EFFECT OF PROSTAGLANDIN B_1 ON THE SYSTEMIC AND REGIONAL HEMODYNAMICS

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The effect of prostaglandin B_1 (PGB_1) on the cardiovascular system was studied in experiments on anesthetized dogs. After intravenous injection of PGB_1 (40 μg/kg in a single dose) arterial hypotension tachycardia, increased myocardial contractility, an increased cardiac output, and a rise of pressure in the pulmonary artery were observed. The total peripheral resistance and total pulmonary resistance were reduced. The work of the right and left ventricles was increased. The coronary blood flow was increased by 29%. The mean velocity of the volume blood flow in the renal and femoral arteries was appreciably increased after administration of PGB_1, but in the common carotid and superior mesenteric arteries the increase was not significant. Changes in the systemic and regional hemodynamics were of short duration.

KEY WORDS: *prostaglandin B_1; systemic regional hemodynamics.*

Prostaglandins (PGs) of the B group are formed during metabolism of PGs of the A group [2]. PGB_1 and PGB_2 have a weak hypotensive action [4]. The relatively weaker activity of PGB than of PGA on the cardiovascular system may be connected with changes in the stereochemical arrangement of the alkyl and carboxyl radicals as a result of the formation of double bonds in the molecule at the 8th and 12th carbon atoms [3]. Despite investigations of the effect of PGB_1 on the systemic hemodynamics and blood flow in particular vascular regions [5-7], the general pattern of distribution of the cardiac output between the organs and tissues after administration of this substance remains unexplained.

The object of this investigation was to study the effect of PGB_1 on the systemic hemodynamics and the distribution of the blood flow between the principal vascular regions in dogs.

EXPERIMENTAL METHOD

Experiments were carried out on mongrel dogs weighing 15-25 kg. After induction of anesthesia with hexobarbital (10 mg/kg intravenously) the animals were intubated, complete muscle relaxation was induced by a single intravenous injection of succinylcholine (1 mg/kg), and the lungs were artifically ventilated with a mixture (2:1) of nitrous oxide and oxygen. The pressure in the left ventricle, ascending aorta, and pulmonary artery was measured in 5 dogs by electromanometers of the Mingograph-81 (Sweden) polygraph. The sensitive elements of an SEM-275 electromagnetic flowmeter (England) were placed on the ascending aorta. Analog signals of the velocity of the blood flow and pressure in the region to be investigated were led through matching amplifiers and an analog-to-digital converter, with a quantization period of 10 msec, to the operative memory of a gE-115/3 computer (France), recorded on magnetic disks, and processed during the experiments in accordance with a special program. The resulting data were printed out by the computer in the form of tables. Every 5 cardiac cycles, tables of parameters of the circulation averaged for these cycles were printed. After the experiments, the results were further processed automatically in order to calculate the maximal velocity of shortening of the contractile elements of the heart under zero loading (V_{max}) [1]. In another five dogs, the sensitive element of the flowmeter was fixed to the left circumflex branch of the coronary artery. A catheter was introduced through the femoral artery into the ascending aorta. The ECG, the pressure, and the volume velocity

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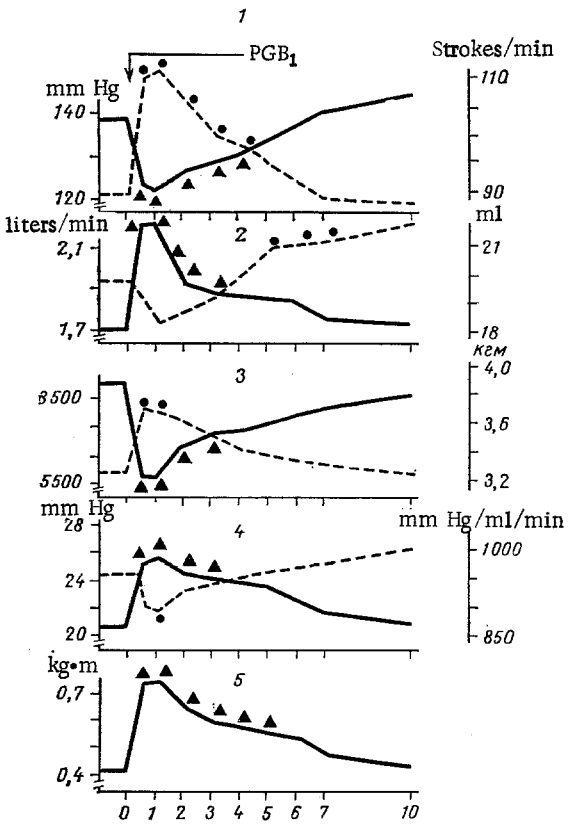

