

# Effect of Artificial Bleeding on Blood Pressure in Hypophysectomised or Neurohypophysectomised Rats

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## Introduction

A low blood pressure was observed after hypophysectomy in rats and dogs<sup>3,8)</sup>. Clark<sup>5)</sup> found an independent release of vasopressin without oxytocin during hemorrhage in cats. There are a number of reports which studied on the release of vasopressin in response to hemorrhage<sup>2,5,8,14,16,20,26,27,29)</sup>. It was recognized that a significant fall in arterial blood pressure caused by hemorrhage released much more vasopressin than severe hypotensions caused by normovolemic conditions<sup>20)</sup>. However, it seems to be no any specific studies on the blood pressure recovery in response to moderate hemorrhage in neurohypophysectomised and hypophysectomised rats.

This experiment was, therefore, carried out to test the hypothesis that the blood pressure in response to hemorrhage in neurohypophysectomised and hypophysectomised rats, would be recovered slower than that of normal rats.

## Materials and Methods

Sexually matured Sprague-Dawley rats were obtained from Seoul National University Experimental Animal Farm, Seoul. The rats were maintained on pellets (Jeil Feed Co.) and tap water *ad libitum* in individual wire cage at least for 3 weeks before use. The rats used were 14 to 15 weeks old. The body weight of the rats were 350 to 400g and 250 to 300g in male and female, respectively.

Neurohypophysectomy and hypophysectomy were performed under ether (Kanto Chemical Co.) anesthesia. Surgery was performed within 30 minutes using

standard surgical procedures under semi-sterile conditions. The technique of surgery was the same as that used by Chung except for a few modifications to release dyspnea<sup>47)</sup>. Tracheotomy was performed to prevent dyspnea. The neurohypophysis and hypophysis were sucked out through Pasteur transfer pipet (Curtin Matheson Scientific Inc.)<sup>11,17)</sup>. After each operation Tardomyocel (0.5ml/rat, Bayer Vetchem Korea Ltd.) was intra-muscularly injected to each animals. The efficiency of the operation was checked by post-mortem histologically (Fig. 1)<sup>7)</sup>.

Blood pressure was recorded from the cannulated artery using physiograph (Narco Bio-System Inc.) or kymograph. Blood coagulation was prevented by heparin (500 IU/kg body wt.) Blood pressure was recorded within 30 minutes after pentobarbital sodium anesthesia, and blood (10ml/kg body wt.) was acutely bled from the cannulated artery. Hematocrit value was checked by microhematocrit centrifuge (International Co., Model MB). Vasopressin(5 IU/100g body



Fig. 1. Hypophysis after neurohypophysectomy in the rat. Neurohypophysectomy was performed 60 days before autopsy. (hematoxylin and eosin stain, X 13.2)

wt., Ferring Co.) was infused via carotid artery at the same time of bleeding in neurohypophysectomised rats. Principles of randomization were applied in all experiments and chi-square test was employed for the statistical analysis.

### Results

In normal rats, the blood pressure of male ( $162 \pm 4$  mm Hg) was slightly higher than that of female ( $157 \pm 5$  mmHg) and hematocrit value of male ( $45 \pm 0.7\%$ ) was similar to that of female ( $43 \pm 0.6\%$ ), but no significant differences were observed. Effect of neurohypophysectomy on blood pressure and hematocrit value were shown in Fig. 2. The blood pressure and hematocrit value of hypophysectomised rat were significantly lower than those of normal and neurohypophysectomised rats ( $P < 0.001$ ). The blood pressure and hematocrit value of normal rats were similar to those of neurohypophysectomised rats.

In neurohypophysectomised, hypophysectomised, and normal rats the blood pressure decreased over 50% after bleeding (10ml/kg body wt.) Effect of bleeding on blood pressure recovery in neurohypophysectomised rats were shown in Fig. 3. The blood pressure of normal rats within 2 minutes after bleeding recovered faster than those of the other groups ( $P < 0.001$ ).

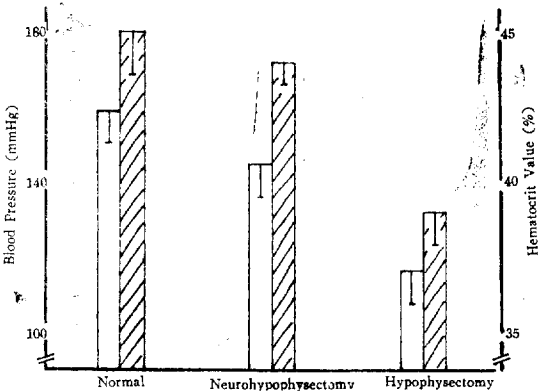


Fig. 2. Mean arterial blood pressure and hematocrit value in normal, neurohypophysectomised and hypophysectomised rats. Vertical lines indicate  $\pm$ S.E.  $\square$  means arterial blood pressure  $\blacksquare$  hematocrit value.

