RESPONSE OF THE MESENTERIC MICROCIRCULATION OF RATS WITH EXPERIMENTAL RENAL HYPERTENSION TO HISTAMINE AND ADRENALIN

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The response of the blood flow and arterioles (the change in their diameter) in the rat mesentery to application of histamine (100-500 μg) and adrenalin (1-10 μg) was studied in vivo. The sensitivity of the microvessels 10-30 μ in diameter to the action of these substances was reduced in hypertension.

KEY WORDS: microcirculation; renal hypertension; biogenic amines.

Disturbances of the microcirculation are among the more important factors involved in the pathogenesis of hypertensive states. In this condition the reactivity of the microvessels is modified. Investigations of the microvessels of the bulboconjunctiva [9] and nailbed [6] of patients with essential hypertension have revealed the high sensitivity of the arterioles to adrenalin. A character of the action of histamine on the microvessels is also determined by their reactivity. This could account for the contradictory results indicating that histamine can induce both dilatation [4, 5, 10, 11] and constriction of the arterioles and other microvessels [7, 8].

The object of this investigation was to compare responses of the microcirculation to application of histamine and adrenalin to the rat mesentery in normal animals and animals with experimental hypertension.

EXPERIMENTAL METHOD

Male albino rats weighing 260-450 g were used. Experimental hypertension was induced by applying a metal coil (lumen 0.3-0.35 mm, length 2.5 mm) of 3-4 turns to the left renal artery, followed (15-20 days later) by removal of the second kidney [2]. The presence of hypertension was confirmed by measuring the blood pressure repeatedly by a bloodless method, without anesthesia, by means of a piezoelectric transducer [3]. The blood pressure of the control animals was 95 ± 3.6 mm and of the hypertensive animals 130 ± 5.6 mm Hg ($P < 0.01$).

Biomicroscopy of the rat mesentery was carried out under urethane anesthesia (1.6 g/kg). The abdomen was opened through a midline incision and a loop of intestine was carefully straightened out on the light conductor of the heated stage (37°C). Drying of the mesentery was prevented by moistening its surface with physiological saline warmed to 37°C and wrapping the intestine in moist gauze strips.

The internal diameter of the microvessels was recorded by an image splitting method [1], using an objective and ocular giving magnifications of 40× and 10×, respectively. Histamine (100-500 μg) and adrenalin (1-10 μg) were applied in 0.1 ml physiological saline. The experiments were carried out 7-126 days after removal of the kidney.

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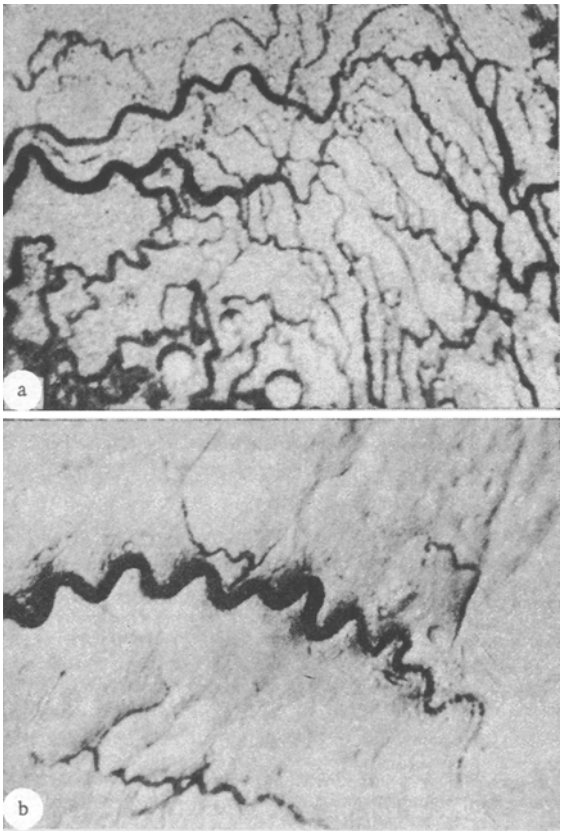

Fig. 1. Intravital microscopy of mesentery of a rat with experimental renal hypertension: a) general view of microcirculation (objective 10×, ocular 1.7×); b) wave-like shape of arteriole (objective 2.5, ocular 1.7).

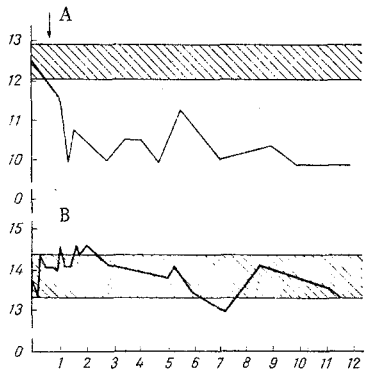

Fig. 2. Changes in diameter of arterioles after application of 10 μg adrenalin (marked by arrow): A) control; B) experimental hypertension. Shaded areas denote range of spontaneous variations of diameter. Abscissa, time (in min); ordinate, diameter of vessels (in μ).

