilot was feasibility of accelerated surgery, i.e. within 6 hours of diagnosis. Further, we collected data on the incidence of a composite of all-cause mortality, nonfatal myocardial infarction, stroke, pneumonia, pulmonary embolism, and major bleeding at 30 days after randomization.

Results: We recruited 60 patients (83% women) in 3 sites. The mean age was 81 years (standard deviation 9). Fifty-five percent (n = 33) of the patients underwent open reduction and internal fixation. Neuromuscular block of a median time of 6.0 hours (Q1-Q3 4.2–8.4) in the accelerated and 24.2 hours (Q1–Q3 11.1–29.5) in the standard care group, respectively (p <0.0001). Five (8.3%) patients died within 30 days. The composite endpoint occurred in 13.3% (n = 4) of the accelerated and 30% (n = 9) in the standard patients (hazard ratio 0.6, 95% confidence interval 0.26–1.39).

Discussion: The target time of 6 hours between hip fracture diagnosis and OR arrival was feasible. The 30-day incidence of major complications and mortality was very high, with promising results in the accelerated care group. We are planning a large-size RCT to test the hypothesis that accelerated surgery repair improves outcomes.


FM 2

Anesthetic Conditioning in Liver Transplantation: A multicenter randomized controlled trial

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Background: Due to organ scarcity and increasing use of older organ grafts for liver transplantation, organ-protective strategies are gaining importance. Pharmacologic conditioning with volatile anesthetics attenuates ischemia-reperfusion injury during liver resection [1, 2]. Whether it improves outcome in the setting of liver transplantation is unknown. The aim of this study was to assess the effect of pharmacological conditioning with sevoflurane on liver graft function and clinical outcome of patients undergoing cadaveric orthotopic liver transplantation.

Methods: Liver recipients were randomized from 03/2009 to 08/2012 at three University Centers (Zurich, Sao Paulo, Ghent). After ethic committee approval eligible patients were randomly assigned to receive anesthesia with either propofol (control group) or sevoflurane (sevoflurane group) during organ procurement. Postoperative peak of the aspartate transaminase (AST) was defined as primary endpoint.

Secondary endpoints included postoperative peak alanine transaminase (ALT), in-hospital complications (grade I–V) and length of hospital- and ICU stay. Data are presented as median (interquartile range) and odds ratio (95% confidence interval). P <0.05 was considered statistically significant.

Results: Ninety-eight patients were included in the study, 50 receiving sevoflurane and 48 propofol for anesthesia. Biochemical endpoints did not differ significantly between groups: Median peak values of AST were 925 (IQR: 512–3274) U/l and 1097 (IQR: 540–2633) U/l in control and sevoflurane group. Similar results were found for ALT. Regarding clinical endpoints overall complication rate did not differ between groups. However, a trend towards less severe complications was found in patients receiving sevoflurane. Median complication score was grade I (II–IVb) in the control group vs. sevoflurane group (OR = 0.51 (0.24 to 1.09), P = 0.08). Delayed graft function was seen in 11 patients (23%) receiving propofol compared to 7 patients (14%) receiving sevoflurane (OR = 0.64 (0.20 to 2.02), P = 0.45).

Conclusion: This first multicenter trial evaluating protective effects of volatile anesthetic sevoflurane compared to intravenous propofol in liver transplantation failed to show significant benefits of sevoflurane. However, sevoflurane application showed a trend towards less severe postoperative complications.


FM 3

A restrictive fluid regimen combined with norepinephrine during open radical cystectomy decreases the postoperative complication rate and accelerates recovery


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Introduction: Anesthesics and neuraxial anesthesia commonly result in vasodilation/hypotension. Norepinephrine could counteract this effect and thus allow for decreased intraoperative fluid administration. We investigated whether this approach may reduce postoperative complication rate in patients undergoing radical cystectomy with urinary diversion.

Materials & Methods: In this single-centre, double-blind, randomized trial, 166 patients undergoing radical cystectomy and urinary diversion were equally allocated to receive 1 ml kg⁻¹ h⁻¹ of balanced Ringer’s solution until the end of surgery and then 3 ml kg⁻¹ h⁻¹ until the end of surgery combined with preemptive norepinephrine infusion at an initial rate of 2 µg kg⁻¹ h⁻¹ (low-volume group; n = 83) or 6 ml kg⁻¹ h⁻¹ of balanced Ringer’s solution throughout surgery (control group; n = 83).

Primary endpoint was the in-hospital complication rate according to Clavien-Dindo classification for cystectomy. Secondary endpoints were the need for intraoperative/postoperative blood transfusion, and length of hospital stay.

Results: Baseline characteristics were equally balanced between the groups. Forty-four patients developed complications during hospitalization in the low-volume group (52%) versus 63 patients (73%) in the control group (P = 0.003). Gastrointestinal complications were lower in the restrictive fluid group (5 [6%] vs. 31 [37%], P <0.001). There were significantly lower incidences of ileus [0 [0%] vs. 8 [10%]; P = 0.007] in the low-volume group. The total number of cardiac events was also lower in the low-volume group (17 [20%] vs. 39 [48%], P <0.001). The number of renal, infectious, pulmonary and thromboembolic complications did not differ between the two groups. Median blood loss was 800 ml (range: 300–1800 ml) in the low-volume group versus 1200 ml (range: 400–3000 ml) in the control group (P <0.001). Fewer patients in the low-volume group (7 [8%]) needed intraoperative blood transfusion than in the control group (26 [31%]) (P <0.001). Twenty-three patients (28%) in the low-volume group needed postoperative blood transfusion versus 40 patients (48%) in the control group (P = 0.01).

Conclusion: In patients undergoing radical cystectomy with urinary diversion, a restrictive deferred intravenous crystalloid hydration reduces the incidence of in-hospital complications and accelerates recovery.
The pediatric supraglottic airway devices AirQ™ and Ambu Aura-i™ – blind intubation cannot be recommended

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Background: The pediatric intubating supraglottic airway devices (SAD) AirQ™ and Ambu Aura-i™ have been successfully used for pediatric tracheal intubation [2]. Advancement of the tube could be visualized, while there was no fiberoptic guidance. Primary outcome was success rate of simulated blind intubation.

Methods: With IRB approval and written informed consent, we included 42 children, ASA class I–III with a weight of 5–50 kg. After induction and effective ventilation through the randomized device, the tip of a fibrescope was placed inside the tracheal tube to simulate blind tracheal intubation [2]. Advancement of the tube could be visualized, while there was no fiberoptic guidance. Primary outcome was success rate of simulated blind intubation.

Results: Demographic data did not differ between groups (p >0.05). Particularly, weight and distribution of mask sizes were equal. SAD insertion was successful at first attempt in all but one AirQ, and in all cases at second attempt (p = 1.00). Intubation times (27 ± 5 vs. 23 ± 10 sec, p = 0.14) and leak pressures (16 ± 4 vs. 16 ± 4 cmH₂O, p = 0.88) did not differ between the AirQ and Ambu Aura-i group. Likewise, epiglottic downfolding (15% vs. 5%, p = 0.34) and number of patients showing a full fiberoptic view of the vocal cords (25% vs. 5%, p = 0.09) did not differ.
were similar. Success of simulated blind tracheal intubation was higher in the AirQ group (20% vs. 0% with the Ambu Aura-i, p = 0.048). In one case, the tube dislodged during removal of the AirQ, but still unsuccessfully blind intubation attempts, the ETT was deviating towards the esophagus. There were no major complications.

