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Paper No: 33.00

Effect of rocuronium on expressions of cyclooxygenase-2 and nitric oxide synthase in vascular endothelial cells

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Introduction: Endothelial cells play an important role in a number of physiological and pathological processes, such as inflammation through the response to and release of various endogenous vasoactive compounds to modulate vascular relaxation and constriction. Pain is the first response to injury or infection in the vascular endothelial cells. Injury and infection activates the immune system to produce inflammatory responses. Rocuronium administration is frequently associated severe burning pain. It has been suggested that the pain induced by rocuronium may be due to the activation of nociceptors by the osmolality or pH of the solution, or by the release of endogenous mediators such as histamine, kinin, and other substances mediating inflammation. But, the exact mechanism of rocuronium-induced localized pain has not been established. In the present study, it was investigated whether rocuronium bromide-induced localized pain involves the induction of inflammation in bovine endothelial cells.
Method: Calf pulmonary artery endothelial (CPAE) cells were treated with rocuronium bromide at concentrations of 1,000 ¥ig/ml, 100 ¥ig/ml and 10 ¥ig/ml for 24 hours. The cells in the control group were left untreated. And then Western blot were performed to analyze cyclooxygenase (COX)-1, COX-2, 5- lipoxygenase (LOX), inducible NO synthase (iNOS) and endothelial NOS (eNOS). Prostaglandin (PG) E2 immunoassay, nitric oxide (NO) detection, and immunocytofluorescence were also conducted. The data were analyzed by one-way ANOVA followed by Duncan¡s post-hoc test. The differences were considered statistically significant at $P<0.05$.
Result: The present results show that rocuronium bromide exerted no significant effect on COX-1 protein expression in CPAE cells. But, COX-2, 5-LOX and iNOS protein expressions were increased as a dose-dependent manner. And PGE2 synthesis was also increased as a dose-dependent manner. On the other hand, rocuronium inhibited eNOS protein expression in a dose-dependent manner, and then NO production is suppressed as a dose-dependent manner in the CPAE cells.
Conclusion: These findings show that rocuronium can cause inflammation in vascular endothelial cells that likely occur via increasing COX-2, 5-LOX and iNOS protein expressions. And vasospasm also can be caused by inhibited eNOS protein expression and NO production.

Paper No: 198.00

Phaxancd®, a captisol®-enabled water soluble preparation of alphaxalone for intravenous anesthesia and sedation: comparison of anesthetic properties with propofol and althesin®

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Introduction: Alphaxalone is a neuroactive steroid that causes anesthesia by positive modulation at GABAA receptors. It was the main ingredient of Althesin®, used widely for intravenous anesthesia from 1971 until 1984 when it was withdrawn from clinical practice because of hypersensitivity to the emulsifying agent (Cremophor EL) used in the formulation (1). Captisol® is sulfobutylether ?-cyclodextrin; a molecule with a lipophilic cavity that enables water insoluble drug dissolution in water for human use.
Objectives:

(1) dissolve alphaxalone in water using Captisol®
(2) assess anesthesia and recovery using this preparation and
(3) compare these properties with propofol and Althesin®.

Methods: Alphaxalone (10mg/ml) was prepared using 13% Captisol® and saline (PhaxanCD® - PHAX). An "Althesin®-like" solution of alphaxalone was prepared in 20% CremophorEL as described in the literature (ALTH) (2). Jugular intravenous catheters were implanted in male Wistar rats (150-200g). Separate groups of ten rats each were given intravenous injections of PHAX or ALTH (1.25, 2.5, 5, 10, & 15 mg/kg), or propofol lipid emulsion [10mg/ml; PROP (1.25, 2.5, 3.75, 5, 10, 15, & 20mg/kg). Onset and recovery from anesthesia was assessed by

righting reflex, tail pinch response and rotarod performance. AD50 and AD95 values for righting reflex and tail pinch responses were calculated from probit analysis.

