Effect of ouabain on O₂ supply/demand in normal and ischemic heart

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Summary

The effect of ouabain (15 μg/kg) on subepicardial and subendocardial blood flow, oxygenation, and small-vessel blood content was studied in anesthetized open-chest rabbits with hearts subjected to acute coronary occlusion. 10 minutes after occlusion, blood flow was 48% lower than in the control region. Ouabain lowered blood flow significantly in the non-occluded region and insignificantly in the occluded area. Small-vessel blood content, a measure of open capillary density, was unaffected by occlusion or ouabain. After occlusion, relative tissue PO₂ fell to a greater extent in the affected subendocardium than the affected subepicardium. Ouabain, therefore, appears to be well tolerated in both the control and ischemic regions in terms of oxygen supply and consumption.

Key words: ouabain, coronary blood flow, open capillary density, tissue oxygenation

Introduction

Ouabain has been shown to increase the degree of injury caused by myocardial infarction, since it increases the heart's needs for oxygen (1). In non-failing hearts, ouabain has been shown to increase cardiac oxygen consumption (2, 3). This increase in oxygen consumption appears related to an increase in the contractile force of the normal heart (4). Marked increases in the velocity of myocardial shortening have been demonstrated with ouabain (5). Others (6, 7), however, have shown that ouabain produced a negative chronotropic effect upon the heart and a decreased end diastolic dimension and ejection fraction of the heart. These changes could reduce myocardial oxygen needs. The effect which ouabain has upon regional myocardial oxygen consumption in the acutely ischemic myocardium remains controversial (1, 8).

There is evidence that ouabain increases resistance in coronary blood vessels (6). In constricted vessels, ouabain may cause dilation (7, 8). We investigated the effect of ouabain on regional flow, oxygenation and small-vessel blood content in occluded and non-occluded regions of the left ventricle and used these data to estimate regional consumption (9). We also considered the difference between the subepicardium and subendocardium in this regard. It is clear that normally the subendocardium has
a higher oxygen requirement (10) and that in stress the relationship between oxygen supply and demand in this region is more precarious (11). The aim of this study was to determine on a regional basis whether ouabain had deleterious effects on the normal and ischemic areas of the heart.

Materials and methods

58 New Zealand white rabbits of either sex, weighing between 1.0 and 2.2 kg were anesthetized with sodium pentobarbital (30 mg/kg) administered into the circumflex ear vein. The left common carotid artery was cannulated. This catheter was subsequently utilized for blood pressure and heart rate measurements, for reference blood flow measurements, ouabain injection, and to obtain arterial blood samples for subsequent analysis. An endotracheal tube was inserted and artificial respiration was instituted using a Harvard respirator. Respiratory rate and volume were adjusted to maintain eucapnia as monitored by a Godart-Statham capnograph. A left thoracotomy was performed at the 4th or 5th intercostal space, and a partial pericardiotomy exposed the heart. The protocol was varied depending on the measurements made on the animal: regional myocardial blood flow, relative tissue PO2, or small-vessel blood content.

Regional blood flow

In 29 rabbits a catheter was placed into the left atrium for injections of radioactive tracer microspheres. Control blood pressure and heart rate measurements were obtained, and blood samples were taken. The left anterior descending coronary artery (LAD) was ligated below its first major branch. 10 minutes later, approximately 7.5 x 10^5 141Ce or 85Sr-labelled microspheres (15 ± 3 μ in diameter) were injected through the atrial catheter in a 0.2-ml bolus and flushed with 1 ml saline. A 3-minute timed sample was withdrawn by peristaltic pump at the rate of 1–2 ml/min, beginning 30 seconds before the microsphere injection. Then 15 μg/kg of ouabain were administered. Blood pressure and heart rate were monitored, and arterial blood samples were obtained, as previously described, 30 minutes after the administration of the ouabain. At this time, an identical procedure to determine blood flow using the “reference sample” method was performed using 141Ce or 85Sr-labelled microspheres (12).

The heart was excised at the level of the atrio-ventricular ring and frozen. The frozen left ventricular wall was divided into subepicardial and subendocardial layers within the occluded and non-occluded areas. Weighed tissue and blood samples were counted to a standard error of less than 2 % on a Hewlett-Packard Gamma Scintillation Spectrometer. Blood flow in ml/min/100 g was calculated (12).

Small-vessel blood content

15 rabbits were divided into 3 experimental groups of 5 each. In the first group, the left anterior descending coronary artery was occluded below its first major branch. 10 minutes later, heart rate, blood pressure measurements were noted, and blood samples were taken. Small-vessel blood content was determined through the use of 59FeCl3, which was used to label the plasma siderophilin. The details of this method have been described elsewhere (11, 13). Briefly, a dose of 25 μCi was administered in an 0.5-ml bolus and flushed into the arterial catheter with saline. 2 minutes later, duplicate blood samples were withdrawn. The heart was excised at the level of the atrio-ventricular ring and placed into ice water. The left ventricular free wall was divided into subepicardial and subendocardial layers within the occluded and non-occluded areas. Weighed tissue and blood samples were counted twice for 10 minutes with a standard error of less than 2 % on an automated gamma