EFFECT OF ATENOLOL AND PROPRANOLOL ON THE SYSTEMIC AND REGIONAL HEMODYNAMICS

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There are data in the literature on the effect of propranolol and other nonselective β-adrenoblockers on the distribution of the cardiac output among the organs and tissues of normotensive and hypertensive experimental animals [4, 5]. The effect of cardioselective β-adrenoblockers (atenolol etc.) on the distribution of the blood flow between organs and tissues has not been studied.

This paper describes an investigation of the effect of the cardioselective β-adrenoblocker atenolol, compared with that of propranolol, on the cardiac output and its distribution among the principal vascular regions.

EXPERIMENTAL METHOD

Experiments were carried out on normotensive male Wistar rats weighing 300-350 g, anesthetized with pentobarbital sodium (40 mg/kg intraperitoneally). The cardiac output and its distribution among the principal vascular regions were determined by the radioactive microspheres method [3, 6]. By means of a catheter introduced through the common carotid artery, 90,000 microspheres (NEN-TRAC microspheres, England), 15 μ in diameter, labeled with ^{46}Sc (specific activity about 1 μCi) in 0.2 ml of 10% dextran solution with the addition of one drop of Tween-80 (to prevent aggregation of the microspheres) were injected into the left ventricle in the course of 30 sec. Simultaneously with the beginning of injection of the microspheres blood was taken from the femoral artery by means of a two-way injector at the rate of 1 ml/min for 1 min (to determine activity of microspheres in a standard sample). The animals were then decapitated. Pieces of heart, lung, kidney, liver, stomach, large and small intestine, brain, skeletal muscles of the lower limbs, and also blood of the standard samples were placed in special test tubes and the ^{46}Sc activity was determined in the test samples by means of a Nuclear Chicago γ-ray counter (USA). Activity of ^{46}Sc in the test samples per gram tissue was expressed as a percentage of the injected dose of isotope. Changes in the fraction of the cardiac output reaching the given organ were determined from changes in the ^{46}Sc content in that organ. Cardiac output was determined by the equation: $A = (B \times C)/D$, where A is the cardiac output (in ml/min), B the rate of collecting blood from the femoral artery (in ml/min), C the content of labeled microspheres in the dose injected into the left ventricle, and D the content of labeled microspheres in the standard sample. The absolute tissue blood flow was determined as the product of the cardiac output and its fraction reaching the given organ. The systemic arterial pressure (AP) was measured by an electromanometer in the femoral artery (through a three-way cock) before and after blood taking, and the total peripheral resistance was calculated by dividing the mean AP by the cardiac output.

The animals were divided into three groups with 8-15 rats in each group. The rats of group 1 received an injection of isotonic NaCl solution through a cannula into the external jugular vein, whereas the rats of groups 2 and 3 received injections of atenolol and propranolol in a dose of 0.5 mg/kg (in this dose both drugs caused complete blockade of the β-adrenoreceptors of the heart) 5 min before injection of the labeled microspheres.

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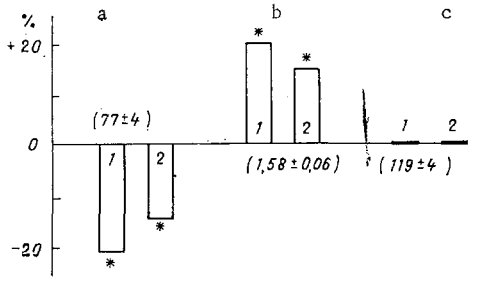

Fig. 1

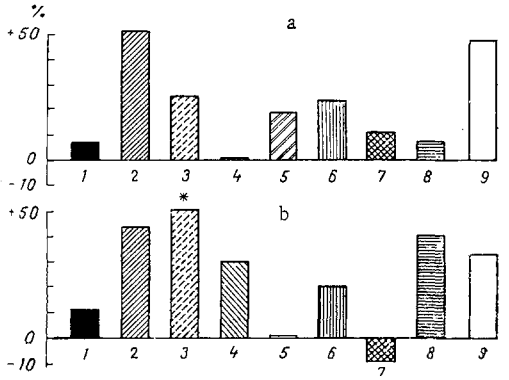

Fig. 2

Fig. 1. Effect of propranolol (1) and atenolol (2) on cardiac output (a), total peripheral resistance (b), and AP (c). Columns denote changes in parameters studied (in % of control). Numbers in parentheses give values of parameters in control: cardiac output (in ml/min), total peripheral resistance (in ml/mm Hg/ml/min), AP (in mm Hg). *P ≤ 0.05.

Fig. 2. Changes in ^{46}Sc activity in different organs and tissues (in % of control) after injection of propranol (a) and atenolol (b). 1) Heart, 2) lung, 3) stomach, 4) liver, 5) small intestine, 6) large intestine, 7) kidneys, 8) skeletal muscles, 9) brain.