Results: Alphaxalone (10mg/ml) dissolved readily in 13% Captisol®-saline to form a clear colourless solution. Intravenous PHAX caused immediate dose-related sedation and anesthesia accompanied by no abnormal movements. The course of anesthesia was smooth with rapid awakening equal with equivalent doses of ALTH and PROP. The doses that caused all 10 rats to lose righting reflex was: ALTH 5; PHAX 5; & PROP 10 mg/kg respectively. Those doses caused loss of righting reflex for (minutes; mean (SD)): ALTH 3.6(2.18); PHAX 1.9(0.84); PROP 2.5(1.15). The AD50 (AD95) doses for loss of righting reflex for ALTH, PHAX, and PROP (mg/kg) were 2.95(4.39), 2.79(4.26) & 4.63(8.40) respectively. The AD50 (AD95) doses for loss of tail pinch response were 6.46(14.09), 6.56(8.56) & 8.4(14.46) mg/kg for ALTH, PHAX, and PROP respectively.

Conclusions: PhaxanCD causes anesthesia with fast onset, and offset timing equal with propofol and Althesin®. PhaxanCD is twice as potent as propofol. PhaxanCD® may be reintroduced into human anesthesia because the clear water-soluble preparation avoids the CremophorEL hypersensitivity. Furthermore, it is filterable with none of the infection and other issues associated with propofol lipid formulations.

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Paper No: 284.00

Anesthesia management of patients undergoing surgery for hydatid cyst removal

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Introduction: Hydatid disease or echinococcosis is an infection of humans caused by the larval stage of Echicoccus granulosus, E.multilocularis, or E.vogeli. It is prevalent in areas where livestock is raised in association with dogs (1). It is endemic in cattle-and sheep-raising regions of the world, including the Middle East . The liver and lungs are the most common sites of these cysts. Slowly enlarging echinococcal cysts generally remain asymptomatic until their expanding size produces a mass effect on the involved organ giving rise to clinical symptoms. Intraoperative anaesthetic management depends on the anatomical site of the cyst and the risk of cyst rupture during surgery which may lead to anaphylaxis (2). This is a report of our experience dealing with a series of 16 patients scheduled for elective resection of hydatid disease at our institution.

Materials and Methods: The medical charts of patients undergoing surgery for hydatid cyst at Al Ahli Hospital in Hebron over a 30-month period (January 2008-June 2011) were included in this retrospective study. The following data were collected: age and gender of the patients, weight, size, and site of the hydatid cysts, preoperative complications and length of hospital stay.

Result: 16 cases were collected during this period. Eight (57%) were female and six (43%) were male. Their ages range from 13 to 80 years and their body weights from 24kg to 83kg (mean 61.66kg). The size of the cysts ranged from 5.5 x 3.7cm to 30 x30cm, with most located in the right hepatic lobes (fig 1) . The median hospital stay was 3 days). The duration of procedure ranged from 50 minutes to 160minutes (mean 90.7 minutes).

All patients received general anesthesia. For prevention of anaphylactic shock 12 patients (86%) received an average intravenous dose of 200 mg of hydrocortisone. Two(14%) cases of anaphylactic shock occurred during surgery, the 1st was a 10 year old female who received adrenaline 0.25mg, while the second one was 23years old required 8mg of adrenaline and 25mg of promethazine followed by additional large doses of vasopressors and mechanical ventilation for 2 days. No patient died during or after the surgery.

Comments Hydatid cyst surgery represents a major challenge for both the anesthetist and the surgeon. Life-threatening complications such as massive hemorrhage and anaphylactic shock can occur at any time during the procedure but especially in relation to rupture of the cyst. For all cases of hydatid cyst removal it is recommended to insert 2 wide bore venous cannula for rapid infusion of intravenous fluids and blood products, and an arterial cannula to monitor arterial blood pressure. Prophylactic hydrocortisone (200 mg) should be given following induction of anesthesia, and in case of anaphylactic shock, adrenaline should be administered I.V without delay.

Paper No: 400.00

Does type of anesthesia influence cytokine output during major surgery?

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Introduction: There is some evidence to suggest that the type of anesthesia influences the post surgery recurrence rate of various solid tumors1. This is possibly due to changes to host defense mechanisms during anesthesia and surgery.

Objectives: Observe for any immunological response to surgery and anesthesia by noting changes to various

cytokines during major surgery as well as in the post-operative period.