Fig. 1

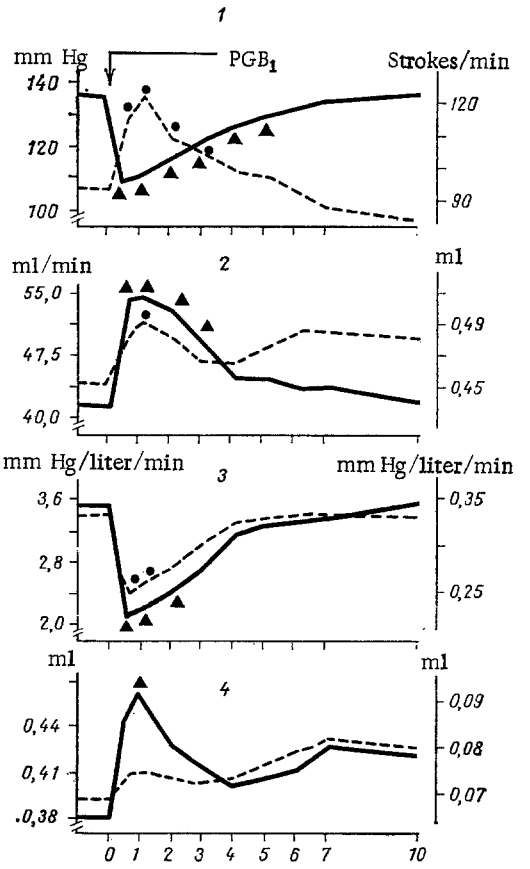

Fig. 2

Fig. 1. Effect of PGB_1 on systemic hemodynamics of dogs. Continuous lines (ordinate, on left): pressure in aorta (1), cardiac output (2), total peripheral resistance (3), pressure in pulmonary artery (4), and work of right ventricle (5); broken lines (ordinate, on right) indicate heart rate (1), stroke volume of the heart (2), work of left ventricle (3), and total pulmonary resistance (4). Triangles and circles indicate times at which indices differ statistically significantly ($P < 0.05$) from initial levels. Ordinate, changes in indices studied. Abscissa, time (in min).

Fig. 2. Effect of PGB_1 on coronary blood flow in dogs. Continuous lines (ordinate, on left): pressure in aorta (1), coronary volume blood flow (2), resistance of coronary arteries (3), stroke diastolic blood flow (4); broken lines (ordinate, on right): heartrate (1), stroke coronary blood flow (2), resistance of coronary arteries in diastole (3), stroke systolic blood flow (4). Remainder of legend as in Fig. 1.

of the blood flow were recorded on the Mingograph-81 polygraph. The coronary stroke blood flow, diastolic and systolic blood flow, resistance of the coronary vessels, and the mean diastolic resistance of the coronary vessels were calculated by integration. In five dogs the pressure in the abdominal aorta, the portal vein, and the superior vena cava and the volume velocity of the blood flow in the carotid, superior mesenteric, renal, and femoral arteries were recorded simultaneously by means of the Nihon Kohden (Japan) four-channel flowmeter.

PGB_1 (Upjohn, USA) was injected intravenously as a single dose of 40 mg/kg over a period of 30 sec.

EXPERIMENTAL RESULTS AND DISCUSSION

PGB_1 lowered the arterial pressure briefly by 14% (Fig. 1). The final diastolic pressure in the left ventricle under those circumstances changed in two different phases: An initial fall (for 3 min) was followed by a rise. Arterial hypotension was accompanied by marked tachycardia. At the time of the maximal increase in heart rate (by 29%) the expulsion