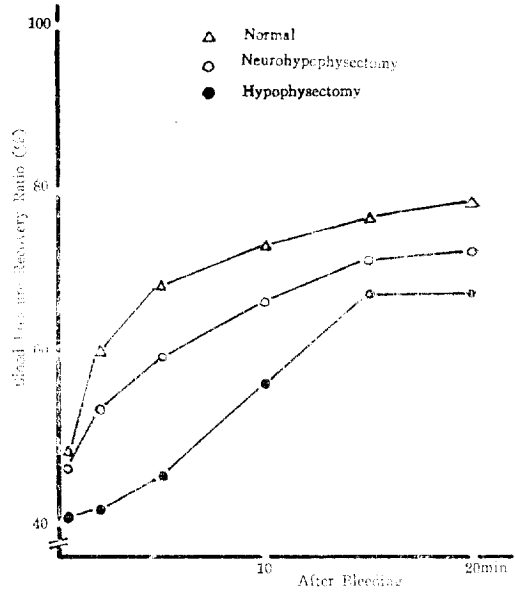


Fig. 3. Blood pressure recovery ratio after bleeding in normal, neurohypophysectomised and hypophysectomised rats. Recovery ratio =  $\frac{\text{blood pressure after bleeding}}{\text{blood pressure before bleeding}} \times 100$

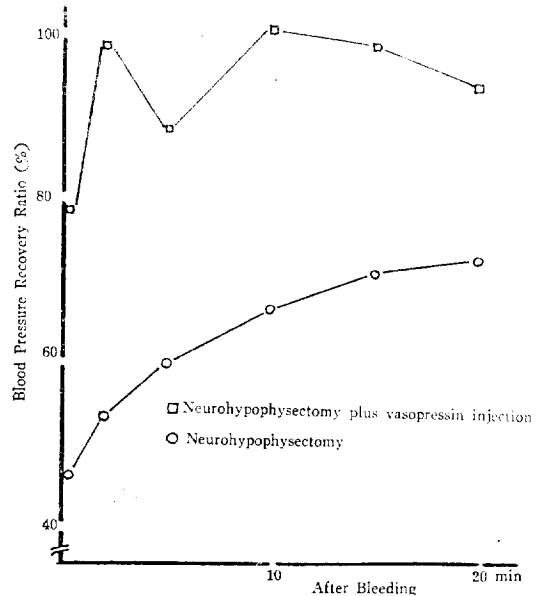


Fig. 4. Effect of vasopressin infusion at the same time of bleeding on blood pressure in neurohypophysectomised rats. Recovery ratio =  $\frac{\text{blood pressure after bleeding}}{\text{blood pressure before bleeding}} \times 100$

Effect of vasopressin infusion on blood pressure at the same time of bleeding in neurohypophysectomised rats were shown in Fig. 4. The blood pressure in the neurohypophysectomised rats following the infusion of vasopressin increased more within 2 minutes after vasopressin infusion than that of neurohypophysectomised rats ( $P < 0.001$ ).

## Discussion

The permissible amount of bleeding in dogs was 3.5 % of body weight, but there were some cases showing death after bleeding of 2.0% of body weight in rats<sup>24,31</sup>. In this experiment some cases were dead after bleeding of 2.0% of body weight in neurohypophysectomised rats, and it was found that blood pressure dropped markedly after bleeding of 1.0 of body weight. The blood volume of rat was 54.3 ml/kg body wt. and 1.0% of body weight was equal to the volume from 15 to 18% of whole blood volume<sup>13,29</sup>.

In this experiment mean blood pressure was 162 mm Hg in normal male rats. Beznak<sup>3</sup> observed that systolic and diastolic carotid artery pressure were 101 and 99mm Hg, respectively. This different result seemed to be due to the experimental environment, devices, and strain difference.

Polydipsia, low blood pressure and body weight loss were observed in neurohypophysectomised and hypophysectomised rats (Fig. 2) as reported previously.<sup>25</sup> The low blood pressure and abatement of hypertension after hypophysectomy were well reported<sup>21-23,30</sup>.

The cause for the low blood pressure after hypophysectomy was due to the decrease in cardiac output<sup>3</sup>. The first change after hypophysectomy was the diminished oxygen need of the animal due to decreased general metabolism, leading to a body weight loss. The cause for polydipsia was the blockade of vasopressin release from the neurohypophysis<sup>1</sup>.