Methods: Blood samples were collected at multiple time intervals. This observational study was part of a larger pharmacological study on intravenous acetaminophen. We estimated cytokines at different time intervals. The data here shows the cytokines at 0 hr (soon after the induction of anesthesia), at 6 hours (end of surgery) and at 48-72 hours (postoperative period). The plasma was stored and later batch analyzed for 27 different cytokines.

Results: There were a total of 20 non-randomized patients in this observational study and the demographic details given in Table 1. One group received only general anesthesia and the 2nd group received spinal or spinal and epidural anesthesia along with a general anesthesia for the surgery. All patients underwent major abdominal surgery. The data were not normally distributed and we used Mann-Whitney U test to compare the 2 groups (Table 2). The results showed some minor changes to the cytokine levels in the postoperative period in those receiving spinal or epidural anesthesia. There were no significant differences between the 2 groups in their clinical observations or outcomes.

Conclusions: This pilot study shows that there is no evidence that inclusion of spinal/ epidural anesthesia reduces the output of cytokines compared to general anesthesia alone to account for the suggestion that cytochemical changes during surgery could account for recurrence of solid malignant tumors.

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Paper No: 507.00

Ulinastatin supresses lipopolysaccharide-induced cyclooxygenase-2 and inducible nitric oxide synthase through the nuclear factor-¥êB inactivation in mouse bv2 microglial cells

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Introduction: Ulinastatin is an intrinsic serine-protease urinary trypsin inhibitor that can be extracted and purified from human urine. Urinary trypsin inhibitors are widely used to treat patients with acute inflammatory disorders such as shock and pancreatitis. And it can be used to reduce blood loss during operation. However, although the anti-inflammatory activities of urinary trypsin inhibitors have been studied, their underlying mechanisms are not yet fully understood.

Methods: In the present study, we evaluated the effect of ulinastatin on lipopolysaccharide (LPS)-induced inflammation using mouse BV2 microglial cells. To accomplish this, we performed a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, reverse transcription-polymerase chain reaction (RT-PCR), Western blot, an electrophoretic mobility gel shift assay (EMSA), nitric oxide (NO) detection, and a prostaglandin E2 (PGE2) immunoassay in mouse BV2 microglial cells.

Results: The results of the present study revealed that ulinastatin suppressed PGE2 synthesis and NO production by inhibiting the LPS-induced expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) mRNA and protein in mouse BV2 microglial cells. Furthermore, ulinastatin suppressed the activation of nuclear factor-¥êB (NF-¥êB) levels in the nucleus.

Conclusions: These findings demonstrate that ulinastatin has analgesic and anti-inflammatory effects that likely occur via suppression of the expression of COX-2 and iNOS through down-regulation of NF-¥êB activity.

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Paper No: 748.00

Correlation between Spectral Edge Frequency (SEF) and implicit memory during general anesthesia

Oded Steiner

Introduction: There are two kinds of memories that might happen after surgery:

1. Explicit memory- recall of events during surgery. Incidence: 0.2-1.2%
2. Implicit memory- behavioral changes towards words /events occurring during surgery. Incidence: ?

It is very important to prevent Awareness under General Anesthesia (AGA), because it may have adverse psychological effects, including Post-Traumatic Stress Disorder-PTSD.

Spectral Edge Frequency (SEF) is a reliable parameter for measuring brain-activity. Its "Optimal range" is between 8-12 Hz. SEF$<$8 Hz – deep anesthesia. SEF$>$12 Hz – superficial anesthesia.

Past studies (1) show that the use of SEF is important during general anesthesia.It helps to prevent AGA.

Reaction Time (RT) is the time that take the patient in response to words heard during anesthesia and read to patient post-operatively.

The purposes of the study:

1. To confirm the relation between SEF during general anesthesia and implicit memory (as measured by RT).

2. To check if there are any differences between reaction-time to neutral words and to emotional words, heard during anesthesia.

