Reduction of Myocardial Reactive Hyperemia during Oxygen Breathing in Dogs

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In 7 open-chest anesthetized mongrel dogs the left anterior descending coronary artery was occluded for 20 sec. Myocardial reactive hyperemia was recorded during air and oxygen breathings. The excess blood flow during the reactive hyperemia was smaller and the duration of the reactive hyperemia was shorter during oxygen breathing than during air breathing. It is suggested that the reduction of oxygen demand during oxygen breathing is a possible reason for the decreased reactive hyperemia and oxygen administration is beneficial in relieving myocardial ischemia.

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Oxygen inhalation therapy for myocardial infarction is still a matter of controversy. The net effect of oxygen inhalation on the myocardium is a reduction in the oxygen availability (Meijne and Straub 1966; Ishikawa et al. 1974a) in spite of the elevated arterial oxygen content during oxygen breathing, because coronary blood flow decreases during oxygen breathing. Myocardial tissue oxygen tension shows only a minimal elevation in the infarcted area (Säyen et al. 1951), and myocardial contractile force is rather reduced by oxygen breathing (Ishikawa et al. 1974a, b). Some investigators postulated that oxygen inhalation therapy may be harmful for patients with myocardial infarction (Thomas et al. 1965; Daniell and Bagwell 1968). Since the administration of oxygen in patients with myocardial ischemia is one of the routine procedures, it may be important to find whether oxygen inhalation therapy is harmful or not for the ischemic myocardium.

Coronary blood flow shows a characteristic increase in response to the ischemic stimulus in consequence of coronary artery occlusion, i.e., myocardial reactive hyperemia (Olsson and Gregg 1965). Duration of myocardial reactive hyperemia is longer if the ischemic stimulus to the myocardium is greater and vice versa (Olsson and Gregg 1965). It is likely that myocardial reactive hyperemia will be reduced if oxygen administration improves the myocardial oxygenation in the ischemic change. The present study was undertaken to find whether oxygen inhalation is beneficial in reducing myocardial reactive hyperemia.

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METHODS

In 7 mongrel dogs, left thoracotomy was performed at the fifth intercostal space under positive pressure breathing via a tracheal tube and pentobarbital anesthesia of 20 mg/kg. The anterior descending branch of the left coronary artery was dissected free and an electromagnetic flowmeter (MF-46, Nihonkohden Co., Tokyo) was placed to record coronary blood flow. A suture ring around the artery was made 3 mm distal to the flowmeter probe to occlude the artery. Electrocardiogram, aortic blood pressure and aortic blood flow were recorded simultaneously.

Under room air breathing, the coronary artery was occluded by the suture ring for 20 sec. Coronary blood flow was increased markedly after release of the suture ring as compared with the control flow (myocardial reactive hyperemia). The mean flow was continuously measured for 4 min after release by means of an electrical integral circuit with the time constant of 1.0 sec. Nine min after release of the occlusion, the second occlusion of the artery was performed. The duration of occlusion was the same as the first time (20 sec). Just at the time when the artery was occluded for the second time, the inspiration was switched from room air to pure oxygen (Fig. 1), so that the oxygen debt of the myocardium due to coronary occlusion (Olsson and Gregg 1965) in the second time would be the same as in the first time. After 4 min recording of myocardial reactive hyperemia, inspiration gas was changed from oxygen to room air. Nine min after release of the second occlusion, that is, 5 min after the onset of room air breathing, the third occlusion of the artery was made by the same procedure as the first occlusion.

![Fig. 1. Relationship between coronary artery occlusion and the timing of administration of oxygen.](image1)

![Fig. 2. Calculation of indices from reactive hyperemia blood flow. The excess flow rate at the peak flow was divided into four. The time interval from the point of release of the artery to the point where the flow rate recovered the first one quarter of the excess flow rate was designated as 25% recovery (a). The time interval to recover the half and three quarters of excess flow rate were named as 50% (b) and 75% (c) recoveries, respectively.](image2)
The following three indices were measured (Fig. 2).

1) Peak flow (ml/min); the largest value of the mean coronary blood flow after release of the occlusion.

2) Reactive hyperemia blood flow (the excess flow during reactive hyperemia) (ml); (total flow during reactive hyperemia) – (duration of reactive hyperemia × flow rate at control). Flow rate at control was measured 3 to 4 min after each release of the occlusion.

3) Percent recovery (sec); time interval necessary to vanish the reactive hyperemia as shown in Fig. 2.

These indices were compared between the first (air breathing) and the second (oxygen breathing) or between the third (air breathing) and the second (oxygen breathing) occlusions, and the significance of differences between obtained values were evaluated by paired t test. The data were discarded when any of the heart rate, coronary blood flow before occlusion, aortic blood pressure and aortic blood flow showed a considerable variation during those experiments.

