Catecholamine in Congestive Heart Failure

Report II

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Through a light on the pathophysiological significance of cardiovascular disturbance related to the sympathicoadrenal system, the quantitative determinations of the plasma and urinary catecholamine in the cases of congestive heart failure were tried ; and studies were undertaken on the variation of catecholamine during the digitalization and a sympathetic blocking agent as well as their effects on clinical progress.

It has been found that concentration of plasma catecholamine is intimately related with its urinary excretory figure, while the plasma concentration in cardiac failure seemed to have increased, giving a higher value than those of controls. In the exercise test, plasma catecholamine tends to show a marked elevation.

It is proved, by the observations of catecholamine in plasma and urine, however, that dynamic changes of this pressor amine would be attributable to improved cardiac condition in the digitalized cases.

ALTHOUGH the sympathoadrenal system exerts a vital influence in biophysiological adjustment of the circulatory function, either increased sympathoadrenal activity or heightened active state induced with exogenous catecholamine would enhance oxygen consumption, furthermore there was an increase in cardiac work load due to constriction of the peripheral vascular system. It has been believed that hyperfunctional sympathoadrenal system would be inimical to the cardiovascular organs because of deleterious influence on the carbohydrate and lipid metabolism of the myocardium. Our previous paper dealt with the variation of urinary catecholamine to clarify further on the pathophysiological significance related to the sympathoadrenal system in the cardiac diseases. The present paper is to add further on the catecholamine variation in plasma and urine in the heart diseases in reference to clinical situations.

METHOD

For concentration of plasma catecholamine, modified Häggendal's method was

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followed. For urinary secretion, modified Imaizumi's Euler-Floding method was adopted. Hitachi's spectrofluorophotometer was used for degree of fluorescence following concentration, separation and decolorization.

RESULTS

1. Plasma concentration of catecholamine in normals and various cardiac diseases are as shown in the Fig. 1. Ten cases of the normals for the

Fig. 1. Plasma concentration of catecholamine of patients with cardiac failure.

Fig. 2. Correlation between plasma concentration of catecholamine and urinary excretion of catecholamine in hour.

contrast were shown to be $0.28 \pm 0.08 \mu\text{g./L.}$, while the heart cases numbering 29 showed the higher value ranging from 0.23 to $1.92 \mu\text{g./L.}$ That is; the plasma concentration of catecholamine is not changed significantly due to the pathogenesis of heart failure, but due to the severity of heart failure.

2. Correlation between the plasma concentration of catecholamine and its urinary excretion during a period of 1 hour, in the midst of which blood specimen was collected, is shown in Fig. 2. There seemed to be a significant positive correlation found between the catecholamine content of blood and the excretory quantity of urinary noradrenaline as well as adrenaline with their related coefficient of correlation and risk rate of $r=0.72$, $P 0.01$, $r=0.62$, $P 0.01$, respectively. Another attempt has been made to compare catecholamine content in plasma and urine. Twenty-four hour urine was collected in 4 divided portions. Blood was withdrawn at the corresponding time to each period of 6 hours. As is shown in Fig. 3 it is demonstrated that there is paralleled diurnal changes of catecholamine content between plasma and urine.

3. Variability of the urinary and plasma catecholamine in reference to hemodynamic changes during venoclysis of the exogenous adrenaline

Healthy subjects were employed and adrenaline in 5% dextrose solution 100, 200, 300 and $400 \mu\text{g./100 ml.}$ was intravenously infused for 1 hour at a rate of 5 ml. per min. Determinations of serum electrolytes and plasma concentration of catecholamine as well as urinary catecholamine changes during venoclysis were made together with the heart rate and blood pressure as shown in Fig. 4.

It is shown that the plasma catecholamine has risen markedly due to

Fig. 3. Diurnal changes of plasma concentration of catecholamine and urinary excretion of catecholamine.

Fig. 4. Changes of urinary excretion of catecholamine and hemodynamic changes induced by adrenaline infusion in normal subjects.

intravenous administration of adrenaline; on the other hand, urinary excretion of noradrenaline has been decreased in contrast to heightened adrenaline. As to serum electrolytes, there occurred decreased potassium with little change in sodium. Hemodynamically, systolic pressure was elevated radically almost always and with accelerated heart rate though the diastolic pressure exhibited reduced pressure.

Fig. 5. Changes of plasma concentration of catecholamine on exertion in cardiac patients (●—●) and normal subjects (○-----○).

4. Variation of oxygen consumption and changes in plasma concentration of catecholamine on exertion in the cardiac patients

As shown in the Fig. 5, the rate of oxygen consumption showed increase when they try to exert themselves. Concentration of the plasma catecholamine of the controls showed the elevated values from $0.10 \mu\text{g./L.}$ to $0.37 \mu\text{g./L.}$, however, in the cardiac patients their rate increased sharply from $0.17 \mu\text{g./L.}$ to $1.40 \mu\text{g./L.}$

5. On the influence of catecholamine variation in plasma and urine and clinical changes when a digitalization or a sympathetic blocking agent was administered to the cardiac patients

Case 1, hypertensive decompensated heart, age 65, male.

Both plasma and urinary catecholamines have shown marked decrease when reserpine was administered. There was reduction in urinary quantity, while the vital capacity seemed to have decreased and the other clinical and laboratory findings were of definite signs and figures of aggravated condition of cardiac insufficiency. Concentration of plasma catecholamine rose radically due to full digitalization, though the rate of urinary catecholamine shifted to increased quantity with resultant improvement in clinical signs (Fig. 6).

Fig. 6. K.K., 65-year-old male with hypertensive decompensation.