Patients and Methodology:

Including criteria:  Hebrew speaking  ASA 1 and 2, aged 18-65 ys.  BMI< 35  Elective surgery: Laparoscopic cholecystectomy Excluding criteria :  Chronic sedative treatment  Psychiatric/Neurologic disorders

 Non-cooperative patient

Implicit memory test:

- Two lists of word-pairs (cue and target).
- First list: Surgical (experimental) - heard during surgical Procedure.
- Second list: Control- not heard during surgical procedure.
- Each list include: ? negatively-emotional valence pairs (e.g. anger-rage) ? neutral pairs (e.g. hill-mountain).
- Four hours post-operatively: patients were provided only with the Cue words (e.g. anger or hill) from both lists: ? surgical ? control (heard for the first time).
- Differences in Reaction-Time (RT) in naming correct target- words Provided to cues from control and surgical lists, were measured.

Results:

Demographic data:  Nr. of patients: 30  Mean age (ys): 43.9  M/F: 7/23

SEF score and End-Tidal Isoflurane:  General SEF levels were significantly negatively correlated with end-tidal isoflurane level ($p < 0.001$).  When the Isoflurane levels were low, the SEF levels were high.

SEF score & Reaction -Time:  SEF level was significantly negatively correlated with RT of correct negatively emotional words in the experimental list ($p < 0.05$).  Patients took less time to provide correct associates (target words) to emotionally negative cues from the experimental list, than to those from the control list.

The findings were correlated with SEF: When the SEF levels were high, the RT was short.

Conclusions:

1. SEF is a sensitive measure of implicit learning and awareness during general anesthesia.

2. Implicit memory can be detected by Reaction Time (RT).

3. There is an inverse relation between a measure of cortical electrical activity (SEF) and implicit memory (as measured by RT to name target words to cue words presented during surgery).

4. Implicit learning during general anesthesia may be stronger for emotionally negative information and is detected by SEF.

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Paper No: 835.00

Comparision of epidural 0.5%bupivacaine with 0.75%ropivacaine on latency and duration for lower limb and lower abdominal surgery

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Introduction: The present study is carried out to compare the latency and duration of action of Bupivacaine and recently introduced Ropivacaine

Objectives: Bupicaine is established regional anaesthetic. But it has got toxic effects on CVS resulting in conduction disturbances, myocrdial depression and CNS effects. Ropivacaine is new regional anaesthetic recently introduced. It has got less toxic effects on CNS and CVS. In the present study, 0.5 % epidural bupivacaine 20 ml is compared with 0.75 % epidural ropivacaine 20 ml to bring out the facts regarding the latency, duration and safety aspects.

Methods: Hospital ethical committee approval and informed consent was taken from all patients. Both males and females were included in the study. ASA grade 1 and grade 2 patients were selected. Age ranged from 20 to 80 years. Patients undergoing elective lower abdominal and lower limb surgeries were selected. Routine investigations and BT, CT were within normal limits. There was no contraindication to epidural anaesthesia. They were divided into 2 groups of 102 patients each; group 1 is bupivacaine epidural, group 2 is ropivacaine epidural. Patient was shifted to operation table. Monitors, pulse oxymeter, NIBP, ECG, ET CO2 were connected. Patient was turned laterally or in seated position. Back was cleaned and draped. Epidural space was identified by loss of resistance technique with 18 G epidural needle and catheter was passed and fixed to back of patient, and patient changed to supine position. After taking necessary precautions, 20 ml local anaesthetic was injected randomly and latency time was noted to loss of pain sensation to pin prick and duration of effect was noted till the loss of regression of 2 segments.

Results: Epidural effects of bupivacaine and ropivacine were studied. Average age is similar in both groups. Sex ratio is similar. Average weight is similar. Latency is similar. Duration of analgesia is prolonged in Ropivacine group with p value <0.0001 (statistically significant). Male: female ratio is similar in both groups (55:47 vs 55:47) average age is similar ($47.49+/-15.37$ years vs $44.23+/-17.17$ yrs) average weight is similar ($64.96+/-5.50$ vs $64.14+/-7.42$) latency is similar ($12.30+/-2.96$ minutes vs $12.37+/-3.31$ mins) duration of action is significantly different($176.02+/-22.05$ mins vs $252+/-45.26$ mins) p value <0.0001

Discussion: In the present study, epidural effects of bupivacaine and ropivacine were studied. Average age is similar in both groups. Sex ratio is similar. Average weight is similar. Latency is similar. Duration of analgesia is prolonged in Ropivacine group with p value <0.0001 (statistically significant). Bupivacaine produces cardiac dysrrhytmias and myocardial depression. In this study no such effects were noted, as dose was kept within therapeutic range. Prolonged effect of ropivacaine is more useful.

