Responses to Epinephrine in Patients with Anorexia Nervosa

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Abstract

To examine the sensitivity to epinephrine in patients with anorexia nervosa, 20-60 ìg/kg body weight/min of epinephrine was infused for 30 min each in 5 patients and 5 controls. The increase in pulse rate and the decrease in diastolic blood pressure were significantly smaller in the patient group. Elevated plasma GH levels in the patients were markedly suppressed by epinephrine infusion. These results indicate the β-adrenergic function is decreased at least in the cardiovascular system in patients with anorexia nervosa.

In the course of examining the responses of pituitary and adrenomedullary hormones to insulin-induced hypoglycemia in patients with anorexia nervosa, we noticed that these patients exhibited minimal clinical manifestations of adrenergic stimulation such as palpitation, tachycardia or sweating. This can be partly explained by decreased secretion of epinephrine in response to hypoglycemia (Nakagawa et al., 1985). However, the coexistence of decreased sensitivity of β-adrenergic receptors in these patients cannot be ruled out.

The present study was undertaken to examine the responses to exogenously administered epinephrine in these patients.

Materials and Methods

Five female patients with anorexia nervosa, age 17–27, and 5 female control subjects of comparable age were studied. The body weights were 34.6±4.1 (mean±SD) kg in the patients and 54.4±5.0 in the controls. Infusions of physiological saline at the rate of 1 ml/min and the automatic recordings of pulse rate and blood pressure every 5 min were started between 9:00 and 9:30 h. After a stable period of 30 min, physiological saline was replaced with that containing epinephrine at a concentration of 20 ìg/kg body weight/ml. The speed of the infusion was doubled for the next 30 min and tripled thereafter. The epinephrine infusion was stopped at 90 min.

Blood was drawn from the indwelled catheters every 15 min during and 30 min after the end of the infusion for the determination of blood glucose, GH (RIA by the method of Nakagawa et al., 1985) and prolactin (RIA with a kit purchased from the Dainabot Co.).

Results

Cardiovascular Responses (Figure 1)

The control subjects showed a dose-related increase in the pulse rate and a
Fig. 1. The changes in pulse rate, blood pressures (systolic, diastolic and pulse pressure) and double product (systolic pressure × pulse rate) in control saline infusion (−30–0 min) and infusion of graded doses of epinephrine (0–90 min). ○—○ controls, ●—● patients with anorexia nervosa. mean ± SE.
decrease in diastolic blood pressure. Their maximal changes at or near the end of the epinephrine infusion (90 min) were $+26.4 \pm 3.3$ (mean $\pm$ SE)/min ($p < 0.001$) and $-22.2 \pm 3.3 \text{ mmHg}$ ($p < 0.001$), respectively, in comparison to those at the point immediately before the beginning of the epinephrine infusion (0 min). The systolic blood pressure tended to rise ($+13.3 \pm 5.6 \text{ mmHg}$, $p > 0.05$). Thus, the pulse pressure ($+37.2 \pm 6.3 \text{ mmHg}$) and double product (pulse rate multiplied by systolic blood pressure; $+4015 \pm 575 \text{ mmHg/min}$) were also remarkably increased. In contrast, patients with anorexia nervosa had

![Epinephrine mg/kg/min](image)

Fig. 2. The changes in blood glucose, plasma GH and prolactin levels in control saline infusion (−30–0 min) and infusion of graded doses of epinephrine (0–90 min). ○--○ controls, ●--● patients with anorexia nervosa. mean $\pm$ SE. GH levels of the patients are shown as a % of the 0 min values, and those of the controls both as a % of the 0 min values (upper broken line) and in ng/ml (lower broken line).
smaller changes in all of these parameters. The diastolic blood pressure lowered maximally with the lowest dose of epinephrine infusion and tended to rise with increased doses of epinephrine. The final change of $-0.6 \pm 4.4$ mmHg in diastolic blood pressure and maximal increase of $+9.4 \pm 1.3$ min in pulse rate, $+19.0 \pm 8.1$ mmHg in pulse pressure and $+1309 \pm 297$ mmHg/min in double product were significantly lower than those in control subjects ($p<0.01$, $p<0.01$, $p<0.05$ and $p<0.01$, respectively).

**Blood glucose** (Figure 2)

The blood glucose levels increased with the epinephrine infusion. The maxima were $+32.4 \pm 5.3$ mg/dl in the controls and $+24.0 \pm 5.6$ in the patients. However, the difference was not statistically significant.

**Plasma GH and prolactin** (Figure 2)

The basal plasma GH levels in the control subjects were $0.4 \pm 0.1$ ng/ml, and, in 2 subjects they slightly increased in the latter part of the infusion. Three other controls did not show any significant change. In contrast, the basal levels in the patients were $7.4 \pm 0.9$ and remarkably decreased during the epinephrine infusion, reaching the nadir of $9.6 \pm 1.1$% of the initial level at 90 min. The GH levels showed a slight rebound after the cessation of the infusion.

There could not be found any significant change in plasma prolactin levels during and after the epinephrine infusion in both groups.

**Discussion**

The present study showed the decreased responses in the pulse rate or blood pressure to exogenous epinephrine infusion in patients with anorexia nervosa. These findings are consistent with our previous observation that these patients manifested clinical signs of adrenergic stimulation less remarkably in response to insulin-induced hypoglycemia.

Epinephrine was used to observe the response to adrenomedullary hormone in the present study. However, epinephrine is not the stimulator specific for $\beta$-adrenergic receptor as isoproterenol (Innes and Nickerson, 1980). The slight increase in systolic blood pressure, though statistically insignificant, is attributable to the stimulation of $\alpha$-adrenergic receptor. The paradoxical rise in diastolic pressure with increasing doses of epinephrine observed in the patient group suggests a decrease in $\beta$-adrenergic function with preserved or rather increased $\alpha$-adrenergic function. Actually, an increase in $\alpha$-adrenergic receptors was reported in patients with anorexia nervosa (Luck et al., 1983) and in starved rats (Spyra and Pirke, 1982).

The response of plasma epinephrine to hypoglycemia was decreased and basal plasma and urine epinephrine were also lower, though not statistically significant, in the other series of patients with anorexia nervosa (Nakagawa et al., 1985). The drop in the plasma epinephrine level would cause an increase in the number and/or affinity of $\beta$-adrenergic receptors. Therefore, the present results indicate that another factor or factors in the patient group affects the receptor or post-receptor mechanism involved. It also remains unclear whether the desensitization to epinephrine in patients with anorexia nervosa is caused simply by weight loss or by other more essential deterioration in these patients.

Plasma GH was suppressed with the epinephrine infusion in patients with anorexia nervosa. Infusion of saline for 120 min in 2 cases or serial blood samplings in all cases did not affect the elevated GH levels. Blood glucose levels increased slightly with epinephrine infusion and this may tend to suppress GH levels. However, plasma GH levels were hardly suppressed with oral glucose loading in these patients. On the other hand, the inhibition of GH secretion by $\beta$-adrenergic stimulation is well established (Blackard and Heidingsfelder, 1968; Imura
et al., 1971). Although the effect of epinephrine itself on GH secretion is controversial, and the suppression of GH levels in the patients could not be compared with the controls because of very low basal levels in the latter, β-adrenergic function seems to be preserved at least enough to maintain nearly normal regulation of GH secretion in patients with anorexia nervosa.

References


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