4AP2-2

**Hemodynamic stability of xenon during general anaesthesia for carotid endarterectomy in old patients**

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**Background and Goal of Study:** General anaesthesia (GA) for carotid endarterectomy (CEA) requires a tight hemodynamic control in order to limit neurological and cardiovascular complications. This study aimed to demonstrate that the hemodynamic stability is better respected with Xenon than with sevoflurane during CEA under GA in old patients.

**Materials and Methods:** This randomized controlled trial was approved by our local ethic committee (CPP ParisVI). Patients older than 65 years scheduled for CEA were included. Anesthesia was induced in both groups with propofol and remifentanil and a non-depolarizing neuromuscular blocking agents (atracurium) was used for tracheal intubation. For the maintenance phase, patients were randomly allocated to either Xenon (60%) or Sevoflurane (1.7%). 30% of oxygen was used for all patients. Both groups received remifentanil targeted concentration of 2 ng/ml and adapted according to clinical needs and spontaneous EEG (BIS) monitoring. Continuous recording of arterial blood pressure (ABP), airway pressure and electrocardiogram was done (Biopac(tm)). Tachycardia, bradycardia, hyper and hypotension were defined as a change of more than 40% compared to the basal state recorded at rest before induction. Intraoperative hemodynamic variability was calculated using sequential analysis of one minute provided by the continuous recordings of ABP. After integration over the time, hemodynamic variability was expressed as a continuous variable in % min. Fisher exact test and non parametric Wilcoxon test were used to compare these endpoints.

**Results and Discussion:** 46 old patients (mean age was 75 +/- 7) were included in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane</th>
<th>Xenon</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=23)</td>
<td>(n=23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0 (0%)</td>
<td>2 (9%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Hypotension</td>
<td>22 (86%)</td>
<td>10 (43%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phenylephrin (ng)</td>
<td>750 +/- 375</td>
<td>300 +/- 300</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ephedrin (mg)</td>
<td>30 +/- 14</td>
<td>16 +/- 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nicardipin (mg)</td>
<td>0 (0%)</td>
<td>2 (9%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Global hemodynamic variability (%.min)</td>
<td>1080 +/-440</td>
<td>230 +/-60</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** 46 old patients (mean age was 75 +/- 7) were included in the two groups.

4AP2-3

**Xenon reduces the gradient of blood pressures between radial blood pressure and occluded carotid artery during carotid endarterectomy: A randomized controlled study**

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**Background and Goal of Study:** During the cross clamping of the carotid required by Carotid endarterectomy (CEA), the brain circulation is mainly supplied by the contralateral carotid . A residual carotid blood pressure (RCBP) reflecting this can be measured. In this study we defined a gradient of pressures (Gp), as the difference between the systemic arterial blood pressure (sABP) and the RCBP. The aim of this randomized study was to compare this Gp during CEA conducted under general anesthesia (GA), with Sevoflurane (S) or Xenon (X).

**Materials and Methods:** This randomized controlled trial was approved by our local ethic committee (CPP ParisVI). Patients older than 65 years scheduled for CEA were included. Anesthesia was induced in both groups with propofol and remifentanil. For the maintenance phase, patients were randomly allocated to either X (60%) or S (1.7%). Both groups received remifentanil targeted concentration of 2 ng/ml and adapted according to clinical needs and BIS monitoring. Continuous recording of systemic arterial blood pressure (sABP), and of RCBP was done (Biopac(tm)). RCBP was obtained by the placement, by the surgeon, of a Fogarty’s probe in the carotid during the cross clamping. The primary endpoint, Gp, was calculated directly, and the means of these Gp over the time were compared using non parametric Wilcoxon test.

**Results and Discussion:** 24 patients were included in this study, 12 in each group. No postoperative neurological adverse event has been observed. The mean cross clamping duration was 22 +/- 5 minutes, and was not different in the groups. Mean Gp of the X Group was inferior (p < 0.001) compared to the one observed in the S group.

![Graph showing hemodynamic stability comparison between Xenon and Sevoflurane](image)

**Conclusions:** The use of Xenon to conduct GA for CEA reduced the observed mean Gp during cross clamping compared to Sevoflurane. This suggests that X provides a better regulation of the cross clamping than S. Nevertheless, these physiological observations need to be confirm by neurological outcomes.

4AP2-4

**Propofol attenuates apoptosis induced by angiotensin II via the PI3-kinase/Akt pathway in neonatal rat cardiomyocytes**

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**Background and Goal of Study:** Propofol protects cells against oxidative injury in several organ, but the mechanism by which it exerts the cardioprotective effect is not well established. Angiotensin II (Ang II) can induce cardiomyocyte apoptosis which has an important role in the transition from compensatory cardiac remodeling to heart failure. In the present study, we evaluated the effects of propofol on Ang II-mediated cardiomyocyte apoptosis.

**Materials and Methods:** Cultured cardiomyocytes from neonatal rats were stimulated with Ang II. Apoptosis was evaluated by measuring caspase 3 activity and by TdT-mediated dUTP nick-end labeling (TUNEL) method. To further investigate the underlying mechanisms, the quantity of cleaved caspase-3, cytosol cytochrome c release, BcL-xL expression, and ROS generation were examined. The effects of propofol on Akt phosphorylation and the involvement of PI3K/Akt pathway also assessed.

