**Title:** METABOLIC CHANGES IN THE MYOCARDIUM FOLLOWING DISCONTINUANCE OF INFUSIONS OF DOPAMINE AND DOBUTAMINE IN DOGS.

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**Introduction:** Both dopamine (DA) and dobutamine (DB) have positive inotropy and maintain aerobic metabolism during infusions. The plasma levels of DA and DB following discontinuation of infusion returned to the levels before infusion, which indicated their rapid elimination. However, abrupt discontinuance of DA and DB infusions causes hemodynamic changes in certain patients. The aim of this study is to investigate the myocardial metabolism following discontinuation of infusions of DA and DB.

**Methods:** Twelve mongrel dogs weighing 10-15 kg were anesthetized with 25 mg/kg of sodium pentobarbital. After endotracheal intubation, animals were mechanically ventilated by a Servo 900-B ventilator under FiO2 of 0.4 under muscle relaxation with pancuronium bromide. Supplemental doses of pentobarbital and pancuronium were administered as required. Tidal volume was set at 15 ml/kg and respiratory rate was adjusted to keep PaCO2 at approximately 40 mmHg.

A Swan-Ganz catheter was inserted and advanced to the pulmonary artery for determination of cardiac output by injection of a 5 ml cold bolus of saline using a thermodilution computer, and cardiac index (CI) was calculated by standard formulae. A pigtail catheter was inserted and advanced into LV. The first derivative of LV pressure was computed and specific points on the signals (dP/dt) was automatically detected.

A pericardiectomy was performed through midline sternotomy. After systemic heparinization, a Mazzaz's cannula was inserted into the coronary sinus. Coronary sinus blood flow was induced to this cannula and detected using an electromagnetic flow probe and a synchronized electromagnetic flow meter. Lactate and pyruvate levels of arterial (A) and coronary sinus (CS) blood were determined enzymatically. Oxidation-reduction electrical potential (Eh) and myocardial lactate extraction (MLEx) were calculated as:

\[ Eh = \frac{204 - 30.7 \times \log [lactate / pyruvate] (mv)}{MLEx} = \frac{lactate(A) - lactate(CS)}{Lactate(A) \times 100 (\%)} \]

The 12 dogs were divided into two groups, DA group and DB group. After the baseline measurements, all dogs of each group received continuous infusion of 10 mcg/kg/min of DA or DB intravenously. The same measurements were obtained after 30 minutes of infusion of each catecholamine. The infusions were then terminated and the same measurements were repeated 15, 30 and 60 minutes following discontinuance of each catecholamine.

All values were expressed as mean±SD and statistical analysis was performed by the paired t-test.

**Results:** Results are summarized in the table and figures. Hemodynamic parameters returned to the almost baseline levels following discontinuation of infusions (Table). MLEx (Fig 1) and the differences of Eh between A and CS (AEh, Fig 2) were significantly decreased immediately after discontinuation of DA infusion and there were significant differences between the groups.

**Discussion:** In this study, we investigated the myocardial metabolism during and following infusions of DA and DB in anesthetized dogs. It is considered that Eh are characterized as redox potential of the myocardium and that reduction of MLEx suggests production of lactate in the myocardium. Therefore, changes in these 2 parameters indicate that anaerobic metabolism of the myocardium is accelerated immediately after discontinuation of DA infusion while aerobic metabolism is maintained after discontinuation of DB infusion. However, the mechanism of this change is unknown and further study is needed.

**Table. Parameters during and following DA and DB infusions**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>during</th>
<th>15min</th>
<th>60min</th>
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</thead>
<tbody>
<tr>
<td>CI DA</td>
<td>2.75±0.9</td>
<td>2.32±0.3</td>
<td>2.54±0.3</td>
<td>2.51±0.5*</td>
</tr>
<tr>
<td>DB</td>
<td>3.1±0.7</td>
<td>3.3±0.9</td>
<td>2.5±0.3</td>
<td>2.61±0.5*</td>
</tr>
</tbody>
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\[ dp/dt (DA) = 1677±248; 2023±262; 1755±323; 1792±393 \]

\[ dp/dt (DB) = 1607±198; 2160±202; 1597±124; 1598±95* \]

*: denotes significant differences between DA and DB groups (p<0.05), t: indicates significant differences compared with value during DA/DB (p<0.05).