**Discussion:** Both SADs are efficient for ventilation. In contrast to our hypothesis, blind intubation success rate was higher for the AirQ, but still unacceptably low (20%). Blind intubation through either AirQ or Ambu Aura-i cannot be recommended. For anesthesia providers who anesthetize children and need a back-up system for emergency airway cases, a suitable fiberscope is mandatory to perform fast and safe fiberoptic-guided intubation through these pediatric intubating SADs.

**References:**


**Automated assessment of difficult ventilation with facial recognition techniques**

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**Introduction:** Failure/difficulty in mask ventilation for patients undergoing general anesthesia represent a significant cause of morbidity and mortality. Upper airway collapse or anatomical features play a role and a close relationship between difficult ventilation and intubation exists. No simple test can effectively predict difficulty and no scale has been unanimously recognized to grade difficulty. We propose a method using computer vision and machine learning to grade and predict difficult ventilation.

**Methods:** Patients necessitating general anesthesia were enrolled at the anesthetic consultation. Besides demographics, video recordings and depth maps of the head and neck were collected with two webcams and a Kinect®. Computer vision models computed morphological features (MF) known as relevant to difficult ventilation or intubation in static, dynamic, frontal and lateral mode. A classifier was trained to assign the patient a grade of mask ventilation difficulty scale against the anesthetist assessment while in the operating room (1 = ventilated by mask 2 + oral airway 3 = 2+necessitating two providers 4 = impossible to ventilate). ANOVA, t-test and Fischer’s exact test were applied as appropriate.

**Results:** In the first 12 months of the study, ventilation difficulty was assessed for 665 patients (Grade 1 = 469, Grade 2 = 136, Grade 3 = 60). No patients were described as impossible to ventilate. Among grade 3 patients, statistically significant factors were male gender (n = 50, 83.3%), patients with denture, especially if upper complete dentures (n = 7, 11.7%) and BMI >26 kg/m² (n = 45, 75.0%) and Mallampati (MP) III classes (n = 11, 18.3%) while MP IV as a single predictor was not significant. Correlation between difficult ventilation and difficult intubation (n = 10, 16.7%) was also found.

Creating a classifier with unbalanced classes allowed fit of over fitting. Therefore, the machine analysis was restricted to 180 patients. The classifier underlined relevance of relationship between mouth opening surface and that of the tongue, the morphology of the tongue (convex, concave or horizontal) and jaw mobility. Analysis of the 2000 next patients is underway and will add precision to identification of morphological features as well as further increase the specification of the classifier.

**Conclusions:** This study presents encouraging results for a fully automatic computer vision based system while identifying new MF to assess the difficulty of ventilation.

**Table 1: Supraglottic airway device performance. Data are n (%) or mean ± SD.**

<table>
<thead>
<tr>
<th></th>
<th>LMA Supreme (n = 80)</th>
<th>Aura Once (n = 73)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway leak pressure (cmH₂O)</td>
<td>17.9 ± 3.5</td>
<td>18.2 ± 3.5</td>
<td>0.60</td>
</tr>
<tr>
<td>Success at first attempt</td>
<td>77 (96)</td>
<td>67 (92)</td>
<td>0.41</td>
</tr>
<tr>
<td>Overall success</td>
<td>79 (99)</td>
<td>71 (97)</td>
<td>0.94</td>
</tr>
<tr>
<td>Difficulty of insertion on a scale from 1-5</td>
<td>77/2/0/0/0/0 (96/4/0/0/0/0)</td>
<td>57/10/2/1/0/0 (61/14/3/1/0/0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Time until successful ventilation (sec)</td>
<td>23.9 ± 5.8</td>
<td>24.8 ± 8.2</td>
<td>0.43</td>
</tr>
<tr>
<td>Epiglottic downfolding</td>
<td>11 (16)</td>
<td>3 (4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fiberoptic view grade 1/2/3/4/*</td>
<td>27/29/10/2 (34/36/13/3)</td>
<td>61/8/0/0 (86/11/0/0)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* 1 = full view of glottis, 2 = partial view, 3 = only epiglottis, 4 = no glottic structures
Evaluation of 6 video-laryngoscopes in a difficult airway scenario. A multicenter trial involving 720 anesthetized patients
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1Department of Anaesthesia and Pain Medicine, Bern University Hospital Inselspital, and University of Bern; 2Anesthesiology Department, University Hospital Center and University of Lausanne, CHUV; 3Division of Anaesthesiology, University Hospitals of Geneva and Faculty of Medicine, University of Geneva

Background: Video-laryngoscopes (VLS) are increasingly used and are aggressively marketed, but independent evaluation of efficacy and success in managing difficult airways is scarce. This multicenter, prospective randomized controlled trial evaluates six different VLS in a difficult airway scenario using a stiff extrication collar in a planned total of 720 elective surgical patients.

Methods: After IRB approval and written informed consent, 720 patients without predictors for a difficult airway, scheduled for elective surgery at the University Hospitals in Bern, Lausanne and Geneva.

Table

<table>
<thead>
<tr>
<th>Devices without a guiding channel for tracheal intubation</th>
<th>Devices with a guiding channel for tracheal intubation</th>
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</thead>
<tbody>
<tr>
<td>C-MAC™ n = 33</td>
<td>Airtraq™ n = 24</td>
</tr>
<tr>
<td>GlideScope™ n = 28</td>
<td>A. P. Advance™ n = 31</td>
</tr>
<tr>
<td>McGrath™ n = 27</td>
<td>King Vision™ n = 36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success at 1st attempt</td>
<td>0.001</td>
</tr>
<tr>
<td>Overall success rate</td>
<td>0.02</td>
</tr>
<tr>
<td>Time necessary for the successful attempt</td>
<td>0.01</td>
</tr>
<tr>
<td>Percentage of glottic opening visible</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* statistically different to C-MAC, GlideScope and McGrath
** statistically different to Airtraq
*** statistically different to all other five devices
Bonferroni correction factor applied

Volatile anaesthetics and positive pressure ventilation impair left atrial performance – A transthoracic echocardiographic study in young healthy adults
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Background: Animal and in vitro studies suggest that volatile anaesthetics affect left atrial (LA) function [1, 2]. We hypothesized that human LA function and dimensions are altered by volatile anaesthetics in vivo.

Methods: We studied 59 healthy adults (aged 18–48 years; 20 female) undergoing minor surgery under general anesthesia. The unpremedicated patients were randomly assigned to general anesthesia with sevoflurane, isoflurane or desflurane. Examinations by transthoracic echocardiography (TTE) were performed at baseline and after induction of anesthesia and placement of a laryngeal mask.