Radioimmunoassay enabled to determine the concentration and half-life of vasopressin in plasma<sup>12,13</sup>. The concentration of vasopressin in plasma increased after hemorrhage in the rat<sup>9</sup>, cat,<sup>5</sup> dog,<sup>27</sup> goat,<sup>20</sup> sheep,<sup>19</sup> monkey,<sup>2</sup> and man<sup>14</sup>. The level of vasopressin rose within 5 minutes after hemorrhage in the

cat<sup>5</sup> and dog.<sup>29</sup> In rats the half-life of arginine vasopressin was  $2.6 \pm 0.3$  minutes<sup>13</sup> and the concentration was relatively constant, averaging  $2.3 \pm 0.9$  pg/ml under basal conditions in unanesthetised rats<sup>9</sup>. Increased plasma arginine vasopressin did not become significant until plasma volume had decreased by 8 per cent or more<sup>9</sup>. Larsson et al.<sup>20</sup> suggested that vasopressin secretion may help to maintain the arterial blood pressure in emergency situations. There are many factors that control the blood pressure recovery after bleeding such as vasopressin, renin, angiotensin, and aldosterone<sup>10</sup>.

We assumed that there will be some the difference in recovery of blood pressure after hemorrhage between normal and neurohypophysectomised rats. In these experiments the blood pressure of neurohypophysectomised rats recovered slower than that of normal rats within 5 minutes after bleeding (Fig. 2). This result supports the result of Larsson et al.<sup>20</sup> Edmunds et al.<sup>10</sup> observed moderate elevation of blood pressure within 20 minutes after vasopressin administration.

If endogenous vasopressin play an primary role in blood pressure recovery, infusion of vasopressin at the same time of bleeding in neurohypophysectomised rats could elevate the blood pressure abruptly within 5 minutes after bleeding. In this experiment the abrupt peak was confirmed within 2 minutes after bleeding (Fig. 3). By the results obtained in these experiments it seemed to be that the release of vasopressin from neurohypophysis might help to elevate arterial pressure after hemorrhage.

## Conclusion

To study the effects of moderate hemorrhage on blood pressure in the neurohypophysectomised or hypophysectomised rats, the blood pressure in operated rats after acutely bled from cannulated carotid artery were recorded by physiograph or kymograph.

The results obtained in this experiment were summarized as follows:

1. The mean blood pressure was  $162 \pm 4$  and  $157 \pm 5$  mm Hg, and the hematocrit value was  $45 \pm 0.7$  and  $43 \pm 0.6\%$  in normal male and female rats, respectively.

2. The mean blood pressure of hypophysectomised rats ( $117 \pm 8$  mmHg) was significantly lower than those of normal ( $159 \pm 9$  mmHg) and neurohypophysectomised rats ( $149 \pm 10$  mmHg) ( $P < 0.001$ ).

3. The blood pressure decreased over 50% after bleeding (10 ml/kg body wt) in normal, neurohypophysectomised and hypophysectomised rats ( $P < 0.001$ ).

4. The blood pressure of neurohypophysectomised and hypophysectomised rats recovered slower than that of normal rats within 2 minutes after bleeding ( $P < 0.001$ ).

5. The blood pressure of vasopressin infused neurohypophysectomised rats recovered faster than that of the neurohypophysectomised rats within 2 minutes after bleeding ( $P < 0.001$ ).

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腦下垂體 또는 腦下垂體後葉을 除去한 쥐에서 放血이 血壓에 미치는 영향

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抄 錄

腦下垂體 全體 또는 腦下垂體後葉만을 除去한 쥐에 있어서 放血이 血壓에 미치는 영향을 관찰하기 위하여 腦下垂體 또는 腦下垂體後葉을 除去한 쥐에서 頸動脈을 통하여 體重 kg 당 10ml의 피를 뽑은 다음 physiograph와 水銀柱를 이용한 kymograph를 사용하여 血壓을 측정하였던바 아래와 같은 결과를 얻었다.

1. 정상 쥐의 血壓 및 hematocrit 값은 수컷이  $162 \pm 4 \text{ mmHg}$ ,  $45 \pm 0.7\%$ 이었고 암컷은  $157 \pm 5 \text{ mmHg}$ ,  $34 \pm 0.6\%$ 이었다( $p > 0.05$ ).

2. 腦下垂體를 제거한 쥐의 血壓은  $117 \pm 8 \text{ mmHg}$ 로서 정상( $159 \pm 9 \text{ mmHg}$ ) 및 腦下垂體後葉을 제거한 쥐의 血壓( $149 \pm 10 \text{ mmHg}$ )보다 낮았다( $p < 0.001$ ).

3. 腦下垂體 또는 腦下垂體後葉을 제거한 쥐와 正常的인 쥐에 있어서 放血後(10ml/kg BW) 血壓은 50%이상 감소하였다( $p < 0.001$ ).