ABSTRACT: In order to investigate whether dopamine combined with bunazosin improves cardiac function, the global and regional cardiac function and regional blood flow of 7 anesthetized dogs were analyzed before and after occlusion of the left anterior descending coronary artery (LAD), then after 10 μg/kg/min dopamine infusion following the LAD occlusion, and again after a bolus infusion of bunazosin 250 μg/kg. Dopamine with bunazosin reduced left atrial pressure from 4.9 ± 0.9 to 3.1 ± 0.5 mmHg (p<0.05) and improved cardiac output from 1.22 ± 0.15 to 1.50 ± 0.14 L/min (p<0.05), maximum positive left ventricular dp/dt from 1721 ± 202 to 3600 ± 663 mmHg/sec (p<0.05) and the time constant from 45.2 ± 5.0 to 27.5 ± 4.6 msec (p<0.01). Bunazosin added to the dopamine reduced the elevated left ventricular peak systolic pressure caused by dopamine from 130 ± 7 to 113 ± 8 mmHg (p<0.01). With regard to the regional wall motion, the impaired LAD-AL (the segment systolic shortening) and LAD-Emax (the slope of peak systolic pressure—endsystolic length relation) following the LAD occlusion improved from 0.5 ± 2.5 per cent to 5.9 ± 2.6 per cent (p<0.01) and from 50 ± 9 to 82 ± 14 mmHg/mm (p<0.01) after the infusion of dopamine with bunazosin. Dopamine greatly increased the Rate Pressure Product (RPP) from 12610 ± 1120 after LAD occlusion to 16950 ± 1420, whereas dopamine in combination with bunazosin did not increase the RPP due to a drop of LV-PSP with little change in regional myocardial blood flow. It was concluded that combining dopamine with bunazosin was useful for improving both the global and regional cardiac functions of the ischemic heart.

KEY WORDS: ischemic heart, dopamine, bunazosin, regional myocardial wall motion, regional myocardial blood flow

INTRODUCTION

Dopamine is widely used in the treatment of heart failure as an inotropic agent. However, it is likely to augment afterload and also induces arrhythmia with dose dependency,

1,2 these side effects being potentially deleterious to the ischemic heart. Bunazosin is a vasodilator whose action results from an α1 blocking effect,3 which reduces preload and afterload against heart failure,4 dilates the coronary arteries,5 and inhibits arrhythmia after coronary reperfusion.6 We therefore were of the opinion that dopamine in combination with bunazosin might possess advantages for the management of cardiac

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failure caused by ischemia. The aim of this study was to evaluate the effectiveness of such a combined therapy for ischemic heart failure following acute coronary artery occlusion in a canine model.

**Materials and Methods**

Seven mongrel dogs weighing between 6.0 and 15.5 kg were anesthetized with intravenous sodium pentobarbital 25 mg/kg and maintained on a respirator. After a thoracotomy had been performed through an incision in the left fifth intercostal space, the heart was exposed and suspended by a pericardial cradle. Swan-Ganz catheter (Edwards, USA) was then inserted into the right pulmonary artery from the left internal jugular vein, and a Muller type micromanometer-tipped catheter inserted into the left ventricular cavity through the cardiac apex. To assess regional myocardial wall motion, a pair of ultrasonic crystals, 1–2 mm in diameter, was implanted in the subendocardium in an ischemic area where the left anterior descending coronary artery (LAD) was occluded and in a normal area perfused by the left circumflex coronary artery (LCX). Two wire-type platinum probes, 100 μm in diameter, were positioned in the middle layer of myocardium for measurement of regional myocardial blood flow by the hydrogen gas clearance method, while one probe was positioned in an area of normal myocardium (LCX-flow), and the other in the ischemic area (LAD-flow) (Fig. 2).

The parameters of hemodynamics consisted of: heart rate (HR), cardiac output (CO), left ventricular peak systolic pressure (LV-PSP), maximum positive LV dp/dt (positive dp/dt), maximum negative LV dp/dt (negative dp/dt) and the time constant of isovolumic pressure fall (TC) calculated by Weiss’s method. Variables studied with regional wall motion on the ischemic and normal areas were end-diastolic segment length (LAD-EDL, LCX-EDL), which was normalized by dividing the observed length by the control end-diastolic segment length before the occlusion of LAD and multiplying it by ten, and segment systolic shortening (LAD-ΔL, LCX-ΔL). The regional myocardial contractility was obtained by the slope of peak systolic pressure—end systolic length relation (Emax), derived from a linear regression analysis on 6–10 beats during the elevation of LV-PSP by means of constriction of the aortic arch gradually with teflon tape. Pressure and regional wall motion were recorded with a Polygraph system 360 (Nippon Denki Sanei, Japan) (Fig. 3). Global cardiac function, regional wall motion and contractility, and regional myocardial blood flow were measured in the stable state of hemodynamics before and after LAD occlusion, after dopamine infusion (10 μg/kg/min), and then again after the infusion of bunazosin (250 μg/kg). With respect to the dose of dopamine, we selected a 10 μg/kg/min infusion of dopamine which clearly