Results: The three volatile anaesthetics similarly reduced AVTI, a’ , LA ejection fraction and force were evaluated by an investigator blinded to the type of volatile anaesthetic.

Conclusions: These findings need to be assessed in further studies.

References:
1 Gare et al. Anesthesiology 2001.

All patients (n = 59)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>SB</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal volume (cm³)</td>
<td>44.2 ± 18.9†</td>
<td>42.2 ± 16.9*</td>
<td>33.3 ± 16.1*</td>
</tr>
<tr>
<td>Minimal volume (cm³)</td>
<td>15.5 ± 8.2</td>
<td>16.1 ± 8.6</td>
<td>15.5 ± 9.0</td>
</tr>
<tr>
<td>A v (cm)</td>
<td>4.1 ± 12†</td>
<td>3.2 ± 11</td>
<td>2.8 ± 10†</td>
</tr>
<tr>
<td>a’ (cm s⁻¹)</td>
<td>7.6 ± 15†</td>
<td>6.1 ± 17*</td>
<td>4.6 ± 16*</td>
</tr>
<tr>
<td>LA Ejection fraction (%)</td>
<td>66 ± 10†</td>
<td>61 ± 12*</td>
<td>55 ± 12*</td>
</tr>
<tr>
<td>Ejection force (dydynes)</td>
<td>12.9 ± 5.8†</td>
<td>8.9 ± 4.1</td>
<td>7.4 ± 4.1†</td>
</tr>
</tbody>
</table>

*baseline vs SB <0.025; † baseline vs IPPV <0.025; # SB vs IPPV <0.025 by ANOVA and Bonferroni adjustment.

Discussion: Not all VLS evaluated reached the desirable intubation success rate of >90%. Most devices required two attempts to reach this success rate. The integrated tracheal tube guidance does not seem to offer any advantages over unguided laryngoscopes in the hands of experienced anesthesiologists.
The maximum effective needle-to-nerve distance for ultrasound-guided interscalene block


Introduction: Direct needle trauma and intraneural injection are important mechanisms of nerve injury associated with regional anesthesia. Despite ultrasound (US) guidance, unintentional intraneural needle tip placement is common, especially during interscalene block (ISB) [1]. While needle-to-nerve proximity is the fundamental requisite for a successful block [2], the maximum effective distance between the needle tip and the target nerve is unknown. This study aimed to determine the maximum distance the needle tip can be placed from the roots of the interscalene brachial plexus while still achieving a successful block for shoulder surgery.

Material and methods: Twenty adult patients scheduled for ambulatory throracic or open shoulder surgery received an US-guided ISB using 20 mL of bupivacaine 0.5% with epinephrine. The first block was performed with the needle tip positioned outside but in contact with the transversus abdominis plexus sheath an exact distance between C5-C6. For subsequent blocks, the Dixon up-and-down method was followed: the distance from needle tip to sheath was increased or decreased by 2 mm for each consecutive patient according to the block success or failure respectively, in the previous patient. The primary outcome was the maximum effective distance required to achieve a successful block in 50% (MED50) of patients.

Results: The MED50 and MED95 were 8.3 mm (95% CI: 6.3–11.1 mm) and 1.6 mm (95% CI: 0.0–7.0 mm), respectively. Among the 11 patients with a successful ISB, the median intraoperative and postoperative tentanyl consumption was 150 µg (Interquartile Range [IQR] 150–175 µg) and 75 µg (IQR 25–75 µg), respectively. The median NRS pain score in Phase I recovery was 2 (IQR 0–3). Median durations of motor and sensory blockade were 19.8 hours (h) (IQR 15.0–22.3 h) and 10.1 h (IQR 8.5–12.2 h), respectively. The time to first dose of oral opioid analgesic at home was 9.6 h (IQR 9.3–12.1 h). No complications were reported.

Discussion: A successful ISB can be achieved with a distance of 8 mm between the needle tip and the brachial plexus sheath in 50% of patients. Our results suggest that it may not be necessary to position the needle tip as close as possible to the nerve roots during US-guided ISB. Future studies are required to explore the concept of maximum effective needle-to-nerve distance for other types of peripheral nerve blocks with a view towards enhancing safety.

References

Acknowledgment
Eric Abrecht is grateful to the department of Anesthesiology, CHUV, Lausanne, Switzerland, which supported his fellowship performed at the Toronto Western Hospital, Toronto, Ontario, Canada.

Ultrasound-guided transversus abdominis plane (TAP) block for laparoscopic gastric-bypass surgery: a prospective randomized controlled double-blinded trial

