Relationship Between Blood Supply to Myocardial Segments and Their Contractility in Dogs with Intact and Ischemic Myocardium

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In dogs with an intact heart, intravenously administered dipyridamole increased the contractility of a myocardial segment 30-80% and the volume rate of coronary blood flow 142±14%. Dipyridamole administered to dogs before their coronary artery was occluded for 3 min did not decrease the contractility of the ischemia-affected myocardial segment. In dipyridamole-treated dogs with well-developed collaterals, blood was redistributed to the intact zone and the blood flow in the vein draining the ischemic zone increased by 168±17%.

Key Words: *ultrasound; coronary blood flow; blood flow redistribution; segment length; dipyridamole*

A very important property of many coronary vasodilators is the ability to stimulate the development of collateral vessels [9,11] and thus improve the contractility of an ischemic myocardium. However, as found in animal experiments, the use of some vasodilators brings about the so-called steal syndrome [6,8,10], in which the blood flow is redistributed in favor of the intact cardiac region, and this appears to have an adverse effect on contraction of the ischemic zone.

The aim of the present study was to establish, as an objective indicator of myocardial status, how an increase in coronary blood flow is related to the contraction of a myocardial segment. To this end, the classic coronary vasodilator dipyridamole (DP) was tested for its effect on the intact dog heart and on a heart subjected to acute or chronic myocardial ischemia.

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MATERIALS AND METHODS

A total of 20 mongrel dogs of both sexes (body weight 6-12 kg) were used. Under general anesthesia (Nembutal, 40 mg/kg intravenously) and artificial ventilation, thoracotomy was performed in the fourth intercostal space on the left, the pericardium was opened, and coronary vessels were dissected out to install sensors of coronary blood flow and segment length and an occluder.

Blood flow was measured by Doppler ultrasonography [3] using bandage-type sensors calibrated in units of linear and volume blood flow rates [2]. Sensors with an inner diameter of 2-3 mm were used for measurements in large vessels (the left coronary artery and the great cardiac vein) and miniature sensors (inner diameter 0.5-0.7 mm) for measurements in smaller vessels (second- and third-order coronary arteries and coronary veins). All sensors operated at the 27 MHz frequency and sent signals to an analog computer to calculate and monitor in real time the balance of blood supply to the cardiac regions under study.

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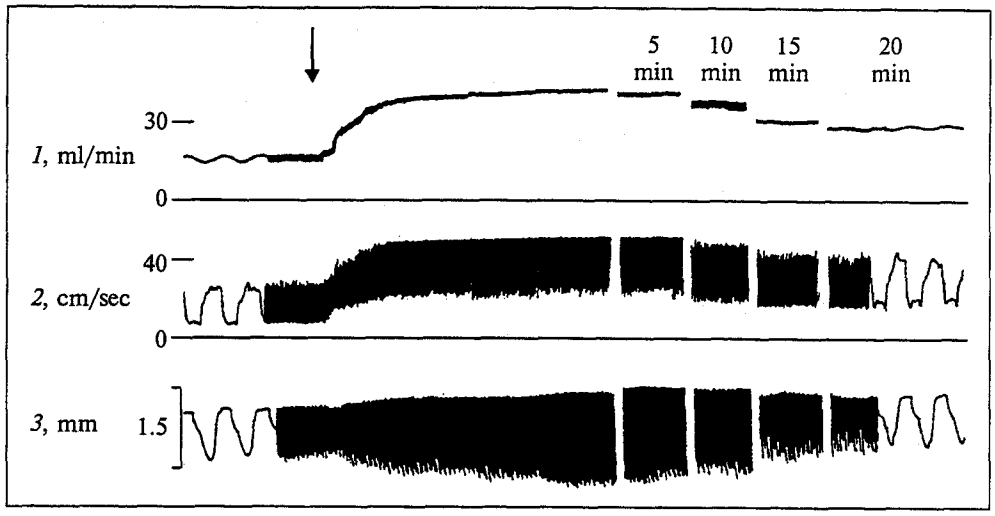

Fig. 1. Effects of DP (1 mg/kg intravenously) on coronary blood flow and on contraction of a myocardial segment in a dog with intact heart. Here and in Fig. 2: *1* and *2*) volume and linear blood flow rates, respectively; *3*) variations in length of myocardial segment. The start of DP administration is indicated by the arrow.

