Effect of sinoaortic denervation on cardiac output

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KRIEGER, Eduardo Moacyr. Effect of sinoaortic denervation on cardiac output. Am. J. Physiol. 213(1): 139—142. 1967.—Cardiac output was measured in 30 rats with neurogenic hypertension of 20, 40, 180, and 360 days duration under light pentobarbital anesthesia. When compared with the values exhibited by 21 normal rats, all the denervated rats (except 4) had normal cardiac outputs, indicating that the major factor responsible for the elevation in blood pressure was an increase in peripheral resistance. Heart rate, blood volume, and hematocrit were also normal in the neurogenic hypertensive rats. For the purpose of comparison the cardiac output was determined in groups of rats with neurogenic, renal, and deoxycorticosterone (DCA) hypertension. The values (ml/min per 100 cm²) found in the denervated (14.4), renal (12.4), and DCA (15.0) hypertensive animals were not significantly different from those exhibited by normal rats (15.4). The blood volume of the rats with DCA hypertension was elevated. The results indicate that the hypertension produced in the rat by sinoaortic denervation, as well as that caused by DCA injection or renal artery constriction, is due to increased peripheral resistance rather than to elevation of cardiac output.

A radical denervation of the sinoaortic baroreceptor areas in the dog produces an elevation of its blood pressure. Still, some doubt exists concerning the exact mechanism (an increase in cardiac output and/or peripheral resistance [10]) responsible for this phenomenon. A close correlation between elevations of arterial pressure and heart rate was described (7, 28), but hypertension persisted when tachycardia was abolished (9, 20). More recently hypertension without tachycardia was found in dogs after isolated denervation of the carotid sinus area (4, 13, 14). In only one experiment was the cardiac output actually measured in neurogenic hypertensive dogs (1), showing that an increase in output rather than an elevation in the peripheral resistance was the major cause of the hypertension.

Neurogenic hypertension in the rat has been produced in our laboratory, and the increase in blood pressure seen in this animal species was not accompanied by as marked a tachycardia as that which has been observed in dogs (16). In the present experiment the cardiac output of rats with sinoaortic denervation was measured by the dye-dilution method. Rats with renal and deoxycorticosterone (DCA) hypertension were also included in this study in order to compare the cardiac output of rats with different types of experimental hypertension.

METHODS

Studies were performed in Wistar rats of both sexes weighing 170–280 g. The aortic (17) and the carotid (15) baroreceptor areas were denervated in a one-stage operation with a technique described elsewhere (16). The cardiac output was measured 20, 40, 180, and 360 days after the denervation. The neurogenic hypertensive rats in the group used for comparison purposes with other types of experimental hypertension were tested 2–6 months after the operation. Renal hypertension was produced by applying a silver clip to the left renal artery (27) simultaneously with right nephrectomy; these rats were used 3–5 months after the operation. Deoxycorticosterone hypertension was obtained by administering 1 mg deoxycorticosterone acetate (generously supplied by Schering, S.A.) daily to unilateral nephrectomized rats given 1% saline to drink; cardiac output was determined 2–3 months after the beginning of treatment. The arterial blood pressure of the unanesthetized hypertensive rats was repeatedly measured by means of a tail plethysmographic method (16).

Prior to the cardiac output determination, the blood pressure of unrestrained quiet rats was measured directly from the femoral artery which had been cannulated 4 hr before under ether anesthesia. Immediately after, the rats were lightly anesthetized with intraperitoneal pentobarbital (1–2 mg/100 g) with no interruption of pressure recording. This small dose of pentobarbital causes only minor changes in the blood pressure of the

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sinoaortic denervated rats or animals belonging to the other groups, as shown in results. The injection of the usual doses of pentobarbital (4 mg/100 g) in the neurogenic hypertensive rats caused a great fall in blood pressure and respiratory depression. The great sensitivity to anesthesia presently observed in rats with sinoaortic denervation has also been described in dogs (4, 23). The dye-dilution technique for the cardiac output determination was adapted from that described by Bullard (3). It consisted of the injection, with a Hamilton syringe, of 0.175 ml T-1824 solution (4 g/100 ml) into the femoral vein and the collection of blood samples from the femoral artery every 0.8 sec. The Stewart-Hamilton formulas were used for calculation of the cardiac output (8). Blood volume was measured in the usual manner from the concentration of dye in the blood samples taken at 10, 15, and 20 min. Body surface area was calculated from the body weight using the formula given by Mitchell (21).