RESULTS

Twenty-six paired experiments were performed (Table 1). Arterial oxygen tension was 81 ± 10 mmHg (mean ± S.D.) on the average during air breathing. This was elevated to 499 ± 28 mmHg during oxygen breathing. In the present experiment, arterial oxygen tension reached a peak value within 20 sec after the onset of oxygen breathing. Excess flow during the reactive hyperemia (reactive hyperemia blood flow) was reduced significantly during oxygen breathing (Fig. 3). There was a slight reduction in the peak flow during oxygen breathing. The duration of reactive hyperemia was slightly shortened by the inhalation of oxygen as it was shown in the reduction of percent recovery (Fig. 4). All of these significant differences between the first occlusion (air breathing) and the second occlusion (oxygen breathing) were again demonstrated between the third (air breathing) and the second (oxygen breathing) occlusions.

**TABLE 1. Comparison of myocardial reactive hyperemia during air breathing and oxygen breathing in 7 dogs**

<table>
<thead>
<tr>
<th></th>
<th>Air (I)</th>
<th>O2 (II)</th>
<th>Air (III)</th>
<th>(II)−(I) × 100</th>
<th>(II)−(III) × 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive hyperemia</td>
<td></td>
<td></td>
<td></td>
<td>p value</td>
<td>p value</td>
</tr>
<tr>
<td>blood flow (ml)</td>
<td>48±18*</td>
<td>43±14</td>
<td>45±18</td>
<td>−9±4 &lt;0.02</td>
<td>−12±5 &lt;0.02</td>
</tr>
<tr>
<td>Peak flow (ml/min)</td>
<td>107±39</td>
<td>100±36</td>
<td>106±37</td>
<td>−2±12 &lt;0.05</td>
<td>−1±12 NS†</td>
</tr>
<tr>
<td>25% recovery (sec)</td>
<td>27.0±5.7</td>
<td>26.5±6.0</td>
<td>26.5±5.3</td>
<td>−4±2 NS</td>
<td>−3±2 NS</td>
</tr>
<tr>
<td>50% recovery (sec)</td>
<td>39.8±8.0</td>
<td>36.5±8.2</td>
<td>38.0±6.6</td>
<td>−11±2 &lt;0.01</td>
<td>−10±3 NS</td>
</tr>
<tr>
<td>75% recovery (sec)</td>
<td>59.9±14.0</td>
<td>56.5±15.3</td>
<td>58.6±14.4</td>
<td>−8±4 &lt;0.01</td>
<td>−13±5 &lt;0.01</td>
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*Mean±S.D.
†Not significant (p>0.05).

DISCUSSION

A reduced excess flow during reactive hyperemia and more rapid recovery from the reactive hyperemia brought about by oxygen breathing may suggest that
Fig. 3. Change of reactive hyperemia blood flow during air and oxygen breathings. The excess flow caused by reactive hyperemia (reactive hyperemia blood flow) is significantly reduced by oxygen breathing.

Fig. 4. Change of percent recovery during air and oxygen breathings. The time intervals necessary to reduce excess flow (% recovery) are shortened during oxygen breathing. The vertical bars indicate s.e. Upper: 75% recovery. Middle: 50% recovery. Lower: 25% recovery. * Difference is significant at the level of p<0.01.
oxygen is beneficial in relieving myocardial ischemia. A similar study has been conducted by Bird and Telfer (1967) using reactive hyperemia of the human forearm. In their study, occlusion of the forearm artery was completed after the arterial blood of the subjects had been saturated with 100% oxygen. Since oxygen debt caused by arterial occlusion was smaller during oxygen breathing because the tissue was over-saturated with oxygen, reactive hyperemia could be smaller during oxygen breathing. In the present experiment, on the other hand, the oxygen debts of the myocardium during air and oxygen breathing experiments were equal since oxygen was given just at the time when the coronary artery was occluded. Accordingly, the reduced magnitude of reactive hyperemia during oxygen breathing indicates that perfusion of arterial blood with a high oxygen tension was effective in paying the myocardial oxygen debt.

Lammerant and Becsei (1972) demonstrated that, even though coronary vessels were forced to dilate maximally by adenosine infusion, coronary flow was decreased by oxygen breathing. In the present study, the peak flow during reactive hyperemia was decreased by oxygen breathing. This would suggest that hyperoxia exerts a direct vasoconstrictive effect on coronary vessels, thus it may reduce the “reactive hyperemia blood flow”. If this is the case, however, rather a prolongation of the duration of reactive hyperemia might be expected in order to pay a certain amount of myocardial oxygen debt. The shortening of percent recovery demonstrated in this study (Fig. 4) cannot support this concept.

Another possible explanation for diminished myocardial reactive hyperemia response during oxygen breathing is that the vasoactive metabolites produced from the ischemic myocardium (Rubio et al. 1969) disappear more rapidly by oxygen breathing. Several studies indicate that myocardial contractile force diminishes during oxygen breathing and this is evident in both normal and ischemic myocardium (Daniell and Bagwell 1968; Ishikawa et al. 1974a, b). The decreased myocardial contractile force is related to a decrease in myocardial oxygen demand. Myocardial contractile force and thus myocardial oxygen demand will be reduced by administration of oxygen even in the state of myocardial reactive hyperemia. These effects might facilitate the normalization of the ischemic myocardium. If the ischemic myocardium is normalized sooner, vasoactive metabolites disappear earlier and myocardial reactive hyperemia will cease more rapidly.

References


