Experimental Studies

Is Coronary Sinus Blood Oxygen Tension Behavior Determined by Myocardial Oxygen Tension Variation during Cardiac Reperfusion?

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SUMMARY
The relationship between coronary sinus blood oxygen tension (CSPO₂) and myocardial oxygen tension (MPO₂) variations during cardiac ischemia and reperfusion was studied in anesthetized open-chest dogs. Oxygen tension was measured by a polarographic method. Ischemia resulted in a slightly decreased CSPO₂ and a more pronounced reduction of MPO₂. After reperfusion the CSPO₂ rose rapidly and transiently before it returned gradually to the control level. By contrast, during the recovery period, the MPO₂ increased slowly, with recovery occurring long after the peak of CSPO₂. These data suggest that during the reperfusion phase, the CSPO₂ variation is probably due to opening of the myocardial arteriovenous shunts instead of an increase of flow through the myocardial capillary bed.

Additional Indexing Words:
Myocardial oxygen tension  Coronary sinus blood oxygen tension
Polarography  Cardiac ischemia  Reperfusion

Previous studies have revealed that coronary sinus blood oxygen tension (CSPO₂) increases rapidly and phasically after coronary occlusion or anoxic cardiac arrest. The mechanism involved in this CSPO₂ response is not well established. The high oxygen saturation of the coronary venous blood is believed to be the result of an increased flow through the capillary bed, causing a decrease in the myocardial oxygen extraction or arteriovenous shunting. The first hypothesis was based on authors who verified that reactive hyperemia is always associated with an elevation of myocardial oxygen tension (MPO₂) values above those observed before coronary occlusion. However, changes in CSPO₂ and MPO₂ were not recorded simul-
Simultaneously and continuously. Simultaneous measurements are needed to test the hypothesis that a quick and transient elevation of CSPO$_2$ is dependent on MPO$_2$ variations. This study was undertaken to determine if the changes in oxygen tension of the coronary sinus effluent after coronary occlusion are determined by changes in intramyocardial oxygen tension. The CSPO$_2$ and MPO$_2$ were recorded simultaneously by a polarographic method during cardiac ischemia and reperfusion.

**Methods**

Studies were performed in 7 male adult mongrel dogs, weighing from 15 to 20 kg. They were anesthetized with sodium pentobarbital (20 mg/kg/iv) and morphine (2 mg/kg/im); additional anesthetic was administered as required. After endotracheal intubation, respiration was maintained with a mechanical respirator and supplementary oxygen was administered to keep the arterial pH, oxygen and carbon dioxide tensions within the physiological range. The thorax was opened and the heart suspended in a pericardial cradle so that the anterior aspect of the left ventricle was exposed. The initial portion of the left anterior descending artery was dissected free so that it could be occluded when desired and the probe of an electromagnetic flowmeter (Biotronex BL610) was applied. A zero-flow reference were obtained by occluding the vessel distal to the probe. The calibration was done with isolated arteries of suitable length and diameter, which were cannulated at both ends and perfused with blood from a gravity feed reservoir into a graduated cylinder. Aortic pressure was measured by means of a catheter placed in the thoracic aorta.

The myocardial oxygen tension was measured in the endocardial layers of the left ventricle perfused by left anterior descending artery (LAD) with a cyanomethacrylate glue insulated platinum electrode (183$\mu$m diameter). The tip of the electrode was freed from insulation for 1 mm. In order to fix the electrode in the surface of dry myocardium, a thin layer of a cyanomethacrylate glue was applied to its base, just before its implantation in the muscle. The electrodes were also sutured in the myocardium.

For the measurement of coronary sinus blood oxygen, a glass insulated platinum electrode (0.1–0.2 mm free of insulation) with 1 mm of diameter was positioned in a silastic tube. This catheter was inserted at least 2–3 cm into the coronary sinus via the right atrium. The entire volume of coronary sinus blood flow was withdrawn at a rate of 12 ml/min, and returned to the dog via the right external jugular vein. Koberstein et al.\(^7\) have demonstrated that the sinus coronary blood may be withdrawn at this rate without atrial
contamination.