Conclusion: The prolonged duration of ropivacine is statistically significant. There were no toxic effects of Ropivacine on CNS and CVS.

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Paper No: 1023.0

Isoflurane sensitivity in complex-I deficient mice

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Introduction: Children with mitochondrial disorders are frequently anesthetized for diagnostic muscle biopsy, but also for a wide range of other operations. These disorders may interfere with vital functions and with response to surgery and anesthesia.

Objectives: Mutations in the NDUFS4 gene cause isolated complex-I dysfunction. NDUFS4 knockout (KO) mice show clinical signs and symptoms resembling those of patients with mitochondrial complex-I disease (1). We examined isoflurane sensitivity in the NDUFS4-KO mouse model, which exhibit an isolated mitochondrial complex-I deficiency.

Methods: We investigated seven NDUFS4-KO mice, five NDUFS4 heterozygous (HZ) mice and five wild type (WT) mice. Animals were placed inside an airtight box, breathing spontaneously while isoflurane was administered. The concentration of anesthetic was measured intermittently at the venting port of the chamber. After equilibration the response to electrical stimulation to the hind paw was recorded. When a response was noticed the anesthetic concentration was increased stepwise, until there was no response. At this point the anesthetic concentration was decreased until there was a return of response. The minimum alveolar concentration (MAC) was determined as the average concentration of isoflurane at loss and return of response to pedal electrical stimulation. Statistical analysis was done using the Students-t-test for unpaired data, $p<0.05$ was significant.

Results: MAC for isoflurane was significantly lower ($p<0.001$) in NDUFS4 KO mice compared to WT and HZ mice: 0.8 (SD 0.29) vs 1.55 (SD 0.29) and 1.55 (SD 0.11) respectively. There was no difference in isoflurane sensitivity between wild type and heterozygous mice. The KO mice showed severe respiratory depression at low isoflurane concentrations. Mean respiratory frequency was 102 (SD 17.0), 104 (SD 11.7) and 79 (SD 10.2) in respectively WT, HZ and KO mice, with significant difference between KO and non-KO mice (p 0.001).

Conclusions: Complex I was the most sensitive of any step in oxidative phosphorylation to inhibition by volatile anesthetics in vitro (2). In a simple animal model, C. elegans, a clear correlation existed between mitochondrial complex I oxidative phosphorylation capacity and volatile anesthetic sensitivity (3). Morgan et al. found profound hypersensitivity to volatile anesthetics in a subset of children with defects in complex I function, requiring very low sevoflurane concentrations to reach a Bispectral Index (BIS) value of 60 (4). In accordance with these previous findings, our study showed an increased sensitivity to isoflurane in complex-I deficient mice.

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Paper No: 1043.0

Stress hormones response in cardiac surgery

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Stress Hormones In Cardiac Surgery, Vicente

Stress response to surgery is modulated by different factors such as the magnitude of the injury, the type of procedure and anesthesia. Stressful experiences induce important hormonal changes in the cardiovascular system and hypothalamic-pituitary-adrenal axis, reflecting a close and bidirectional relationship.

Aim: To study hormonal changes induced by cardiac surgery. Steroid hormones glucocorticoids (ACTH – cortisol), mineralocorticoids (aldosterone), androgens (dehydroepiandrosterone or DHEA) and renine were determined in cardiac surgery patients.

Method: A set of hormones were determined in 50 patients, free of endocrine diseases undergoing programmed cardiac surgery. Hormone tests included steroid glucocorticoids (ACTH–cortisol), mineralocorticoids (aldosterone), androgens (dehydroepiandrosterone or DHEA), renine and growth factor insulin type I (IGF-I. Blood samples were extracted at baseline (48h prior), first 24 hours and by the 5th day following cardiac surgery.