**Results and Discussion:** It was found that incubation with Ang II (0.1 µM) for 48 h increased cardiomyocyte apoptosis. Administration of propofol (3-10 µM) significantly decreased this Ang II-induced apoptosis. These results suggest that propofol abates cardiomyocytes from Ang II-induced apoptosis possibly via reduced the quantity of cleaved caspase-3, and cytosol cytochrome c, and increased BcL-xL expression, and inhibiting the increased ROS generation. In addition, propofol was found to increase the Akt phosphorylation in cardiomyocytes. The siRNA transfection for Akt significantly reduced propofol-induced Akt phosphorylation and propofol’s protective...
tive effect. Pretreatment with the PI3K inhibitors wortmannin and LY294002 inhibited serine phosphorylation of Akt in dose-dependent manners. These findings indicate that propofol induces Akt phosphorylation via the PI3K/Akt pathway. Our data provide the first evidence that the anti-apoptotic effect of propofol may be an important underlying mechanism accounting for its cardioprotect-
tive action.

Conclusion(s): Propofol might potentially be developed to treat heart failure or other apoptosis-related heart diseases if further studies were performed to define and clarify rationale for its clinical use.

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4AP2-5
Isoflurane and Mg²⁺ as regulators of Ca²⁺ uptake in cardiac mitochondria
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Background and Goal of Study: Mitochondrial (m) free Ca²⁺ ([mCa²⁺]) may regulate oxidative energy metabolism, is implicated as an upstream factor that regulates mitochondrial (m) Ca²⁺ uptake despite a slight fall in mCa²⁺ in response to different concentrations of CaCl₂ in the presence or absence of mitochondria

MATERIALS AND METHODS: Rodent cardiac mitochondria were isolated by differential centrifugation, energized with pyruvate with or without malate, and state 3 respiratory function was tested with a Clark-type electrode during states 2-4 respiration, i.e. before, during and after adding 250 μM ADP.

Results and Discussion: Adding 0.25 and 0.5 mM CaCl₂ to the buffer containing 1 mM EGTA increased [mCa²⁺] in a dose-dependent manner at 0 MgCl₂; the presence of 0.5 and 2 mM MgCl₂ reduced the mCa²⁺-uptake in both groups. Adding 0.5 mM MgCl₂ did not increase mCa²⁺, but 2 mM MgCl₂ increased mCa²⁺- uptake in both groups. State 4 was faster with added MgCl₂. Isoflurane at 0.5 to 2 mM dose-dependently increased mCa²⁺-uptake despite a slight fall in ΔΨm, but increased duration of state 3 respiration as well as the duration of the ADF-induced rise in [mCa²⁺]; moreover, isoflurane increased redox state (increased NADH), possibly by inhibiting complex I.

Conclusions: Mg²⁺ interferes with mCa²⁺-uptake via mCU whereas isoflurane enhances mCa²⁺- uptake, possibly by modulating mCU function. Together, these factors appear to modulate mCa²⁺-uptake and thereby alter mitochondrial function in different ways so that in health or disease a change in Mg²⁺ may alter the mitochondrial effects of isoflurane.

4AP2-6
Genetic effects on propofol induced hypotension
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Background and Goal of Study: Providing an optimal brain oxygenation is a mainstay during Carotid Endarterectomy (CEA) and the Near-Infrared Spectroscopy (NIRS) method provides data on cerebral oxygen saturation level (rS02). A decrease of more than 12% of rS02 during carotid clamping has been correlated with an increase of post-op neurological damage after CEA (1). Xenon gas properties on hemodynamic control could be of benefit for general anesthesia of CEA (2-4).

This study evaluated the effect on rS02 values modification during CEA surgery when performed under Xenon (Xe) or propofol (P) general anesthesia (GA).

Materials and Methods: Prospective controlled study in patients scheduled for CEA. After informed consent and following a cluster design, patients were assigned to Xe (80% inhaled) or P (Target Controlled Infusion (TCI) group for the maintenance of GA, with 32% FIO2 and remifentanil TCI adapted according to clinical needs. Induction was identical for groups (propofol, cisatracurium & remifentanil). For each patient rS02 was measured by InvoSom (Somanetics), haemodynamic parameters by invasive blood pressure and arterial Pulse Pressure Variation (PPV)(IntelliVue®,Philips ), anesthesia depth by BIS® (Aspect). Values were compared using Wilcoxon and Fisher tests.

Results and Discussion: 74 patients were included, 37 per group (Xe or P), with no difference in general, medical history, baseline treatments, and surgical characteristics. In the Xe group, -to maintain a similar level of blood pressure within groups and during clamping, fluid load (850±240 vs 1020±315ml, p= 0.01) and ephedrine amount (9±11vs 16±18 mg, p < 0.04) were lower, -patients with > 12% decrease of rS02 were 1/3 less numerous (p=0.041) during carotid clamping, -perop use of nicardipine (n:8 vs 1p= 0.041) and increase in remifentanil dose (4.5± 2 vs 3.3± 1.2 ng/ml,p=0.001) were higher, - all patients could be “on table” extubated whereas for 30% in the P group the extubation was delayed (mean 25±13min).

Conclusion(s): In CEA, the use of Xe for the GA maintenance allows a better rS02 than P during carotid clamping. This benefit has to be confirmed in randomized controlled study more particularly for patients at post-operative neurological risk.

Acknowledgements: Project Grant, 2008