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Introduction: Despite the laparoscopic approach, patients can suffer moderate to severe pain following bariatric surgery [1]. The transversus abdominis plane (TAP) block has been demonstrated to improve pain-related outcomes after both laparoscopic [2] and open [3] abdominal procedures. This randomized controlled double-blinded trial investigated the analgesic efficacy of ultrasound-guided TAP blocks for laparoscopic gastric-bypass surgery (LGBS).
Accuracy and procedural time of ultrasound-guided cervical facet joint nerve blocks
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Background: Ultrasound (US)-guidance to block the cervical facet joint nerves has been described in both healthy volunteers and pain patients. Still most practitioners prefer fluoroscopy because of concerns related to accuracy and procedural times with US. We determined the accuracy of US-guided cervical facet joint nerve blocks in chronic neck pain patients and compared the procedural time with the classic fluoroscopic technique.
Methods: 61 patients were randomized to an US-group (n = 47) or control-group with fluoroscopy (n = 14). The joints to be tested were selected depending on the areas of pain. In the US-group, the needle was guided to the target with US-imaging and 0.2 ml of contrast dye was injected. Fluoroscopic imaging was then performed to evaluate the accuracy of needle placement. The procedural time for the first nerve block of each US-procedure was recorded and compared with the procedural time of the control-group.
Results: A total of 98 needles were placed in the 47 patients of the ultrasound-group. Successful block rate (corticosteroid block rate at bony target) varied from 86% (95% CI 76–96%) for a C3 and C7 medial branch block to 100% for C5 and C6. The mean procedural time was 86 seconds (SD: 25) in the US-group and 71 seconds (SD: 21) in the control group (p = 0.14).
Conclusions: Ultrasound-imaging is an accurate technique to perform cervical facet joint nerve blocks. Although the procedural time was slightly longer in the US-group than in the control-group, this can be considered as clinically irrelevant.
Assessment of labour pain using hand grip force
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The most effective treatment for labor pain is epidural analgesia, but in case of contraindications or maternal preference patient-controlled analgesia (PCA) with intravenous remifentanil may be an alternative. A practical problem during the use of remifentanil PCA is timing of the bolus application. A bolus at the beginning of a contraction is too late for optimum maternal comfort, since the delay of onset of remifentanil action is about 30 sec, and there is a further delay to peak action. A method to predict future contractions would be useful to improve timing of remifentanil bolus. The tocographic signal is too unreliable to be used as a predictor. An alternative may be a signal generated by voluntary action of the parturient. Here, we tested the possibility to use hand grip force measured by dynamometer to signal the pain experienced during the contractions and create a time series for prediction of further contractions. The aim of the study was to evaluate A) if the dynamometer signal is sufficiently reliable to predict further contractions and B) if a correlation between hand grip force and pain intensity evaluated on a numeric rating scale can be obtained.
Methods: 42 parturients were included in an observational study. A dynamometer was calibrated for individual hand muscle strength corresponding to the 10 numeric intensities of 5 and 10 on a 0–10 numeric rating scale (NRS). Pain was recorded during early and late labor for 10–20 min using dynamometer and NRS. Primary endpoint was the correlation coefficient (Pearson) between NRS ratings and the intensity of the peaks recorded by the dynamometer.
Results: All contractions recorded by the external tocogram were also registered by the dynamometer. Hand grip force in early labor was only moderately correlated with the subjective pain level expressed on the NRS (r = 0.36).
Discussion: The signal of a hand dynamometer appears to be reliable enough to be used to calculate a time series to predict a future contraction and thus guide remifentanil administration. The correlation between hand grip force and pain intensity, however, is too weak to be used to adjust bolus dose. The future application of the dynamometer to improve remifentanil PCA use during labor will depend on the performance of a mathematical model to predict the occurrence of the next contraction. Longer time series data are needed to develop such a model.
Effect of Rufinamide and Oxcarbazepine on peripheral nerve excitability
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Systemic sodium channel blockers are successfully used in the treatment of neuropathic pain. However, their impact on the peripheral nervous system remains unclear. The aim of this study was to evaluate the effect of rufinamide and oxcarbazepine on axonal excitability of peripheral sensory nerves.
Methods: After obtaining institutional ethics committee approval (KEK-ZH-Nr. 2010-0088) and written informed consent, we included 24 healthy volunteers in a randomized, double-blinded, placebo-controlled, crossover study. Over a 10-day period the drugs were gradually increased up to a therapeutic level. We measured nerve excitability parameters of sensory afferents on the median nerve (strength-duration time constant, the recovery cycle after a supramaximal stimulus and threshold electrotonus) using computerized threshold tracking technique (QTRAC®).
Results: Rufinamide affected significantly superexcitability, depolarizing threshold parameters and refractoriness of both, sensory and motor nerve fibers. Oxcarbazepine showed similar changes on motor fibers. However, oxcarbazepine changed significantly peak response, subexcitability and refractoriness in sensory fibers.
Conclusion: Threshold tracking techniques are a suitable tool to measure effects of systemic sodium channel blockers on peripheral nerve excitability. Oxcarbazepine showed a differential effect on sensory peripheral nerve.
Long-term exposure to sevoflurane or desflurane attenuates pulmonary inflammatory response in-vitro
Patrick Keilner1, Inge Harrmann1, Martin2, Philipp Euginer3, Beatrice Beck-Schimmer1,2
1Institute of Anesthesiology, University of Zurich, Zurich, Switzerland; 2Institute of Physiology, Zurich Center of Integrative Human Physiology
Background: Acute lung injury (ALI) and ventilator associated pneumonia (VAP) are still contributing to high morbidity and mortality in intensive care units (ICU) patients [1, 2]. Long-term sedation using volatile anesthetics may attenuate ALI and possibly prevent VAP.
Material & Methods: Rat alveolar epithelial cells type II (L2-AEC; CC-149) were grown until 80% confluence and stimulated with lipopolysaccharide (LPS) to simulate acute pulmonary inflammation in target cells. Cells were incubated in air-tight chambers with 5% CO2, adding 0.5 MAC sevoflurane (1.1 Vol%), 0.5 MAC desflurane (3.0 Vol%) or air (control) for 24, 48 and 72 hours. To demonstrate validity of the results and the impact on cell death cytotoxicity was measured determining lactate dehydrogenase assay (LDH). Viability was assessed using MTT assay. Interleukin-6 (IL-6) and cytokine-induced neutrophil chemottractant-1 (CINC-1) as two key inflammatory mediators were measured in the supernatants with the help of ELISA technique. Results were analyzed using linear regression.
Results: Stimulation with LPS provoked a time-dependent increase of IL-6 (+190 pg/mL, p < 0.001) and CINC-1 protein levels (+7580 pg/mL, p < 0.001) in the supernatants. This increase in inflammatory mediators was attenuated when cells were exposed to sevoflurane (IL-6: -3727 pg/mL, p = 0.006; CINC-1: −1870 pg/mL, p < 0.001), but in an even more pronounced way, when incubated with desflurane (IL-6: −3970 pg/mL, p = 0.002; CINC-1: −2030 pg/mL, p < 0.001). In the presence of volatile anesthetics LPS-stimulated cells had slightly higher MTT values in relation to controls (+0.9%, ±0.003), LDH levels were not influenced by LPS, sevoflurane, or desflurane.
Conclusion: In this in-vitro study we demonstrate for the first time, that the inflammatory response in AEC is attenuated in the long-term presence of volatile anesthetics, without affecting cell viability. These findings suggest that this in-vitro model should be further validated in-vivo. Volatile anesthetics could be a future option in ICU patients to treat ALI and to decrease the number of VAP.
References:
Involvement of Inflammatory Cytokines in Nociceptin Receptor Expression in Human Blood Cell Cultures

Laizh Zhang, Frank Stüber, Ulrike M. Stamer
Department of Anaesthesiology and Pain Medicine, Inselspital and Department of Clinical Research, University of Bern

Introduction: The nociceptin receptor (NOP) is a G protein-coupled receptor which has high homology with other opioid receptors. It is widely expressed throughout the human immune system and plays a role in immune response and pain. NOP is expressed in human peripheral blood [1, 2] and detected in all leukocyte subsets [3]. However, modulation of NOP in peripheral blood cells is still not clear to date. The aim of this study was to investigate regulation of NOP in human peripheral white blood cells under inflammatory conditions and explore possible mechanisms contributing to the modulation.

Methods: After approval of the ethics committee and written informed consent, 30 healthy volunteers were enrolled in this observational ex vivo study. Peripheral blood was cultured for 0, 3, 6 and 24 hrs with or without lipopolysaccharide (LPS), tumour necrosis factor (TNF)-α, interleukin (IL)-1β, IL-10 or interleukin (IFN)-γ. NOP mRNA in white blood cells was detected by quantitative RT-PCR. Cytokine concentrations in supernatants of cultures were measured using ELISA. An additional intervention experiment using anti-cytokine antibodies was conducted to evaluate possible mechanisms involved in the modulation of NOP by LPS.