Diurnal changes of catecholamine in plasma and urine, and some clinical features during the treatment with reserpine and digitalis.

Fig. 7. K.K., 65-year-old male with hypertensive decompensation.

Successive observation of variations on plasma concentration and urinary excretion of catecholamine in short time period before and during rapid digitalization.

Fig. 8. M.M., 52-year-old female with mitral stenosis and insufficiency.

Diurnal changes of catecholamine in plasma and urine, and some clinical features with the treatment with Propranolol.

Fig. 7 is the same case which has shown clinical improvement and showed hourly progress of catecholamine as well as clinical effect of the digitalis.

Case 2, mitral stenosis and insufficiency, age 19, female.

This illustrates the case in which administration of Propranolol, a sympathetic

blocking agent for β -receptor of the sympathetic nerve, has caused aggravated signs of the cardiac condition and the therapy changed to the digitalization. Catecholamine values of plasma and urine revealed to show high but with digitalis treatment there was decreased tendency in plasma concentration after a transient rise. The clinical picture turned for the better (Fig. 8).

Case 3, mitral stenosis, age 52, female.

Administration of Propranolol was tried with this patient whose clinical signs presented the decompensated heart of moderate degree. It was found that the

Fig. 9. K.Y., 19-year-old female with mitral stenosis.

Diurnal changes of catecholamine in plasma and urine, and some clinical features during the treatment with digitalis.

Fig. 10. T.I., 68-year-old female with myocardial infarction.

Diurnal changes of catecholamine in plasma and urine, and some clinical features during the treatment with digitalis.

drug has caused increase in both plasma and urinary catecholamines. The patient got worse as his urinary output began to reduced and with changes in body weight. Discontinuance of medication gave rise relatively early clinical improvement.

Case 4, myocardial infarction, age 68, female.

The cardiac decompensated patient gave a previous history of myocardial infarction in which catecholamines in blood and urine shifted to increase upon digitalization. As shown in Fig. 10, the patient upon treatment showed definite improvement in their clinical signs along with catecholamine enhancement.

DISCUSSION

With stimulation of the sympathetic nerve, it has been known that catecholamine is released either at the postganglionic endings or by the adrenal medulla. Its part is released in circulatory blood while the circulating catecholamine is not entirely metabolized but excreted in urine as such. When the sympathetic nerve is in the state of hypertonicity it is reasonable to assume that catecholamine would be enhanced in plasma as well as in urine.

Awareing that the catecholamine can exert a predominating influence in the regulation of circulatory function, it is quite possible to expect abnormal sympathetic tone in the cardiac insufficiency due to altered circulatory malfunction.

Our previous report on the variation of urinary catecholamine in heart disease has revealed the fact that when an exogenous catecholamine was administered, no appreciable effect of the reduced function of the liver or kidney could be observed on the urinary excretion of catecholamine. On the other hand, when adrenaline alone was administered the urinary noradrenaline output would be decreased. This could be interpreted as either due to biochemical mechanism of maintaining internal organic milieu or compensatory action of the administered drug. Present studies threw some lights on the direct relationship between plasma concentration of catecholamine and urinary excretory catecholamine. Variable urinary output may reflect the sympathetic tonicity though the administration of the exogenous catecholamine may not give rise the same effect as in the state of sympathetic stimulation. Ruschmer has stated that organic reaction at the time of exertion test seems to closely resemble that of the administration of exogenous catecholamine. Our results have demonstrated that plasma concentration of catecholamine has definitely increased during the exercise test.

We have failed to observed significant relationship between plasma concentration of catecholamine and various forms of cardiac diseases which are associated with cardiac decompensation as have already been pointed out

concerning urinary catecholamine. The quantitative variation is found to be depend upon degree of involved cardiac disease rather than original disease conditions.

With administration of the sympathetic nerve blocking agent, the kind of drug used would make difference in the catecholamine content of blood and urine. Reserpine is known to cause marked decrease of plasma and urinary catecholamines, whereas beta receptor blocking agent, Propranolol, would increase them, but either drug would likely to cause reduction in the sympathetic tonicity of the heart, hence the clinical signs of the heart disease would be aggravated.

The fact that both plasma and urinary catecholamines tend to be increased under the influence of digitalis, resulting in immediate clinical benefit, would imply that the cardiac contractility would be strengthened due to combined effect of digitalis with fortified catecholamine quantity. As it has been seen, no particular relationship could be observed between etiological factors on cardiac insufficiency in low output type and digitalis effects or fluctuation of plasma or urinary catecholamine. It is assumed, however, that there should be specific relation between the digitalis effect and catecholamine quantity.

Thus, for the cardiovascular system, augmented catecholamine serving as the activator it is our interest to know further the mode of its action on the myocardium or on the vascular system and also metabolic process. It is equally important for us to investigate not only for an effect of catecholamine on the hemodynamics but also its role in energy production in metabolic process.

CONCLUSION

Plasma and urinary catecholamines were measured of the cardiac patients with reference to clinical progress.

(1) Positive correlation was found between plasma and urinary levels of catecholamine using urine collected during the period of about 1 hour in the midst of which blood was withdrawn.

(2) In the majority of the cardiac patients, plasma concentration of catecholamine presented higher values than the control group though no such relationship could be detected with etiological factors on cardinals.

(3) Elevation of catecholamine in plasma along with increased oxygen consumption rate would be markedly greater than the control group when cardiac cases were submitted of exercise test.

(4) In congestive heart failure due to various causes, the effect of sympathetic blocking agent seemed to give clinical unfavorable. Their case histories were presented.

Comments were made on the pathophysiological significance of the heart diseases concerning the sympathetic nervous system.

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