EXPERIMENTAL RESULTS AND DISCUSSION

In the course of development of experimental hypertension in the animals their gain in weight was retarded. The animals became aggressive, their fur lost its sheen and became yellowish in color, and some of the hair came out.

In the early periods of development of hypertension (7-30 days) the mesentery became extremely sensitive to mechanical injury associated with its removal from the abdomen. This was shown by the development of stasis in the capillaries and in the small arterioles and venules.

Later (40-126 days) sensitivity to trauma became less than that usually observed and the blood flow in all the vessels remained normal after removal of the mesentery, so that stasis never developed.

This could evidently be explained by the increased pressure in the vascular system coupled with the simultaneous decrease in sensitivity of the vessel wall.

A noteworthy feature was the development of a network of vessels containing numerous metarterioles, precapillaries, capillaries, venules, and arteriolovenular anastomoses in these rats. For example, whereas in the control animals an arteriole 20 μ in diameter gave off on the average 5-11 vessels of smaller diameter, including metarterioles, precapillaries, and capillaries as branches, in experimental hypertension an arteriole of the same diameter gave off no fewer than 15 analogous vessels. The mesenteric microcirculation in hypertension gradually acquired the appearance of a network consisting chiefly of precapillaries, capillaries, and postcapillaries anastomosing with each other (Fig. 1a). Characteristically the arterioles and, in particular, the venules were wave-like in shape. Whereas normally one arteriole 20-25 μ in diameter may have up to 6 waves, in hypertension an arteriole of the same diameter may form up to 13 waves (Fig. 1b).

Changes in the blood flow in the microvessels of the mesentery 10-30 μ in diameter in response to application of histamine and adrenalin are shown in Table 1.

In the control animals histamine, in doses of 100 to 300 μg, caused slowing of the blood flow followed by stasis, which were abolished by rinsing with physiological saline. Histamine in doses of 400-500 μg led to irreversible stasis. Larger doses (300-500 μg) were needed to induce initial slowing of the blood flow in the animals with hypertension. However, after rinsing the blood flow was restored even after application of these larger doses of histamine.

TABLE 1. Changes in Blood Flow in Arterioles 10-30 μ in Diameter in Rat Mesentery in Response to Application of Histamine and Adrenalin

Substance	Dose (μg)	Control			Hypertension		
		slowing of blood flow	stasis	recovery of blood flow after rinsing off	slowing of blood flow	stasis	recovery of blood flow after rinsing off
Histamine	100	+	±	±	−	−	+
	200	+	+	+	−	−	+
	300	+	+	+	±	±	+
	400	+	+	±	−	−	+
	500	+	+	−	+	−	+
Adrenalin	1	+	+	±	+	+	+
	2	+	+	±	+	+	+
	3	+	+	−	+	+	+
	5	+	+	−	+	+	±
	10	+	+	−	+	+	±

Legend: +) change observed; −) no change; + or −) change present in some vessels and absent in other.

In the control series, application of adrenalin always caused slowing of the blood flow followed by the development of irreversible stasis in doses of 3-10 μg. In animals with hypertension the same doses of adrenalin never caused irreversible stasis.

Changes in the diameter of the microvessels showed that application of histamine in the control animals led to initial constriction (by 6-7% of the initial diameter of the lumen), followed by dilatation (by 3-6% of the initial diameter). In rats with experimental hypertension the response of the vessels to histamine was not significantly changed.

Application of adrenalin in the control animals led to constriction of the arterioles by 8-28%, whereas the same substance caused constriction by not more than 9-18% in the hypertensive animals. In other words, with an increase in the dose of adrenalin, constriction of the arterioles was increased by a lesser degree in the hypertensive than in the normal animals. The reduced sensitivity of the arterioles to adrenalin in hypertension is illustrated in Fig. 2.

In rats with experimental renal hypertension, the sensitivity of the mesenteric arterioles 10-30 μ in diameter to adrenalin is therefore reduced. Meanwhile there are reports in the literature to the effect that the sensitivity of the arterioles of the human bulboconjunctiva to adrenalin is increased in hypertension [9]. This contradiction can evidently be explained by species differences and by differences in the types of hypertension, the location of the microvessels tested, and the doses of the preparations used.

The response of the blood flow to application of histamine and adrenalin as described above also demonstrates a decrease in the sensitivity of the mesenteric microvessels of rats to this substance in experimental renal hypertension.

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