Results: NOP was constitutively expressed in human peripheral white blood cells (median normalized ratio (1st/3rd quartile): 1.1 (0.8-1.3)). LPS dose-dependently down-regulated NOP mRNA expression at a concentration range between 0.5–100 μg/ml with an EC50 of 15 μg/ml. LPS 10 ng/ml significantly suppressed NOP when compared to baseline measurements (median under the mRNA-expression-time curve (1st/3rd quartile): 5.4 (4.6/6.9) vs 22.7 (17.1/25.3) normalized ratio - hr, p < 0.001). TNF-α 3 ng/ml, IL-1β 3 ng/ml, IL-10 50 ng/ml and IFN-γ 10 ng/ml decreased NOP mRNA levels to varying extents (p < 0.05 for all). Anti-TNF-α, anti-IL-1β and the combination of these two antibodies increased NOP mRNA expression 1.6 (95% CI: 1.2–2.0), 1.4 (1.0–1.6) and 1.8 (1.4–2.1) fold compared to the control (LPS + isotype Ab) (p < 0.001 for all). Anti-IL-10 and anti-INF-γ had no effect.

Conclusions: Inflammatory mediators influence NOP mRNA expression in human whole blood cultures. Pro-inflammatory cytokines TNF-α, IL-1β are involved in the LPS induced down-regulation of NOP mRNA.

References:
Posters

P 1

Standard of care in Transfusion Management: Is the same if Patient participates in a clinical trial or not? E. Lugauer, M.D., Maren Kleine-Brueggeney, M.D., Lorenz Theiler, M.D., Reto Kofmehl, Kuno Lehmann, Michael T. Ganter

Introduction: We previously investigated the impact of point-of-care (POC) coagulation monitoring of prothrombin time on intraoperative transfusion management and outcome in a randomized controlled trial (RCT). Here, we analyse if patients who were randomized to “standard of care” in the RCT were treated different than patients not included in a study. Our hypothesis was that inclusion in a RCT about transfusion management decreases transfusion compared to patients not participating in a study.

Methods: Data from patients undergoing elective surgery with an estimated blood loss exceeding 20% of the estimated total blood volume (70 ml/kg) were analyzed. In a retrospective way, we compared two groups: 1. Patients who were randomized to the standard of care group in the RCT and 2. Patients who underwent major orthopedic surgery during the same time period but did not participate in the RCT for organizational, language or other reasons. Outcome parameters were FFP, PRBC and platelets concentrate transfusions, transfusions from a cell salvage device, PACU stay, ICU stay and days in hospital.

Results: Demographic characteristics were comparable in both groups. Of 423 patients not enrolled in the RCT, 139 bled more than 20% of their total blood volume and threfore met the inclusion criteria. In the RCT standard care group 46 (54%) received any allogenic blood products versus 36 (27%) in the daily care practice group (p = 0.52). In the RCT 27 (32%) received FFP versus 37 (27%) in daily clinical practice (p = 0.41). 42 (40%) received PRBC in the RCT vs. 66 (47%) in daily clinical practice (p = 0.78). Number of patients transferred to the PACU (p = 0.58) or ICU (p = 0.19) and duration of hospitalization (p = 0.53) showed no difference between both patient groups.

Discussion: This retrospective analysis did not detect a difference in transfusion management or outcome parameters between patients included into an RCT and patients in daily clinical practice.

Summary: We compared transfusion management and postoperative outcome of patients with major intraoperative bleeding in patients enrolled in a RCT with a retrospective control cohort not enrolled in a study. Results showed no difference, indicating that participating in a study per se does not influence transfusion management and outcome.

References:


P 2

Model-based cost-consequence analysis of postoperative Troponin T screening in patients undergoing noncardiac surgery – 1-year Giovanna Lurati Buse1, André Lamy2, Braden Manns3, P.J. Deveraux2

Department Anästhesiologie Universitätsspital Basel, Population Health Research Institute, Hamilton, Canada; 3 Alberta Health Services, Calgary, Canada

Introduction: Myocardial ischemia after noncardiac surgery (NCS) is associated with 30-day mortality [1]. The majority of these events are asymptomatic [1].

Methods: We conducted a model-based cost-consequence analysis from the perspective of the Canadian public health care. We compared a postoperative Troponin T screening vs. standard care, i.e. Troponin T measurements triggered by ischemic symptoms. We measured the health consequences as the number of prevented death at 1 year and life-years (LY) and years lived (YLL) at a horizon of 5 years after NCS. Detected myocardial injury after NCS (MINS) during the screening period was defined by a Troponin T ≥0.03 μg/L after NCS without alternative explanation. The model was structured as a decision tree and it assumed the same treatment effect in MINS as in nonoperative myocardial infarctions as aspirin, B-Blockers, ACE-inhibitors and statins. Cost estimates (2011 Canadian dollars [CAD$]) included intervention costs and cost related to subsequent events. Model inputs based on Canadian and international patients enrolled in the Vascular events In Non-cardiac Surgery patients cOhort evaluation (VISION) Study, a large international cohort study that enrolls patients aged ≥45 years undergoing NCS with overnight hospitalisation. We run probabilistic sensitivity analyses with 10,000 iterations (Microsoft Excel spreadsheets). We conducted extensive sensitivity analyses.

Results: The data were based on 6,021 patients (47.9% men) aged a mean of 65 years (standard deviation 12). The cost to avoid missing an event amounted to CAD$ 1,567 for MINS. The cost-effectiveness of the postoperative Troponin screening was higher in patients’ subgroups at higher risk for MINS, e.g. patients undergoing urgent surgery ($1,119) or with coronary artery disease ($1,025). In the worst and best case scenarios in terms of resource utilisation, the cost to avoid missing a MINS were $2,045 and $1,097. The 30-day mortality of MINS was 9.6% (95% confidence interval 8.0–11.4%).

Discussion: Based on the estimated incremental cost per health gain, the implementation of a postoperative Troponin T screening after noncardiac surgery seems appealing, in particular in patients at high risk for MINS.

References:


P 3

Model-based cost-consequence analysis of postoperative Troponin T screening in patients undergoing noncardiac surgery – case dection

Giovanna Lurati Buse1, André Lamy2, Braden Manns3, P.J. Deveraux2

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References:


P 4

Anaesthesia in patients undergoing cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy: A single centre experience

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References:

given. Major surgical complications occurred after 13 interventions (23%) leading to death in 2 patients (4%). Anaesthesia and operation time, blood transfusion and fluid administration were associated with a significantly higher risk for major complications. Odds ratio for major complications was 6.6 (95% confidence interval: 1.3–33.3) if operation time was exceeding the initially scheduled time. Postoperative ventilation was needed in 2 patients (3%). Besides primary disease and complexity of surgery, the type and amount of fluids administered, blood loss, transfusions and anaesthesia management might have an impact on the patient’s outcome.

Beta-defense gene copy number variations in sepsis patients

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Background: Sepsis is a systemic inflammatory response after infection, trauma or large operation. Beta-defensins are a group of small cationic antimicrobial peptides which are effective against bacteria, fungi, and enveloped viruses. They are mainly expressed in skin and mucosae and they are strongly inducible by invasive pathogens (1). In addition, beta-defensins have cytokine-like effect to modulate immune system. Beta-defensin genes (DEFB) were found to be variable in copy number (2 to 12 per diploid genome). Gene copy number (CN) of DEFB4 was reported to be proportional to mRNA expression in lymphoblastoid cell lines. Significant association between higher DEFB CN and risk of psoriasis were reported. Based on the functions in immune system and genomic variation for beta-defensins, it is reasonable to investigate the association between DEFB CN and the predisposition to and the clinical course of sepsis.