The electrodes used to measure oxygen tension were polarized at $-0.6 \, \text{V}$ and the circuit was completed using a reference calomel half-cell electrode with a saline bridge connected directly to the subcutaneous tissue of the animal. The polarographic current flow resulting from the diffusion of oxygen to the platinum electrodes was measured by a current amplifier* with a time constant of 1.1 sec. Since the polarographic current is directly proportional to the concentration of oxygen, the relative current variation allows one to infer the relative $\text{PO}_2$ variations.

The "in vitro" response of each single electrode was determined for different concentrations of oxygen in saline solution at room temperature. To verify if the electrodes were responding properly after myocardial fixation, LAD occlusion was performed before each experiment. Simultaneous recordings of $\text{MPO}_2$ and $\text{CSPO}_2$ were made before ($t_0$ time), after 60 sec of myocardial ischemia ($t_1$ time) and after release of coronary occlusion. In the post anoxia period the variables were measured at the peak oxygen saturation of coronary sinus blood ($t_2$ time). The arterial pressure, mean coronary blood flow and oxygen tension were also recorded on a multichannel recorder (DR8—Electronic for Medicine).

At the completion of the study, the dogs were sacrificed, the hearts examined and the positions of the coronary sinus catheter and the depth of the tissue electrode were verified. Blocks of myocardial tissue surrounding each electrode were removed and submitted for histologic study.

Values are expressed as mean ± SEM. Statistical differences between the three parameters were evaluated by the analysis of variance for repeated measures and between two parameters by paired Student’s t-test.

Results

Histological studies: The histological examination of the myocardium showed minimal compression, degeneration and necrosis of the muscle fibers near the electrode tip. Hematomas, fibrin or leukocyte exudates were not observed.

Oxygen tension and hemodynamic changes: A typical response to coronary occlusion is shown in Fig. 1. Simultaneous $\text{CSPO}_2$ and $\text{MPO}_2$ measurement during myocardial ischemia showed a slight decrease of $\text{CSPO}_2$ and a more pronounced $\text{MPO}_2$ decrease. After coronary reperfusion $\text{CSPO}_2$ rose transiently above baseline values; thereafter, there was a gradual return.

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* Polarograph was made by Prof. P. H. Lucchiari, from the Department of Biophysics, State University "Julio de Mesquita Filho", State of São Paulo, Brazil.
Fig. 1. Effect of coronary occlusion on coronary sinus blood oxygen tension (CSPO$_2$), myocardial oxygen tension (MPO$_2$), mean coronary blood flow (CBF) and blood pressure (BP).

Table I. Effects of Coronary Occlusion on Cardiac Variables

<table>
<thead>
<tr>
<th>SAP/DAP</th>
<th>CBF</th>
<th>MPO$_2$</th>
<th>CSPO$_2$</th>
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<tbody>
<tr>
<td></td>
<td>ml/min</td>
<td>%</td>
<td>mmHg</td>
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<tr>
<td>$t_0$</td>
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<td>108/88</td>
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<td>98*</td>
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<tr>
<td>$t_2$</td>
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$\bar{x}$ 109/83 101/73 108/79 23 49 77 -56.5 -14.3 -5.0 +35.9
SEM 3.5/3.2 3.5/3.9 3.4/3.2 2.1 7.7 10.1 13.3 1.5 4.3

SAP=systolic aortic pressure; DAP=diastolic aortic pressure; MPO$_2$=myocardial oxygen tension; CSPO$_2$=coronary sinus blood oxygen tension; CBF=mean coronary blood flow. $t_0$: recording time of variables before coronary occlusion; $t_1$: recording time of variables during coronary occlusion; $t_2$: recording time of variables after coronary occlusion in the peak oxygen saturation of coronary sinus blood; $\Delta_1$: variation between $t_0$ and $t_1$; $\Delta_2$: variation between $t_2$ and $t_0$; mmHg: millimeter of mercury; %: percent of variation; ml/min: millimeter by minute; $\bar{x}$: mean of values; SEM: standard error mean. * mean arterial pressure (this value was not used for calculation of the $\bar{x}$ and SEM of SAP and DAP).
to control level. In contrast, the MPO$_2$ presented a slow elevation, and a full recovery occurred far from the peak of CSPO$_2$.