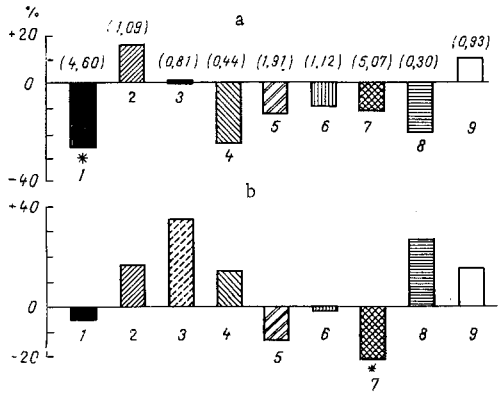

Fig. 3. Changes in tissue blood flow in different organs and tissues (in % of control) under the influence of propranolol (a) and atenolol (b). Numbers in parentheses show mean values of blood flow (in ml/min/g tissue – 15 experiments). *P ≤ 0.05. Remainder of legend as to Fig. 2.

EXPERIMENTAL RESULTS

Atenolol does not differ from propranolol in its effect on the systemic hemodynamics. Both drugs reduced the cardiac output and increased the total peripheral resistance, with the result that no significant change in AP took place (Fig. 1). Other workers obtained similar results [1, 2].

Atenolol and propranolol had a similar effect on the distribution of fractions of the cardiac output but differed from one another in their effect on the blood supply to the organs. Both drugs caused redistribution of the cardiac output in favor of the stomach, lungs, large intestine, and brain but did not change the coronary and renal fractions of the cardiac output (Fig. 2). Atenolol, but not propranolol, also led to some increase in the fractions of the cardiac output reaching the liver and skeletal muscles.

Atenolol caused a significant decrease in the renal blood flow proportional to the decrease in the cardiac output but had no significant effect on the blood supply to the heart, brain, gastrointestinal tract, lungs, or

skeletal muscles (Fig. 3). Unlike atenolol, propranolol caused a clear decrease in the blood supply to the heart. The change in the blood flow due to propranolol in the other vascular regions (including the kidneys and brain) was not statistically significant.

These data on the effect of propranolol on the regional hemodynamics in normotensive rats differ somewhat from results obtained in acute experiments on waking monkeys [4], but coincide almost completely with the results of experiments conducted on anesthetized normotensive and hypertensive rats during chronic administration of propranolol [5]. It was shown in the first investigation cited above that infusion of propranolol for 60 min leads to a decrease in the blood flow in the heart, kidneys, gastrointestinal tract, spleen, liver, and skeletal muscles proportional to the decrease in the cardiac output, but not in the brain. The second of the investigations cited, like the present experiments, showed that propranolol causes a greater decrease in the coronary and muscular blood flow than in the blood flow in other vascular regions. These differences in the effects of propranolol on the regional hemodynamics could be connected with differences in the experimental conditions (species of animals, effect of general anesthesia, etc.).

The results now obtained, showing a decrease in the coronary blood flow after administration of propranolol and in the renal blood flow in response to atenolol, accompanied by a negligible change in the corresponding fractions of the cardiac output are evidence that these effects of atenolol and propranolol are due to their influence on the vessels of the heart and kidneys. So far as the negligible effect of atenolol and propranolol, in the dose tested (0.5 mg/kg), on the blood supply to other vascular regions is concerned, this may be the result of a different functional role of β-adrenoreceptors in different vascular regions.

LITERATURE CITED

1. A. M. Barrett, Postgrad. Med. J., 33, Suppl. No. 3, 58 (1977).
2. B. J. Clar, in: Beta-Adrenoceptor Blocking Agents, Amsterdam (1976), pp. 45-78.
3. H. Flohr, H. W. Dahners, and W. Breull, Arzneimittel-Forsch., 25, 985 (1975).
4. A. S. Nies, G. H. Evans, and D. G. Shand, Am. Heart J., 85, 97 (1973).
5. K. Nishiyama, A. Nishiyama, M. A. Pfeiffer, et al., Blood Vessels, 15, 333 (1978).
6. A. M. Rudolph and M. A. Heimann, Circ. Res., 21, 163 (1967).

EFFECT OF LITHIUM HYDROXYBUTYRATE ON BRAIN SEROTONIN LEVEL IN INTACT RABBITS AND DURING HYPERACTIVITY OF CENTRAL SEROTONINERGIC SYSTEMS

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Lithium salts play an active role in central serotonin metabolism [17]. A decrease in the serotonin concentration has been demonstrated in the rat brain stem, midbrain, striatum, and hypothalamus during a course of lithium chloride [12] and carbonate [9]. Lithium prevents a rise in serotonin level caused by precursors of its synthesis, L-tryptophan and 5-hydroxytryptophan (5-HTP) [3], and increases the content of deaminated metabolic products of serotonin in the brain both of intact animals [15] and after electrical stimulation of the medial nucleus raphe in the midbrain [10].

The new original psychotropic agent lithium hydroxybutyrate [1] prevents amphetamine excitation [8] and 5-HTP- and nicotine-induced hyperkinesia [5], reduces electrical excitability of various subcortical structures

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