Method: 721 sepsis patients with complete clinical data and 283 healthy controls were enrolled in this study. Genomic DNA was isolated from peripheral whole blood. DEFB CN was determined by Multiplex Ligation-dependent Probe Amplification (MLPA).

Result: The medians of DEFB CN in both sepsis patients and healthy controls were 4 (P = 0.91), and the distributions of DEFB CN in two cohorts were not significantly different (three categories including CN ≤3, 4 and ≥5, P = 0.72). In sepsis patients, the median of DEFB CN in non-survivors (5) was significantly higher than that in survivors (4) (P = 0.028). Moreover, a linear trend between DEFB CN and mortality was found (P = 0.024). Logistic regression analysis also showed DEFB CN was an independent factor to determine the outcome. Finally a linear regression model was established between DEFB CN and mortality (r² = 0.86, P = 0.0075), and the equation suggests that each increase by 1 copy from 2 copies adds 6.8% (95% confidence interval: 2.0, 10.6) mortality risk. The association between DEFB CN and risk of death was stronger in females than males (1.3–10.3 for females; 1.3–4.2 for males).

Conclusion: DEFB CN is not associated with the predisposition to sepsis, whereas, DEFB CN is associated with outcome of sepsis in female patients. However, increased DEFB CN is associated with the predisposition to and the clinical course of sepsis.

Validation of Multiple Inert Gas Elimination Technique by Micropore Membrane Inlet Mass Spectrometry in an In-Vitro Lung Model of Lung Compartmental With Low-to-Normal Ventilation-Perfusion Ratios


University Hospital Bern, Dept of Anesthesiology & Pain Medicine, Bern, Switzerland

Background: MMIMS-MIGET has been designed as rapid and direct method to assess the full range of V/AQ distributions [1, 2]. In an in vitro lung model (IVLM), MMIMS-MIGET shunt has been shown to correlate well with preset model shunt [3]. In this study we aimed to compare low (0.005–0.2) to normal (0.1–10) V/AQ compartments determined by MMIMS-MIGET and MM-VQ with reference low-to-normal VAQ compartments as preset in the IVLM (IVLM-VQ).

Method: One single oxygenator (QUADROX-ID Pediatric; MAQUET): was used: (i) sweep gas (air) flows were set to random at 0.05, 0.1, 0.2, 0.4, 0.6, 0.8 and 1 L (V) and (II) saline flow rate was fixed to 2.5 L min⁻¹ (Q) using a micro-diagonal pump (DeltaStreamDP-II, Medos), resulting in defined IVLM V/Q ratios. Inert gas solution (6 solubilities) was infused at a rate of 1.5 ml min⁻¹. Perfusion for duplicate samples were taken at each preset IVLM-VQ (0.02, 0.04, 0.08, 0.16, 0.24, 0.32, 0.4) simultaneously from up- and downstream mixing chambers of the gas exchange assembly (representing arterial and venous vascular beds), and were analyzed by MMIMS-MIGET to determine MM-VQ from retention data [5]. V/Q ratios (geometric means of V and Q peaks representing MM-VQ) were taken from MM-V/Q distributions for comparison with preset IVLM-VQ.

Results: The IVLM performed well, allowing stable control of compartmental saline and gas flows, as well as reproducible inert gas transfer. Fourteen pairs of preset IVLM-VQ (range 0.02 to 0.4) and MM-VQ (range 0.035 to 0.652) were feasible for analysis. Overall coefficient of variation for MM-VQ was 10.3%.

Conclusions: Low-to-normal V/Q ratios generated in an IVLM are detected by MMIMS-MIGET with good accuracy and precision. This IVLM appears as convenient system to validate and test MIGET systems and underlying assumptions by generating known V/Q relationships.

References:
Funding: SNF 320030_133046

Nears-Real Time Pulmonary Shunt and Deadspace Measurement With Multiple Inert Gas Elimination Technique (MIGET) by Micropore Membrane Inlet Mass Spectrometry

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University Hospital Bern, Dept of Anaesthesiology & Pain Medicine, Bern, Switzerland

Background: MIGET using gas chromatography (GC) is a well established but time consuming method to determine ventilation/perfusion (V/Q) distributions. A MIGET variant (Micropore Membrane Inlet Mass Spectrometry, MMIMS) fitted with a single-pore probe already reduced analytic complexity substantially compared to GC [1, 2], with shunt data correlating well with the Riley model [2, 3]. Recently a multi-pore probe was introduced, enhancing MMIMS sensitivity 400-fold. This reduces inert gas solution load to a third of the single-pore MMIMS system. This study evaluated MIGET by multi-pore MMIMS and aimed to compare fractional (I) MMIMS-MIGET shunt (MMS) with Riley shunt (RS) and (II) MMIMS-MIGET deadspace (MMVD) with deadspace based on volumetric capnography (VCVD) [4].

Method: With animal care committee approval, anaesthetized pigs (24 ± 1 kg; lavage injury, n = 15; autologous clot pulmonary embolism; n = 10) were studied. A dissolved inert gas (IG) mixture [2] was infused at a rate of 8 ml/kg h⁻¹. Arterial, mixed venous and mixed expired samples were collected at baseline and after lung injury induction in 15 minutes intervals. Samples were analyzed for IG partial pressures using a multipole MMIMS system (Oscillogy LLC, Folsom PA). Resultant retention and excretion data were transformed to V/Q distributions [5]. As compartments of interest, fractional MMS and MMVD were determined as shunt = V/VAQ <0.005, deadspace = V/VAQ >100. RS and VCVD fractions were calculated as previously reported [2, 3].

Results: Analysis was based on n = 349 data pairs, comparing MMS to RS and MMVD to VCVD. As indicator of experimental error, the MMIMS dataset had a residual sum of squares (RSS) <3.5 in 27.8% cases, RSS <10.6 in 51.3% and RSS <16.8 in 63%.

Conclusions: MMS and MMVD correlate well with conventionally determined RS and VCVD. Whether systematic negative effects reflect superior resolution by MIGET at the extremes of V/Q distribution, requires further study. MMIMS-MIGET emerges as a near real-time technique for true V/Q distributional analysis.

References:
Epidural Catheter: sutured or glued?

Aaron Genini, Viviana Riva, Marco Baggi
Servizio di Anestesia, Ospedale Beata Vergine, 6850 Mendrisio

Background: Despite different devices are available, the fixation of epidural catheters still seems to be an unsolved problem, since the possibility of dislodgment of the catheter can be reduced, but not excluded. Studies in literature show that, according to various fixation devices, epidural catheters dislocate at a rate between 5 and 30% [1, 2].

Methods: 90 patients ASA physical status I-II scheduled for surgery requiring general anaesthesia combined with epidural analgesia were prospectively enrolled in the period between 1/12/11 and 1/12/12. The patients were randomized into two groups: in the Mastisol Groupe the fixation of the epidural catheter was performed with synthetic glue (Mastisol®, Ferndale Laboratories, Inc., Ferndale, MI 48220, USA); in the Suture Groupe the catheter was sutured to the skin with non-absorbable polyamide (Ethilon II 2-0, Johnson & Johnsons, USA).

