THE REACTION OF DOGS TO STIMULI OF VASCULAR TONE AT VARIOUS INTERVALS AFTER HYPOPHYSECTOMY

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Reports in the literature concerning the importance of the pituitary and adrenals for vascular tone are inadequate, and are mainly concerned with the renal circulation.

In hypophysectomized frogs [4, 5] and dogs [1, 2], the sensitivity of the vessels to subthreshold doses of adrenalin and acetylcholine is increased. In hypophysectomized dogs [3] the arterial pressure is lowered, although they reacted to injection of 1 ml pituitrin and 0.5 ml adrenalin in the same way as dogs possessing a pituitary. Various workers [6, 7] have found an average fall in the arterial pressure of totally hypophysectomized animals of 18%; after removal of the posterior lobe it remained normal or slightly low [7, 8]. After rapid bleeding (1.5% of the body weight), the arterial pressure in these dogs was restored more slowly (on the average after 95 min) than in controls (on the average after 45 min).

We have studied the arterial pressure in hypophysectomized dogs after application of stimuli of a pressor (pituitrin, adrenalin) or depressor (acute bleeding, acetylcholine) character during the operation or after an interval of 1-2 days. The investigations showed that the arterial pressure in these animals was lowered significantly (by 50-80 mm) and that they were more sensitive to pituitrin and adrenalin, and especially so to acute blood loss.

Because our results were possibly attributable to the fact that during the first day or two after hypophysectomy the animals had been unable to develop compensatory adaptations, we were interested in examining the changes in vascular tone at later periods after the operation.

EXPERIMENTAL METHOD

Experiments were carried out on 5 dogs at different intervals (from 1 month to 2 years) after hypophysectomy. The arterial pressure was studied in these dogs before and after the action of adrenalin, pituitrin, and acute blood loss, and also after blood loss followed by administration of these drugs.

The arterial pressure was measured in a vascular loop exteriorized in the neck, using a combination of auscultation and palpation, for a period of 30-40 min before and after application of these stimuli. Adrenalin (0.2 ml 1:1000) and pituitrin (0.2 ml) were injected into the auricular vein. Bleeding (to a volume of 20 ml of blood per 1 kg body weight) was performed from the femoral artery under local anesthesia; in one dog (in which the vascular tone was more labile) repeated bleeding was performed under local anesthesia, because the effect of pain during the first bleeding caused a considerable increase in the arterial pressure.

The arterial pressure was measured for 10 days starting from the first day after bleeding; meanwhile the dogs received injections of adrenalin or pituitrin every other day. In one dog, on the first day after repeated bleeding, the arterial pressure was measured every 10-15 min for a period of 2 h.

Hypophysectomy was performed by the temporal route. In two dogs total hypophysectomy was performed, and in three animals the anterior lobe was removed and the posterior lobe divided.

EXPERIMENTAL RESULTS

In all the dogs the arterial pressure was lowered after operation, but this fall varied in degree and duration. In the totally hypophysectomized dogs (with an initial pressure of 125 and 145 mm) it fell steadily by 25-30 mm and remained at this level throughout the period of investigation (from 2 months to 1 year); in one partially hypophysec-

tomized dog (with an initial pressure of 110-120 mm) a considerable (by 30 mm) and lasting decrease in the arterial pressure also was observed (study begun 1 month after operation and continued for 9 months); in two partially hypophysectomized dogs (with initial pressures of 130 and 140 mm) the arterial pressure fell very slightly (by 10-20 mm) and remained at that level for only 2 months after operation, then it rose again to, or actually above, its initial level, but was very labile and fluctuated considerably during the application of stimuli such as a conversation behind the wall, a prick with a needle, and so on.

From 15 to 30 sec after injection of adrenalin, the arterial pressure in the totally hypophysectomized dogs rose by 75-80 mm for a period of 3-4 min. The reaction was of equal magnitude both 1-2 and 9-12 months after the operation.

In the partially hypophysectomized dogs 1-2 months after operation, an increase of 55-70 mm in the arterial pressure took place 15-30 sec after injection of adrenalin, but 4-5 months after operation the increase was only 25-50 mm; the velocity and duration of the reaction remained unchanged. In all the dogs the injection of adrenalin before operation caused a smaller (55-60 mm) increase in the arterial pressure; the rate and duration of the reaction were the same as after the operation.

