

**Title** : EFFECTS OF HYPEROXEMIA ON MYOCARDIAL BLOOD FLOW AND OXYGEN CONSUMPTION IN AN ISOLATED RABBIT HEART.

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**INTRODUCTION.** Breathing an enriched O<sub>2</sub> mixture is usually recommended in patients with coronary artery disease (CAD) during the perioperative period. Indeed, breathing O<sub>2</sub> may decrease coronary blood flow (CBF) as a result of a reduction in myocardial O<sub>2</sub> consumption (MVO<sub>2</sub>) due to a decrease in heart rate mediated by the automatic nervous system (1). However, the decrease in CBF, might also be the consequence of a direct vasomotor effect from arterial O<sub>2</sub> partial pressure (PaO<sub>2</sub>) (1). In this hypothesis, high PaO<sub>2</sub> might paradoxically limit myocardial O<sub>2</sub> supply. A denervated isolated heart preparation is a well suited model to test this last hypothesis.

**METHODS.** Standard human stored blood was washed, centrifuged and resuspended in Krebs-Henseleit Buffer. Blood was equilibrated and oxygenated to achieve a normal acid-base balance, PaO<sub>2</sub> and O<sub>2</sub> content (CaO<sub>2</sub>). Then, blood was shared into 2 separate oxygenation circuits to achieve 2 distinguishable PaO<sub>2</sub> levels : CONTROL BLOOD and HIGH PaO<sub>2</sub> BLOOD. Hemoglobin concentrations (Hb) were adjusted to obtain the same O<sub>2</sub> content for the 2 PO<sub>2</sub> levels. Nine New Zealand albino male rabbits were anesthetized with ether. The heart was quickly excised by thoracotomy and prepared for cannulation under immersion in a cold isotonic saline solution. The aorta was mounted on a cannula and retrograde perfusion was performed with control blood. The speed of the coronary pump, which reflects coronary blood flow (CBF), may vary to maintain a perfusion pressure (PP) of 70 mmHg constant (FREE CBF). The coronary sinus drainage was collected via a cannulated pulmonary artery. A cannulated fluid-filled balloon was placed via a left atrial incision in the left ventricle (LV) and attached to a pressure transducer to monitor LV pressure. The balloon was inflated to maintain constant LV volume and to produce a LV end-diastolic pressure (LVEDP) of 15 mmHg. The right ventricle was paced at a constant rate of 190 b/min. After a rewarming period of 30 min, the first set of measurements was performed under CONTROL BLOOD. The second set was obtained after switching to HIGH PAO<sub>2</sub> blood.

Additional experiments were conducted in 6 hearts. In these experiments, coronary blood flow was maintained constant (CONSTANT CBF). The perfusion pressure may vary and reflects changes in coronary vascular resistances. Measurements were performed at the 2 levels of PaO<sub>2</sub>.

Measurements included : CBF, LV developed pressure (LV systolic pressure minus LVEDP) (LVDevP) and its first positive and negative derivatives (dP/dt max and dP/dt min), PaO<sub>2</sub>, CaO<sub>2</sub>, coronary sinus PO<sub>2</sub> (PcsO<sub>2</sub>) and O<sub>2</sub> content (CcsO<sub>2</sub>). MVO<sub>2</sub> was derived. Data were analysed using the paired Student's t-test, and expressed means  $\pm$  SD.

**RESULTS** are expressed in table 1.

Switching from CONTROL to HIGH PaO<sub>2</sub> BLOOD with FREE CBF induced a significant decrease in CBF and MVO<sub>2</sub>. LVDevP and its positive and negative derivatives did not vary significantly. These effects were reversible.

Switching from CONTROL to HIGH PaO<sub>2</sub> BLOOD with CONSTANT CBF induced a significant rise in perfusion pressure. CcsO<sub>2</sub> significantly increased and MVO<sub>2</sub> decreased. No change in myocardial performance was observed.

**DISCUSSION.** Since the heart was denervated, the coronary vasoconstriction in response to high PaO<sub>2</sub> at a constant CaO<sub>2</sub>, observed in these experiments cannot be explained by reflex adaptations mediated by the autonomous nervous system. Although its main determinants did not change, a decrease in MVO<sub>2</sub> was associated with the coronary vasoconstriction. In addition, experiments at constant CBF excluded an influence of O<sub>2</sub> supply on MVO<sub>2</sub>. This decrease may be likely explained by either a decrease in capillary density or an increased flow heterogeneity. Thus, high PaO<sub>2</sub>-induced vasoconstriction might be explained by a direct vasomotor effect of PaO<sub>2</sub> (arteriolar PO<sub>2</sub> sensors) (2). These results may be clinically relevant when an enriched O<sub>2</sub> mixture is administered in patients with CAD.

**Table 1** : Coronary hemodynamics, myocardial performance and consumption.

	FREE CBF		CONSTANT CBF	
	CONTROL	HIGH PAO <sub>2</sub>	CONTROL	HIGH PAO <sub>2</sub>
PaO <sub>2</sub> mmHg	125 $\pm$ 6	380 $\pm$ 27**	148 $\pm$ 3	432 $\pm$ 28**
CaO <sub>2</sub> ml/100ml	12.8 $\pm$ 0.2	13.0 $\pm$ 0.2	15.3 $\pm$ 0.3	15.2 $\pm$ 0.2
CBF ml/min/g	2.55 $\pm$ 0.37	1.91 $\pm$ 0.24**	1.98 $\pm$ 0.12	1.98 $\pm$ 0.12
PP mmHg	74 $\pm$ 2	75 $\pm$ 1	80 $\pm$ 2	104 $\pm$ 4**
PVO <sub>2</sub> mmHg	37 $\pm$ 1	39 $\pm$ 1	30 $\pm$ 1	32 $\pm$ 1
CvO <sub>2</sub> ml/100ml	10.2 $\pm$ 0.5	10.2 $\pm$ 0.5	8.5 $\pm$ 0.2	9.4 $\pm$ 0.2*
MVO <sub>2</sub> ml/min/g	0.10 $\pm$ 0.01	0.08 $\pm$ 0.01**	0.13 $\pm$ 0.01	0.11 $\pm$ 0.01*
LVDevP mmHg	78 $\pm$ 6	74 $\pm$ 6	81 $\pm$ 3	79 $\pm$ 2
dP/dtmin mmHg/s	1132 $\pm$ 109	1141 $\pm$ 117	1532 $\pm$ 142	1493 $\pm$ 116
dP/dtmax mmHg/s	-673 $\pm$ 32	-687 $\pm$ 46	-920 $\pm$ 76	-912 $\pm$ 64

\* : p < 0.05 vs CONTROL, \*\* : p < 0.01 vs CONTROL

#### REFERENCES.

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