RESULTS

Control and neurogenic hypertensive rats. The cardiac output of 21 normal rats of different sizes under light anesthetization by Nembutal was 18.5 ml/min per 100 cm² or 26.8 ml/min per 100 g, with a significant correlation ($r = 0.64, P < 0.05$) between the cardiac output and the body surface area. Figure 1 shows the confidence limits ($y = b_0 + b_1 x$) for any single predicted value of cardiac output per minute per surface area calculated from the data of the normal rats. By this criterion only 4 of the 30 neurogenic hypertensive rats of Table 1 had elevated cardiac output, indicating that elevated flow is not the main factor responsible for the hypertension exhibited by the sinoaortic denervated rats. The femoral arterial pressure of the control rats during the cardiac output determination was: systolic 142 (160/110), diastolic 90 (110-70), and mean 111 (127-90) mm Hg.
CARDIAC OUTPUT IN NEUROGENIC HYPERTENSION

TABLE 2. Mean cardiac output in control and experimental hypertensive rats

<table>
<thead>
<tr>
<th>Group and No. of Rats</th>
<th>Mean Direct R.P., mm Hg</th>
<th>Heart Rate, beats/min</th>
<th>Cardiac Output, ml/min per 100 cm²</th>
<th>Blood Volume ml/100 cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control, 10</td>
<td>109±2 (114±4)</td>
<td>210±11</td>
<td>15.4±1.0</td>
<td>0.86±0.11</td>
</tr>
<tr>
<td>Neural hypertension, 10</td>
<td>169±8 (168±6)</td>
<td>211±18</td>
<td>14.4±0.9</td>
<td>3.00±0.11</td>
</tr>
<tr>
<td>Renal hypertension, 9</td>
<td>167±9 (175±7)</td>
<td>432±9</td>
<td>12.4±1.1</td>
<td>3.06±0.12</td>
</tr>
<tr>
<td>DCA hypertension, 9</td>
<td>153±3 (162±4)</td>
<td>421±9</td>
<td>13.0±0.9</td>
<td>3.57±0.04†</td>
</tr>
</tbody>
</table>

Values are expressed as means ± se. * Blood pressure before anesthetization (1-2 mg/100 g pentobarbital). † Significantly different from other means.

The mean heart rate of the unanesthetized, unrestrained, control rats was 386 ± 53 (sd), becoming 408 ± 49 (sd) after the administration of the small dose of pentobarbital with 506 (X ± 2 sd) as the upper rate limit. The individual values of all the neurogenic hypertensive rats of Table 1 were less than 506 beats/min, in spite of the finding that four of the animals had increased cardiac output.

Blood volume per 100 cm² in the denervated rats was not statistically different from control animals, which had 2.89 ml/100 cm² (3.41 - 2.08). Hematocrit values were also similar in both the neurogenic hypertensive and the control groups (44 ± 5 and 45 ± 5, respectively).

Other types of experimental hypertension. All rats in the four groups of animals presented in Table 2 had uniform body weight (250-290 g). There was no significant difference between the mean cardiac output exhibited by these groups of rats. However, the blood volumes of the DCA hypertensive rats were significantly elevated. Light anesthesia with pentobarbital (1-2 mg/100 g) produced only a minor decrease in the blood pressure, approximately the same in the different groups, as shown in Table 2.

DISCUSSION

The results herein presented indicate that the hypertension produced in the rat by a radical denervation of the sinoaortic depressor areas is due to an increase in peripheral resistance. Cardiac output in neurogenic hypertensive rats was found to be normal not only when compared with normal animals but also when compared with rats with renal hypertension, which are considered to have normal outputs, as shown by Lendingham and Cohen (18). These authors observed that after an increase in cardiac output in the first days after operation, it returned to normal values, the renal hypertension being caused by an increase in peripheral resistance. Recently Olmsted and Page (22) studied the hemodynamic events in renal hypertensive dogs with implanted probes, confirming previous determinations by the Fick method (11), which showed that cardiac output is normal in the chronic state of renal hypertension.

It is well known that DCA in the rat causes hypertension and disturbances in water and electrolyte metabolism (2). The results of the present study show that, although the DCA hypertensive rats do have increased blood volume, their hypertension is produced by increased peripheral resistance with normal blood flow. The absence of a direct relationship between cardiac output and blood volume in different physiological conditions has been stressed by many authors (6).

The different behavior of cardiac output in the neurogenic hypertensive rat and dog (1) is not clear. The fact that the output of the heart remains normal in the rat after sinoaortic denervation may be due to the circumstance that all the efferent vagal fibers are left intact and also because the heart rate, in this species, is under almost maximal sympathetic tonus (5, 12). Several authors have obtained neurogenic hypertension in dogs without tachycardia (4, 13, 14). It is well established also that the reflex hypertension elicited in dogs by acute occlusion of the carotid arteries is mostly due to vasoconstriction rather than to increased cardiac output (19, 24).

Pentobarbital anesthesia decreases cardiac output of the normal rat, as observed by Popovic and Kent (25). In order to prevent the circulatory and respiratory depression produced in the neurogenic hypertensive rats by full anesthetization we used, for the cardiac output determinations, only one fourth or one half the usual dose of pentobarbital. The values of the cardiac output per minute found in our rats with this light anesthetization (18.5 ml/min per 100 cm² or 26.8 ml/min per 100 g) were quite similar to those described by Popovic and Kent (28.8 ml/min per 100 g) in the unanesthetized animals.

An increase in total blood volume apparently due entirely to an increase in cellular fraction of the blood was observed in dogs with neurogenic hypertension (26). In the present study this fact was not confirmed in the rat.

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REFERENCES