Results: Our patients were middle aged, overweight males (70% males, mean age 59.6 y-o, BMI 26,2) and preserved ejection fraction (56 +16). Total surgery duration was 240 minutes of anesthesia, 66 minutes of cardiopulmonary bypass, and 111 minutes of myocardial ischaemia on average. The mean time to extubation was 14 hours, with 3.4 +1.2 days of ICU stay; only 4% required intra aortic balloon. As shown in table 1, most hormones increased significantly with surgery, approaching baseline values by the by the 5th day. IGF-I remained unchanged, Significant and early changes in cortisol, aldosterone and renine levels were found attributable to surgical stress, volume depletion and hydroelectrolyte imbalance.

Conclusion: our data show an early and swift activation of the hypothalamic-pituitary-adrenal axis responding to stress and volume or hydroelectrolyte imbalance.

Baseline	First	24 h	5th day
Cortisol μg/dl	19.23	53.5 ($p<0.005$)	37.6 ($p<0.005$)
ACTH pg/ml	13.93	16.14	11.65
DHEA μg/dl	948.66	1270	1367($p<0.005$)
Aldosterone ng/dl	97.34	163.98 ($p<0.005$)	140.87
Renine ng/dl	12.48	19.68 ($p<0.005$)	14.10

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Paper No: 1048.0

Transient functional hypothyroidism induced by cardiac surgery

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Functional Hypothyroidism in Cardiac Surgery, Vicente

It is well known that thyroid and growth factor hormone levels change in response to stress, fear or emotions. But little is known of the magnitude and duration of this response.

Aim: To evaluate the changes in the thyroid axis, growth hormone and growth factor insulin type I (IGF-I) following cardiac surgery, their timing and the possible causes, we studied 50 patients, without thyroid disease. All patient underwent programmed cardiac surgery (PCS), half were coronary artery bypass graft surgery and half valvular. Hormones were determined in the previous 48h, in the first 24 hours following the procedure and by the 5th day.

Method: Up to 70% of our cases were males, with a mean age of 59.6 years old, the body mass index was 26,2 and ejection fraction 56+16 on average. The total surgery duration was divided in subsets: anesthesia 240 minutes, cardiopulmonary bypass 66 minutes, myocardial ischaemia 111 minutes on average. The mean time to extubation was 14 hours and the ICU stay was 3.4+1.2 days. Intra aortic balloon was used in 4%.

Results: GH increased significantly in the first 24 hours, decreasing to baseline values by the 5th day. On the other hand IGF-I remained unchanged. Conclusions: A temporary hormonal downfall of thyroid hormones occurs following cardiac surgery; functional hypothyroidism could be related to protection mechanisms responding to surgical injury. Growth hormone responds to cardiac surgery as a stress hormone, whereas IGF-I remains unchanged even though it's expression is mediated by GH.

Baseline	First	24 h	5th f-u day
TSH (μ/ml)	2.24	1.12 ($p<0.05$)	2.56
T3 (ng/dl)	0.85	0.45 ($p<0.05$)	0.70
Free T3 (ng/dl)	4.88	3.95 ($p<0.05$)	4.44 ($p<0.05$)
Inverse T3 (ng/dl)	30.51	55.29 ($p<0.05$)	37.18 ($p<0.05$)
T4 (μ/dl)	83.60	63.12 ($p<0.05$)	79.09
Free T4 (ng/dl)	1.34	1.13 ($p<0.05$)	1.33
GH (ng/ml)	1.64	7.8 ($p<0.05$)	2.5
IGF1 (ng/ml)	189.87	180.60	167.0

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Paper No: 1109.0

Central and peripheral opioid receptor blockade prevent propofol-induced hypotension in rats