Myocardial contractility was evaluated by using piezoelectric sensors having a fixed base 8 mm long to measure variations in the length of individual myocardial segments. These sensors were placed in both the ischemic and intact portions of the myocardium. Pressure was recorded in the left ventricle and, in some dogs, in the ischemic zone as well.

In the first part of the study, DP was tested for its effects on coronary blood flow and contractility of myocardial segments in intact dogs and the same dogs after their coronary artery had been occluded for a short time. In the second part, the effect of DP on the blood supply in an ischemic myocardium of dogs with a well-developed collateral circulation was evaluated. This part consisted of two stages. In the first stage, the anterior descending branch of the left coronary artery was ligated in its upper third, while in the second stage, performed 2 months later, the dogs were subjected to an acute test. Ultrasonic sensors were placed in the great cardiac vein and in the coronary vein draining blood directly from the ischemic zone.

DP was administered intravenously in a dose of 1 mg/kg in a 3-ml volume at a rate of 1 ml/min. Control dogs received physiological saline by the same route and in the same volume.

RESULTS

The DP dose of 1 mg/kg caused a considerable augmentation of the coronary blood flow, which usually began to increase 1 min after the start of infusion to reach its peak by minutes 3-5 and then returned to the baseline level by minute 30. The volume flow rate increased by 142±14% and the linear flow rate by 118±11%. Analysis of the blood flow curves (Fig. 1) showed that this difference was mainly due to the augmented blood flow during systole. These findings generally agree with the results of our previous experiments with anesthetized rats [1], but the coronary blood flow in the rats did

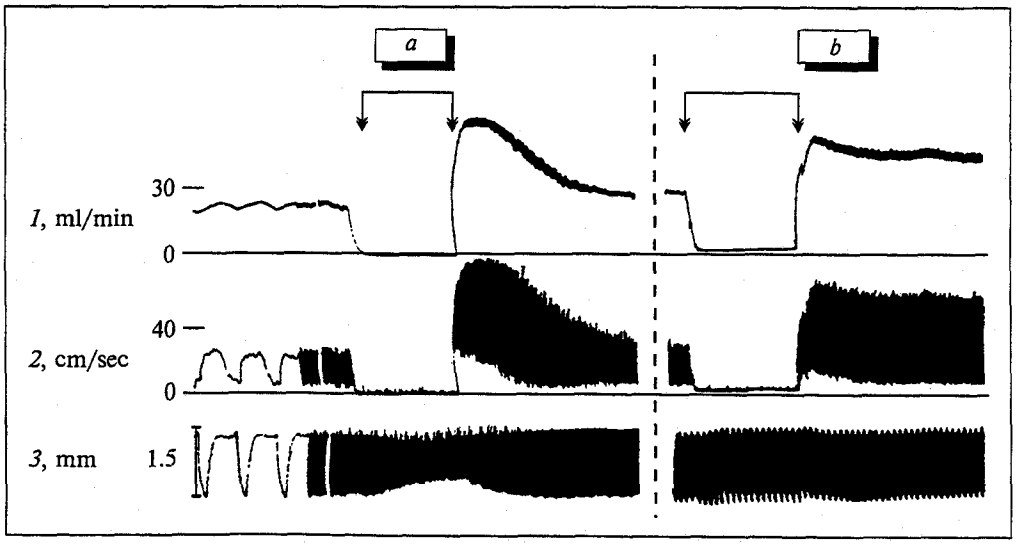

Fig. 2. Effect of DP on the contraction of a myocardial segment in the zone of ischemia produced by acute (for 3 min) occlusion of a coronary artery. *a*) control dog with occlusion after physiological saline; *b*) test dog with occlusion after DP (1 mg/kg intravenously). Arrows indicate the beginning and end of occlusion.

not increase by more than 30%, probably because the myocardial vasculature in this species is less well developed than in dogs. In rats the ultrasonic sensor was installed at the descending branch of the left coronary artery. In dogs coronary blood flow was measured simultaneously in different regions of the intact left ventricular myocardium, and inter-regional differences in the volume blood flow rate in the same DP-treated dogs were found not to exceed 10%, indicating that the drug did not cause an appreciable redistribution of the blood supply between different portions of the intact left ventricle.