Results: The two groups did not present significant differences with regard to sex, age, weight, height, BMI, ASA risk class, duration of surgery and surgical specialties. During the follow-up, 2 patients were transferred to another hospital before the end of the epidural analgesia and in 6 patients some variables were not collected. Therefore we analyzed 42 patients in the Mastisol group and 40 in the Suture group. In 33/42 patients of Mastisol group and in 33/40 patients of Suture group, the analgesic therapy lasted until the end of the indication. At the level of its insertion to the skin, the displacement of the epidural catheter was detected in 8/42 patients belonging to the Mastisol group and in 5/40 patients inside the Suture group: there was not a significant difference between the 2 groups.

Discussion: Synthetic glue appears to be a viable alternative for the establishment of epidural catheters since, according to our study protocol, its dislocation rate did not differ significantly with respect to the suture.

Currently we believe that the use of synthetic glue offers advantages over the suture, as well as being less invasive, and simpler to apply (unlike the suture, it doesn't require an initial training).

Conclusions: Both suture and synthetic glue appear to be two good alternatives for the fixation of epidural catheters.

References

Activity Monitoring as Outcome Measure for Neuromodulatory Therapy Using Smartphones – A Feasibility Study

Lucian M. Macrea, Julia Seiter, Sebastian Feese, Oliver Amft, Bert Amrich, Gerhard Tröster, Konrad Maurer Institut für Anästhesiologie; Interdisziplinäres Schmerzambulatorium; Pain Research Unit, USZ; ACTLab, Signal Processing Systems; Institut für Anästhesiologie; Interdisziplinäres Schmerzambulatorium / ETH Zurich, Switzerland

Background and aims: Monitoring physical activity has been shown to be an important outcome measure in the clinical management of chronic pain.

Methods: We performed a feasibility study in two patients with neuropathic pain before and after neuromodulatory therapy using a smartphone system providing physical activity measurements from acceleration, barometer and location GPS data.

We measured the following smartphone parameters: daily recording time, number of location clusters visited, number of transitions in between different location clusters, number of steps, number of instances climbing stairs and the time the patient walked at a certain speed. The clinical evaluation included: pain intensity, physical functioning and patients ratings of overall improvement. We also evaluated the health related quality of life.

Results: Our results suggest that the changes in smartphone parameters before and after neuromodulatory therapy were considerable. Improvement of activity was achieved particularly in the home environment reflected by an increase in walking, a gain in fast cadence activities and a decrease in rest cadence. Activity questionnaires, however, did not correlate with these measurements. There was a significant increase in the three clinical core outcome domains and in the quality of life.

Conclusions: We conclude that smartphone based activity monitoring has the potential to provide objective information to clinicians with a minimal interference in the patient’s daily life.

Prediction of acute postoperative pain following breast cancer surgery using the pain sensitivity questionnaire

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Service d’anesthésiologie, HUG

Introduction: Postoperative pain treatment may be improved by identifying patients at risk for severe postoperative pain before surgery. Previous studies have indicated that preoperative pain sensitivity correlates with postoperative pain intensity. However, testing of pain sensitivity is time-consuming and painful. In volunteers it has been shown that pain sensitivity can also be assessed by self-rating, and a “pain sensitivity questionnaire (PSQ)” has been developed.

To evaluate whether the PSQ can also be used to predict acute postoperative pain we tested individual pain sensitivity in patients scheduled for breast cancer surgery both objectively and subjectively using the PSQ.

Methods: Following ethics committee approval and written informed consent, 90 patients scheduled for breast cancer surgery were included. Pain sensitivity was objectively assessed using electrical stimuli applied to the sural nerve and a hot water bath. Patients self-rated their pain sensitivity on the PSQ and were told to imagine the postoperative pain intensity on a 0–10 NRS scale (imagined pain score). Patients also completed questionnaires to assess anxiety (STAI) and depression (BDI).

Postoperative outcome criteria were: maximum and average pain during the first 24h, and average pain during the first 6 postoperative days. Pearson correlation coefficients were calculated using SPSS vs21.

Results: Significant correlations (Pearson) are presented in the following table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>PSQ score</th>
<th>Imagined Pain Score</th>
<th>STAI-state score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum pain during the first 24h</td>
<td>.28</td>
<td>.44</td>
<td>.27</td>
</tr>
<tr>
<td>Average pain during the first 24h</td>
<td>.18</td>
<td>.46</td>
<td>.26</td>
</tr>
<tr>
<td>Average pain during the first 6 days</td>
<td>.29</td>
<td>.38</td>
<td>.34</td>
</tr>
</tbody>
</table>

None of the objective criteria of pain sensitivity had a significant correlation with any outcome parameter. The PSQ score was correlated with neither the objectively measured parameters of pain sensitivity nor the imagined pain score. It was, however, weakly correlated with the BDI depression score and the STAI state anxiety score.

Discussion: In the context of breast cancer surgery, the PSQ score, but not objective measures of pain sensitivity, are correlated with postoperative pain intensity.

Interestingly, the simple question “how intense do you imagine the pain after your surgery” was even stronger correlated with postoperative pain intensity. Potentially factors such as anxiety and catastrophizing are more important determinants of postoperative pain in this context than pain sensitivity itself.

The analgesic efficacy of ultrasound guided transversus abdominis plane block (TAP BLOCK): a meta-analysis

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Background and aims: Meta-analyses on the TAP block have reported to improve postoperative pain [1, 2], but they included enthusiastic trials using anatomical landmarks. Thereafter, prospective studies based on ultrasound-guided techniques described conflicting results. This meta-analysis aimed to evaluate the postoperative analgesic efficacy of ultrasound-guided TAP block.

Methods: The authors searched the electronic databases MEDLINE and EMBASE among others. The primary endpoint was IV morphine consumption at 6h postoperatively, analysed according to the type of surgery. Secondary endpoints were IV morphine consumption at 24h postoperatively, pain scores at rest and on movement at 6 and 24h postoperatively, rates of PONV and pruritus at 24h postoperatively, and complications. Meta-analyses were performed with “Review Manager” software (RevMan version 5.1.6).

Results: Twenty trials were identified. Ultrasound-guided TAP block reduced cumulative IV morphine consumption at 6h postoperatively by 43% (mean difference: -4.5 mg, 95%CI: -6.5, -2.6 mg; p < 0.00001). Other endpoints are summarised in table 1. No complications were reported.
Conclusions: Ultrasound-guided TAP block reduces morphine consumption and pain scores at 6h postoperatively.