Table I depicts the changes in MPO$_2$, mean coronary blood flow (CBF) and blood pressure behavior in the experiment. At the release of occlusion (t1), there was a significant decrease in systolic arterial pressure (p<0.05). A consistent finding was a substantial decrease in MPO$_2$ (-56.5±10.1%), while CSPO$_2$ suffered only a slight reduction (-5.0±1.5%). After coronary reperfusion (t2) the CBF increased to 263.9±58.2% (23±2.1 to 77±7.7 ml/min; p<0.001) of the control level. The MPO$_2$ values remained below the basal state (-14.3±13.3). The corresponding values of CSPO$_2$ were substantially larger that the control level (+35.9±4.3%). In all except one experiment, the MPO$_2$ was smaller than CSPO$_2$ t2 time.

**DISCUSSION**

Since the pioneering work of Davies and Brink,13) the implanting of microelectrodes in animal tissues has been used for the measurement of oxygen tension.8),14)-24) The interpretation of oxygen tension measured by the bare-tipped platinum electrode technique requires an accurate estimation of the possible errors. The potential problems associated with the polarographic method have been well described:

1. the cathode current is dependent on the diffusion constant of oxygen in tissue;
2. the negatively polarized electrode itself consumes oxygen;
3. denaturation of protein on the electrode;
4. movement of either the electrode tip or the fluid around the tip;
5. damage to local tissue by electrode dimensions. All these shortcomings have been discussed in previous reports. 9),18),19),22),23),25)-28)

Errors like 1 and 2 mentioned above are inherent in every polarographic measurement; the other errors are dependent upon needle electrodes. Taking into account that in the present investigation the tissue damage was minimal, the electrode appeared to be well fixed in the myocardial surface, the flow rates around the electrode tip positioned into the coronary sinus catheter was constant and the time between two successive records was short, we believe that the oxygen tension measurement reflects PO$_2$ conditions.

Coronary artery occlusion promoted an important decrease in the subendocardial oxygen tension and a slight decrease in the CSPO$_2$. The MPO$_2$ behavior is in agreement with other studies.15)-17),21),22),29),30)

Similar to previous studies,1) 3) we have observed in all the dogs, im-
Immediately after coronary reperfusion, that CSPO₂ rose in a quick and transitory fashion above its control level. On the other hand, the MPO₂ showed a slow ascending slope during reactive hyperemia. In only one dog, a rapid and important enhancement of MPO₂ was observed. The MPO₂ behavior is quite similar to data reported by Sayen et al, 1958¹⁶ and Winbury et al, 1971.²¹ These authors have emphasized that the overshoot of myocardial oxygen tension was not consistent in the post anoxia period; in the great majority of experiments a gradual increase of MPO₂ occurred.

The MPO₂ behavior which was observed in the present investigation raises the hypothesis that the high oxygen saturation of the coronary venous blood probably is due to the opening of myocardial arteriovenous shunts instead of an increase of flow through the myocardial capillary bed. In one dog, the rapid and transitory rise of MPO₂, resulting in a decrease in the myocardial oxygen extraction due to an increase in coronary flow, could explain the quick and transitory elevation of CSPO₂. However, the slow MPO₂ variation in all the other dogs is not in accordance with the fast CSPO₂ changing during reactive hyperemia. In conclusion, this study suggests that the increase in the CSPO₂ values post cardiac ischemia could be related to the opening of arteriovenous shunts.

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