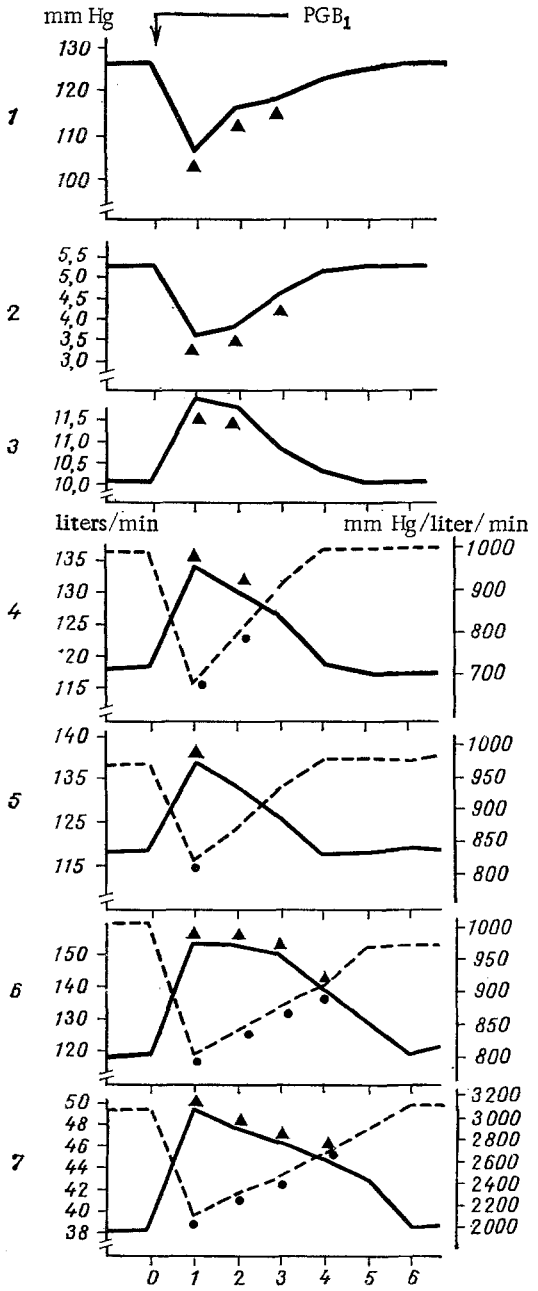

Fig. 3. Effect of PGB_1 on regional hemodynamics in dogs. Continuous lines (ordinate, on left): pressure in aorta (1), in superior vena cava (2), in portal vein (3), volume blood flow in common carotid artery (4) in superior mesenteric artery (5), in renal artery (6), and in femoral artery (7); broken lines (ordinate, on right):resistance in common carotid artery (4), in superior mesenteric artery (5), in renal artery (6), and in femoral artery (7). Remainder of legend as in Fig. 1.

time of blood by the heart was reduced from 0.20 to 0.18 sec. The stroke volume of the heart fell initially after injection of PGB_1, then increased. The minute volume of the heart increased under these circumstances, to reach maximum (by 25%) after 30 sec. Against the background of the action of PGB_1 the total peripheral resistance fell at most by 31%. An increase in the volume load (minute volume of the heart) led to an increase in the work of the left ventricle. The pressure in the pulmonary artery increased by 25% after injection of PGB_1. However, the total pulmonary resistance under these circumstances fell. The work

of the right ventricle rose sharply (by 71%) on account of an increase in the volume load. The indices of myocardial contractility (the peak rate of shortening of the contractile elements of the heart and the maximal velocity of their shortening against zero load) increased after injection of PGB_1 at most by 18 and 22% respectively. Other evidence of increased contractility of the myocardium was given by an increase in the maximal velocity of the blood flow in the ascending aorta and maximal acceleration of the ejection of blood by the left ventricle. Arterial hypotension caused by PGB_1 was thus due to a decrease in the total peripheral resistance. The myocardial contractility increased following administration of PGB_1. This was possibly connected with the direct inotropic effect characteristic of the other prostaglandins PGE and PGA [8], or it was due to activation of the sympathico-adrenal system in response to the fall of arterial pressure. The cause of the increase in the minute volume of the heart was evidently the increased venous return resulting from arteriolar vasodilatation, together with the tachycardia and increased myocardial contractility. The increase in pressure in the pulmonary artery was connected with the increase in minute volume of the heart.

The mean velocity of the volume blood flow in the coronary artery (Fig. 2) rose immediately after injection of PGB_1 to reach a maximum (an increase of 29%) after 1 min. The stroke coronary blood flow also was increased. The resistance of the coronary vessels and the mean diastolic resistance of the coronary arteries were reduced under these circumstances. The increase in the coronary blood flow following administration of the PGB_1 was thus due both to tachycardia and to dilatation of the coronary vessels.

Besides the brief aortic hypotension, a decrease in pressure in the superior vena cava and an increase in pressure in the portal vein were observed after injection of PGB_1 (Fig. 3). The mean velocity of the volume blood flow in the renal and femoral arteries rose appreciably, but in the common carotid and superior mesenteric arteries the increase was not significant. It can accordingly be concluded that the fraction of the cardiac output reaching the vessels of the skeletal muscles, kidneys, and heart is increased. To judge from the response of the renal and femoral arteries, PGB_1 has a vasodilator effect on the vessels of the skeletal muscles and kidneys. The decrease in tone of these vessels evidently plays the leading role in the reduction of the total peripheral resistance following administration of PGB_1.

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