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Introduction: Propofol is an anesthetic agent that is largely used in general anesthesia and intensive care and that occasionally exerts a prominent hypotensive effect via myocardial and vascular mechanisms.
Objective: The objective of the present study was to evaluate the role of opioid receptors in the hypotensive effect of propofol.
Methods: In this experimental pharmacological study, pentobarbital-anesthetized rats were submitted to one of the following two protocols: Protocol 1, systemic (intravenous) or central (intracisternal) infusion of propofol with simultaneous analysis of the dose-response curve of the mean arterial pressure (MAP) and mesenteric intravital microscopy; and Protocol 2, systemic or central pretreatment with naloxone followed by intravenous or central administration of propofol.
Results: Protocol 1: Intravenous administration of propofol induced a significant dose-dependent reduction in the MAP (6%, 31% and 36% reductions with the 2.5, 7.5 and 25-mg/kg dose, respectively; $P < 0.05$ for the 7.5 and 25 mg/kg doses). Intracisternal propofol induced a significant dose-dependent reduction in the MAP (9%, 5%, 20%, and 31% reduction with the 0.1, 1.0, 10, and 100-μg dose, respectively; $P < 0.05$ for the 10 and 100-μg doses). Neither intravenous nor intracistenal propofol induced alterations in the mesenteric microcirculation ($P > 0.05$). Protocol 2: Intravenous (7.5 mg/kg) or intracistenal propofol (10 μg) induced significant hypotensive effects of 45% and 35% reductions in the MAP, respectively ($P < 0.05$).
Discussion: Neither the systemic nor the central pretreatment with naloxone (5 mg/kg and 100 μg, respectively) induced any significant alterations in the MAP in any group. However, both systemic and central pretreatment with naloxone prevented the hypotensive effect of the systemic or central injection of propofol.
Conclusion: This experimental pharmacological study demonstrated that the blockage of central and peripheral opioid receptors prevents propofol-induced hypotension, suggesting that these receptors may be involved in the cardiovascular alterations elicited by propofol administration in anesthetized rats.

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Upregulation of HMBG1 and TLR -4 cardiac right atrium mRNA expression during CABG surgery – the effects of sevoflurane conditioning and postconditioning

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Introduction: Immune system activation and the inflammatory response are important components of ischemia/reperfusion injury (I/R) during cardiac surgery with the cardiopulmonary bypass (CPB). High-mobility group box-1 (HMGB1) protein released by activated immune cells is a crucial mediator of inflammation. Toll-like receptors (TLR2, TLR4) are key mediators in myocardial injury and inflammation in the settings of I/R, and they participate in the HMGB1 signalling pathways. Sevoflurane exhibits protective, anti-inflammatory effect on the myocardium in response to I/R injury, both in pre and postconditioning fashion.
Objectives: We evaluated the sevoflurane conditioning and postconditioning effect on the mRNA expression of HMBG1,TLR2 and TLR4 in the cardiac right atrium, and HMBG1 serum kinetics, together with the pro-inflammatory biomarkers release (IL-6, TNF-alpha) in patients scheduled for first-time elective CABG-CPB surgery.

Methods: Based on the anesthetic technique used, patients were divided into 3 groups: those who received sevoflurane conditioning (n=20), sevoflurane postconditioning (n=20), and those who received TCI propofol (n=20) anesthesia. Blood samples for HMBG1, IL-6, TNF- alpha, and Troponin I were collected before the induction of anesthesia, and at 6 and 24 hours after the surgery. Serum changes in HMBG1 level were determined with ELISA method .Total RNA was isolated twice (pre-CPB and post-CPB) from the right atrial appendage tissue samples using the AllPrep® DNA/RNA/ Protein Kit. The relative amount of HBOX1, TLR2, and TLR4 mRNA was determined by quantitative real time PCR with 7900HT Fast Real-Time PCR System.

Results: Serum HMBG1 protein concentrations increased significantly from 1,6 ± 1,0 ng/mL at baseline to 2,8 ± 1,7 ng/ mL at 6 hours after the surgery (p=0,006), and remained high 24 hours after surgery (2,6 ± 1,2 ng/mL, p=0,03). The level of IL-6, TNF- alpha, and Troponin I was significantly higher 6 and 24 hours after the surgery in all patients, compared to the baseline values. The mRNA expression for HMBG1 was elevated during the surgery (RQ 1,41 ± 0,66) and correlated with higher protein concentration of HMBG1 measured in serum at 6 h after the surgery (R=0,53, p=0,04).The mRNA expression for TLR4 increased in all study groups during the surgery (RQ 1,49 ± 0,61); there was no change in mRNA expression for TLR2 (RQ 2,0 ± 4,33).

Conclusion: CABG-CPB surgery stimulated a significant inflammatory response, but the method of anaesthesia did not have any major influence on the intensity of this response. Cardiac right atrium HMBG1 and TLR4 mRNA expression was upregulated in the early post bypass period but it was not modulated by sevoflurane anesthesia.

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