The contraction amplitude of the myocardial segment in which it was measured also increased, but returned to baseline before the blood flow rate did so (by minutes 15-20 postinjection *vs.* minute 30). The contraction amplitude was highest at minutes 2-3, at which time it was 30 to 80% above baseline. This scatter of values can be explained by the differential contractile activities of different portions of the left ventricle, wherein each segment exhibits its own contraction pattern [5]. In the present study, sensors of segment length were so installed in the myocardium as to take measurements along the longitudinal axis of the left ventricle. However, the contraction vector of cardiac fibers in the monitored region did not always coincide with the direction in which sensor measurements were optimal, and this resulted in underestimates. It was difficult to position the segment length sensor exactly in the blood supply region monitored by the blood flow sensor. It was probably for these reasons that no direct proportionality could be found between the changes elicited by the contraction amplitude of the segment and those it caused in blood flow, although a relationship between the two parameters was evident.

In the experiment with acute ischemia, the segment length sensor was installed in the area to be made ischemic and the other sensor in an area that was to remain intact. The coronary artery was occluded for a short time (3 min) 30 min after the occluder and blood flow sensors were applied so as to allow the contraction amplitude and coronary blood flow to stabilize at the baseline levels. The contraction amplitude of the segment in the ischemic area fell as soon as the artery was occluded (Fig. 2, *a*), but stabilized after 30-60 sec of occlusion, its level then ranging from 50 to 80% of the baseline value throughout the period of occlusion. In some dogs, the initial momentary fall of the amplitude was immediately succeeded by a sharp rise. A phasic analysis of the recorded curves showed that the latter phenomenon was associated with the superior oblique muscle of the left ventricle: contraction of this muscle started earlier than that of the circular muscle and occurred at the beginning of isovolumic cardiac contraction. Contraction of the circular muscle, which provides the main force for cardiac output, is the critical factor to be considered when left ventricular contractility is being evaluated [4]. The superior oblique muscle can probably manifest its activity during the work of the circular muscle when the latter's contraction force is considerably weakened because of the ischemic produced in the myocardium. When contractions in the ischemic zone are recorded, the degree to which this activity is manifested will depend on how deep sensitive elements of the sensor extend into the myocardium. In our study, sensors were inserted 3-12 mm deep.

During the period of occlusion, the contraction amplitude of the segment recorded in the intact area remained unchanged in some dogs and increased by 10-15% in others, probably because the load was redistributed to the intact myocardial regions; it returned to baseline in 30 to 60 sec after the artery was opened (i.e., reperfusion was started) and remained stable thereafter. Blood flow in the coronary arteries was at its peak (2 to 4 times above baseline) at the time the occluder was released and returned to baseline 5 to 7 min later. It should be noted that the contraction amplitude of the segment normalized much earlier.

At minute 30 of reperfusion, DP was injected intravenously at 1 mg/kg and the coronary artery was occluded again. No decrease in the contraction amplitude of the segments was observed; rather, a 10 to 15% increase was recorded in some dogs. This indicates that the drug improved the contractility of the ischemic cardiac muscle (Fig. 2, *b*).

In the second part of the study, DP was administered intravenously in the same dose to dogs with a well-developed network of collaterals and blood flow was found to be increased in both the great cardiac and coronary veins. The nature, intensity, and duration of the response to DP were similar to those recorded for coronary arteries in the first part of the study. The average increase in blood flow reached 168±18% relative to the baseline. During these tests, the ratio of blood flow via the great cardiac vein to that from the ischemic zone was continuously recorded [7]. Analysis of the data showed that the balance between the blood supply to the heart as a whole and to its ischemic zone was altered immediately after DP administration (Fig. 3). The alteration involved blood redistribution in favor of what appeared to be intact areas of the ischemia-affected left ventricle, amounted to 20-30% relative to the baseline, and continued for 15-