References

Keywords
Analgesia, Analgesic adjunct, Perioperative medicine, Postoperative pain, TAP block, Ultrasound

Table 1 Secondary endpoints. Significant results are highlighted with an asterisk.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>References</th>
<th>TAP group</th>
<th>Placebo group</th>
<th>Mean difference (95% CI) or RR (95% CI)*</th>
<th>Test for overall effect (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV morphine consumption (mg) at 24 h postoperatively</td>
<td>Baaj 2010, Belavy 2009, Costello 2009, El-Dawlatly 2009, Kane 2012, Niraj 2009, Siriramka 2012</td>
<td>257</td>
<td>238</td>
<td>-11.7 (-20.2,-3.1)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Pain scores (VAS, VRS or NRS 0-100) at rest at 6 h postoperatively</td>
<td>Atim 2011, Baaj 2010, Bollag 2012, Costello 2009, Griffiths 2010, Melinikov 2012, Kane 2012, Kim 2012, Ra 2010, Shin 2011, Tsuchiya 2012</td>
<td>294</td>
<td>305</td>
<td>-12.2 (-19.4,-4.77)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Pain scores (VAS, VRS or NRS 0-100) on movement at 6 h postoperatively</td>
<td>Atim 2011, Bollag 2012, Costello 2009, Griffiths 2010, Kim 2012, Melinikov 2012, Shin 2011</td>
<td>179</td>
<td>188</td>
<td>-12.4 (-19.4,-5.4)</td>
<td>0.0005*</td>
</tr>
<tr>
<td>PONV at 24 h postoperatively</td>
<td>Baaj 2010, Belavy 2009, Bollag 2012, Hoggood 2012</td>
<td>11/92 (12%)</td>
<td>11/96 (11%)</td>
<td>0.97 (0.46, 2.01)</td>
<td>0.93</td>
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<td>Pruritus at 24 h postoperatively</td>
<td>Belavy 2009, Bollag 2012</td>
<td>16/48 (33%)</td>
<td>17/54 (31%)</td>
<td>1.0 (0.61, 1.63)</td>
<td>0.30</td>
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PIEB – a new addition to the epidural labour analgesia family

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Neuraxial analgesia is the most effective labour analgesia. While the influence of the unborn baby on minimal, neuraxial labour analgesia can influence labour per se and there seem to be more instrumental vaginal deliveries (i.e. forceps and vacuum) in patients receiving epidural labour analgesia, Ambulation per se does not affect the mode of delivery, but motor block seems to have an important impact. In addition parturients with no or minimal motor block have a higher satisfaction with labour analgesia.

Modern neuraxial labour analgesia is delivered as a patient-controlled epidural analgesia (PCEA). The addition of a background continuous epidural infusion (CEI) reduces clinical interventions and increases patient satisfaction. The downside of CEI is accumulation of local anesthetics over time and development of motor block. Recent research has aimed at improving local anaesthetic distribution by delivering the local anaesthetic as a timed bolus rather than a CEI. A couple of months ago the first commercially available pumps with programmed intermittent epidural bolus (PIEB) became available.

Methods: In a pilot study we wanted to acquire experience with this novel model of labour analgesia. Bupivacaine 1 mg/ml (n = 7) or 0.25 mg/ml (n = 3) 10ml 2% MgSO4 was used. The loading dose was 15–20 ml. The pump was set to deliver a PIEB of 5 ml every hour. PCEA settings were 5 ml bolus with a lockout time of 20 minutes.

Discussion: PIEB is a promising new mode to administer epidural labour analgesia. Further studies need to investigate the development of motor block over time and the mode of delivery.

Time course of conditioned pain modulation in patients with acute and chronic low back pain

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Background and aims: The endogenous pain modulatory system can be evaluated in humans by conditioned pain modulation (CPM). CPM occurs when pain with a test stimulus is inhibited by an additional conditioning painful stimulus, reflecting efficient endogenous pain modulation. Disturbed endogenous pain modulation is likely one of the mechanisms underlying central hypersensitivity and might be a contributing factor for the development and maintenance of chronic pain. We tested whether CPM is altered in patients with acute and chronic low back pain, as compared to pain free controls. Two women developed motor block some degree of motor block, while two did not want to ambulate.

Methods: We studied 40 patients with acute low back, 34 patients with chronic low back, and 50 healthy controls. Test-stimulus was pain tolerance threshold to pressure at the 2nd toe (PPTT). Cold pressor test was the conditioning stimulus (hand immersed into ice water). PPTT was measured immediately, after 3, 5 and 10 minutes after cold pressor test. PPTT was calculated as the difference between PPTT after and PPTT before ice water test. The data were analyzed by linear regression models.

Results: CPM was equally functioning in all the groups immediately after cold pressor test. However, CPM declined significantly faster in the two patient groups, compared with the control group. This was evident already three minutes after cold pressor test (P = 0.009 and 0.03 in acute and chronic low back pain, respectively).

Conclusions: The rapid decline in the inhibitory effect of the conditioning stimulus indicates that the endogenous pain modulatory system is less investigated and might provide interesting information about anesthetic immobility mechanisms. Our study aimed at evaluating the role of the stimulation paradigm on the depressive effects of isoflurane on a limb withdrawal reflex in pigs. The hypothesis was that depression of both reflex and purposeful movements would occur at MAC.

In this prospective experimental trial, 10 pigs were anaesthetized twice with isoflurane only. First the individual MAC was determined, and then the effects of increasing end-tidal isoflurane concentrations, from 1.6 to 2.8% on withdrawal reflexes were assessed. Single, 10 and 60 repeated electrical stimulations were used to evoke withdrawal reflexes recorded and quantified by electromyography. Recruitment curves for reflex amplitude for increasing stimulation intensities and isoflurane concentrations were built.

Discussion: PIEB is a promising new mode to administer epidural labour analgesia. Further studies need to investigate the development of motor block over time and the mode of delivery.

Efectos de magnesio y calcio en el dolor neuropático

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Background and aims: An important limitation of clinical nerve excitability studies is the difficulty of interpreting pathological changes in excitability properties and attributes changes to defined cellular or extracellular abnormalities. The current study aimed at investigating the impact of extracellular MgSO4 and Calcium on nerve excitability parameters.

Methods: We used a computerized threshold-tracking program (QTRAC). The stimulus was a train of 60 repeated electrical stimulations were used to evoke withdrawal reflexes recorded and quantified by electromyography. Recruitment curves for reflex amplitude for increasing stimulation intensities and isoflurane concentrations were built.

Results: Low concentrations of MgSO4 and Calcium led to increased excitability whereas higher concentration had less effects. Both, low and high concentrations resulted in longer strength-duration time constants (s). After a train of preconditioning stimuli, threshold increased with low calcium but decreased with low MgSO4. Relative refractoriness was longer with low concentrations of calcium whereas the different concentrations of MgSO4 did not change the relative refractory period. Low concentrated MgSO4 induced a significant increase of excitability at the end of the 100 ms-lasting subthreshold depolarisation. After a long hyperpolarising conditioning current low concentrated calcium but not MgSO4 significantly inhibits inwardly rectifying currents (i).

Conclusion: The results presented in this study show that application of extracellular divalent ions MgSO4 and calcium have different effects on sensory A compound action potentials; Persistent sodium channels, slow potassium channels and inwardly rectifying channel (iH) are all modulated by MgSO4 and calcium.
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