After injection of pituitrin, in all the (totally and partially) hypophysectomized animals the arterial pressure increased by 20-40 mm irrespective of the interval (1-4 months or $1\frac{1}{2}$ years) after operation; the reaction began 30 sec after the injection and lasted 4 min. Before hypophysectomy, the injection of pituitrin into these dogs caused no reaction or led to a very slight (5-10 mm) and transient (1.5-2 min) rise of arterial pressure, while the rate of the reaction was slightly slower (1 min).

Acute bleeding of the totally hypophysectomized dogs caused a reaction which varied with the time elapsing after the operation. In one dog 3 months after the operation the arterial pressure after bleeding fell by 25 mm and was restored over a period of 12 days; in another dog the pressure was very slightly lowered (by 5-10 mm) 7 months after the operation, and was restored to its initial value after 4 days.

In the partially hypophysectomized dogs, 3-18 months after operation, acute bleeding caused no change in the arterial pressure. In one of these dogs with a labile pressure, repeated bleeding under general anesthesia was followed by measurement of the arterial pressure every 10-15 min for 2 h. Immediately after bleeding the pressure fell by 60 mm, but after 15 min it began to rise, and after 1 h it reached its initial value; during the following days it remained unchanged.

In all the dogs before hypophysectomy, acute bleeding did not alter the arterial pressure.

Injection of pituitrin after bleeding into totally hypophysectomized dogs caused a considerable (by 30-40 mm) increase in the arterial pressure, and if injected into partially hypophysectomized animals – an increase of 15-20 mm.

In similar experimental conditions after bleeding, the totally hypophysectomized dogs reacted by a larger increase (by 80-100 mm) in arterial pressure than the partially hypophysectomized animals (by 60-70 mm). Before operation, in similar experimental conditions, the arterial pressure rose in all the dogs by 50-60 mm.

It follows from the findings described above that after total hypophysectomy in dogs a lasting decrease in the arterial pressure takes place. Removal of the anterior lobe and division of the posterior lobe of the hypophysis cause a less marked decrease, more evident during the first 2 months after operation; in the other cases the arterial pressure is not lowered, but merely becomes more labile. It has been found [7, 8] that after removal of the posterior lobe alone, the arterial pressure is unchanged or is lowered very slightly; it may therefore be suggested that the lowering of the arterial pressure is due to removal of the anterior lobe. It is possible that the posterior lobe of the pituitary left behind in our dogs contributed to the development of compensatory adaptations, so that the fall in the arterial pressure in these animals was more marked only during the first few months after the operation.

The reaction to adrenalin after total hypophysectomy was more marked than after partial; it became weaker as the interval after operation grew longer.

The reaction to pituitrin was more marked after total hypophysectomy, and we did not find that it depended on the time elapsing after operation. The difference between our results and those of other writers [3] is probably explained by the fact that they used larger doses of adrenalin and pituitrin, for the change in the sensitivity to small doses is more marked.

Acute bleeding causes a considerable fall in the arterial pressure only in totally hypophysectomized dogs during the first 2-3 months after operation; later, this reaction becomes less evident. The injection of adrenalin or pituitrin after bleeding causes a reaction of greater magnitude in totally hypophysectomized dogs.

It follows from the results obtained on the first days and at later periods after operation, that the fall in the arterial pressure and the change in the sensitivity to adrenalin, pituitrin, and to acute bleeding several months after hypophysectomy are gradually compensated, and that this compensation is more evident in the dogs undergoing partial hypophysectomy.

SUMMARY

Chronic experiments were staged on hypophysectomized dogs. At various intervals following the operation (from 1-3 months to 2 years) a study was made of the blood pressure and its shifts due to the effect of adrenalin pituitrin, acute blood loss and after the action of these substances against the background of blood-letting. The blood pressure in dogs sinks appreciably after total hypophysectomy. Following partial hypophysectomy the blood pressure reduction was not as great or it even remained on the former level but became more labile. In total hypophysectomy the reaction to adrenalin was more pronounced than after partial hypophysectomy. This declined with the progress of time after the operation. The reaction of dogs to pituitrin was more marked after total hypophysectomy; no relation to the time lapse after the operation was noted. An acute blood loss caused a pronounced blood pressure reduction only in dogs subjected to total hypophysectomy during the first postoperative months; later this reaction became less marked. A more pronounced reaction occurred upon the administration of adrenalin or pituitrin to totally hypophysectomized dogs after blood-letting.

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