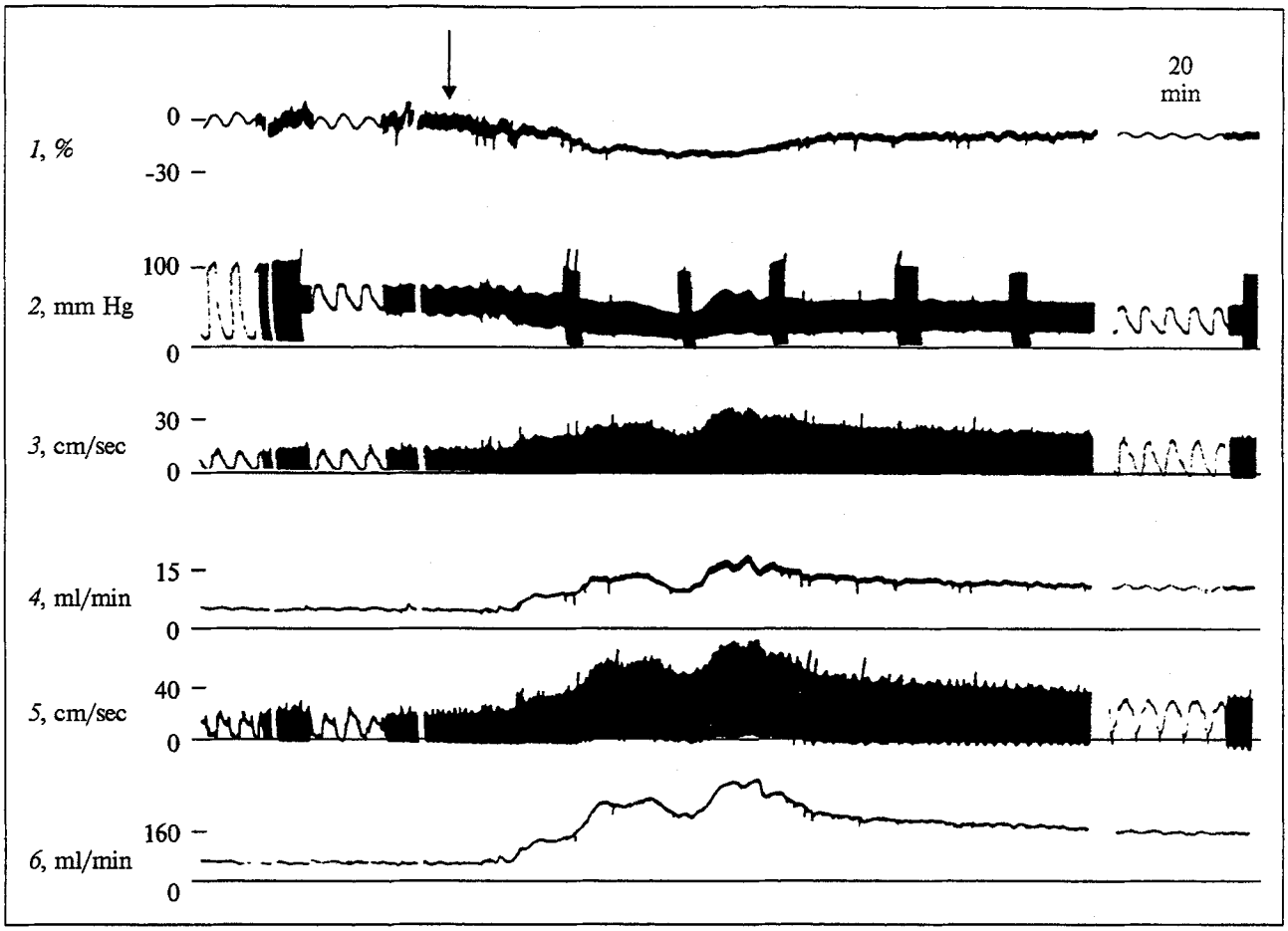

Fig. 3. Effects of DP (1 mg/kg intravenously) on blood flow in the coronary and great cardiac veins of an ischemic myocardium. *1*) blood flow redistribution in the left ventricular myocardium; *2*) blood pressure in left ventricle and retrograde arterial pressure in occluded coronary artery; *3*) linear blood flow rate in coronary vein; *4*) volume blood flow rate in coronary vein; *5*) linear blood flow rate in great cardiac vein; *6*) volume blood flow rate in great cardiac vein. The start of DP administration is indicated by the arrow.

20 min, after which the balance was restored. In contrast, no alteration in the balance was recorded in the saline-injected control dogs with an ischemic myocardium. These findings agree with the observation that blood flow redistribution in favor of intact rather than ischemic cardiac regions occurs because arterioles are dilated in the intact regions [8].

Clinical manifestations of ischemic heart disease are known to depend not only on the deterioration of the myocardial blood supply but also on the state of myocardial contractility. The shift in the balance between the blood supply to the intact and ischemic cardiac regions that is to the detriment of the ischemic region should be considered in relation to the amount of blood entering the latter region after DP administration, which, as the present experiments show, considerably improves the contractility of both the ischemic and nonischemic parts of the myocardium and thus compensates in large measure for the unfavorable blood redistribution induced by this drug.

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