Studies on Cerebral Circulation and Metabolism in Hypertensive Diseases

II. Relation between the Cerebral Circulation and Metabolism and Clinical Findings in Essential Hypertension

By

Mitsuaki Tateyama

(館山 光昭)

From the Department of Internal Medicine, Sendai National Hospital, Sendai. Director: Dr. T. Kato, Professor Emeritus of Tohoku University

(Received for publication, March 30, 1959)

It is rationally suggested that in hypertension the blood circulation and intermediate metabolism in the brain undergo the influence of the presence of various clinical findings and complications of the disease and vice versa. Many problems, however, concerning those relations are not yet adequately elucidated. In the present report, these phases have been strongly studied and the correlation between the values representing the cerebral circulation and metabolism and the clinical findings on 51 patients with essential hypertension and its pathophysiological meaning have been discussed.

EXPERIMENTAL

Method

As subjects, 51 patients with essential hypertension were used and the method of measurement of the cerebral circulation and metabolism is the same as given in the first report¹⁾. 35 of the cases were examined on their arm-to-ear circulation time by Matsuoka's method²⁾*, 11 on their renal hemodynamic data [renal blood flow (RBF) and renal vascular resistance (RVR)] by sodium para-aminohippurate clearance method, 28 on renal function with 15 min. phenolsulphonphthalein excretion test and all the subjects on the haemoglobin content of the arterial blood with Shigiya's method³⁾.

RESULTS AND DISCUSSION

1. Retinal findings and cerebral circulation and metabolism

* Acetosulfonamide solution is given in cubital vein and blood blots are obtained from ear lob every one second. The first point where acetosulfonamide appears in blot is measured by using aldehyd reagent.

It is generally accepted that the retinal findings and the prognosis of essential hypertension are closely correlated; the present author has also suggested in the study reported previously¹⁾ that apparent disturbances in the circulation and metabolism of the brain are found in the cases with severe sclerosis of the retinal arterioles. In Fig. 1 are shown the individual

Fig. 1. Relations between retinal findings according to Keith-Wagener's classification and cerebral circulation and metabolism.

0-IV: Keith-Wagener's grade of retinal findings.

---: Mean values in normotensive subjects.

values concerning the cerebral circulation and metabolism in the patients of the essential hypertension divided into four groups according to the Keith-Wagener's classification of the retinal changes. With the progress of the retinal findings from the group of O grade (no change) to IV grade group, CBF and $CMRO_2$ tended to lower and CVR to rise, and in particular, CVR was found in closest parallelism with the retinal changes. The same fact is reported also by Aizawa⁴⁾ and Kato⁵⁾. Leopold *et al.*⁶⁾ who adopted a finer gradation of the retinal findings based on Keith-Wagener's classification principle, have found that CVR changes in parallel with those finer gradation too, while Hafkenshiel⁷⁾ and Bernsmeier⁸⁾ denied such a correlation. The present results seem to suggest a close correlation between the retinal changes and the organic vascular changes in the brain.

2. Cardiovascular findings and cerebral circulation and metabolism

Essential hypertension is often accompanied by cardiac disturbances. Frequently in the cases, in which no notable anatomical changes in the brain could be observed, but succumbed to apoplectic strokes, the existence of cardiac factors has been presumed⁹⁾. So, it must be of importance from clinical point of view to study the changes in the circulatory and metabolic

functions of the brain in essential hypertension with the cardiac disturbances, which repeatedly occur as complication. For this purpose, the author examined in subjects with essential hypertension the possible relations between the heart roentgenographic and the electrocardiographic findings and the circulation time on the one hand, and the values concerning the cerebral circulation and metabolism on the other.

First, the subjects were divided into the two groups of those showing and those free of left ventricular hypertrophy on their X-ray findings. Their individual values concerning the cerebral circulation and metabolism are shown in comparison by groups in Fig. 2. In the group with the hypertrophy, the frequency of the cases with lowered CBF and $CMRO_2$ and increased CVR was higher than in the hypertrophy-free group. Fig. 3 shows in comparison the values in the group of the subjects showing pre-

Fig. 2. Relations between X-ray findings in heart and cerebral circulation and metabolism.

Group (-): Cases without left ventricular hypertrophy.

Group (+): Cases with left ventricular hypertrophy.

---: Mean values in normotensive subjects.

Fig. 3. Relations between electrocardiographic findings and cerebral circulation and metabolism.

Group (-): Cases without ECG findings such as myocardial damage, coronary insufficiency or left ventricular hypertrophy.

Group (+): Cases with those findings.

---: Means values in normotensive subjects.

sence of left ventricular hypertrophy, coronary insufficiency or myocardial damage and of those free of such findings, as diagnosed electrocardiographically. In the former group, CBF and $CMRO_2$ were lowered and CVR

elevated in a larger number of the cases than in the latter.

In Fig. 4 is shown the relation of the arm-to-ear circulation time to CBF and CVR. A slight tendency of lower CBF and higher CVR was found in the cases with prolonged circulation time.

Fig. 4. Relations between arm-to-ear circulation time and cerebral circulation.

Yokomatsu¹⁰⁾ has found higher CVR and lower CBF and $CMRO_2$ in the hypertensive group with myocardial damage in complication than in the group free from the complication; also Kato⁵⁾ states that among cases with lowered CBF cardiac hypertrophy and myocardial damage are frequently found. Those findings are in agreement with the present author's cited above. Thus, it is obvious that in essential hypertension the cerebral circulatory and metabolic changes are closely correlated with the cardiac disturbances; but it cannot be decided off-hand whether those changes in the brain are caused merely by the reduction of cardiac function or by other factors coexisting in such cases. This question requires further studies.

3. Renal function and cerebral circulation

Disturbances in renal functions are also frequently found in essential hypertension and some relation between the renal functions and the circulatory changes in the brain seems to be presumable. In the present studies the relation between the hemodynamics and dye excretion function of the kidney on the one hand and the cerebral circulation on the other has been investigated. In Fig. 5 are shown the relation between CBF and RBF and that between CVR and RVR. In some instances with lowered RBF, CBF is also found lowered, but such cases are small in number and no close correlation can be established between these two values. Between RVR and CVR a slight parallelism is confirmed.

Fig. 5. Relations between renal hemodynamics and cerebral circulation.
 RBF: Renal blood flow. RVR: Renal vascular resistance.
 ---: Mean values in normotensive subjects.

Fig. 6 demonstrates the relations of *P.S.P.* excretion value from the kidney in 15 minutes versus CBF and CVR. In the cases with lowered *P.S.P.* excretion there are tendencies of lowered CBF and elevated CVR, a parallelism to some extent being established between *P.S.P.* excretion value and the other two values.

Fig. 6. Relations between phenolsulphonphthalein excretion value in 15 min. and cerebral circulation.

Aizawa¹¹⁾ has found a significant positive correlation between CBF and RBF in essential hypertension; Atarashi¹²⁾ also states that in older patients of essential hypertension there exists an apparent correlation between CBF and RBF, both these values dropping abreast, while Kato⁵⁾ insists that RBF tends to be lowered the further, the lower the CBF and the $CMRO_2$, but that no definite correlation can be established between these values.

From the data of the present investigation, it may be suggested that there is a correlation to some extent between the renal function and the cerebral circulation, while no such close parallelism as found between the retinal and cardiac findings and the cerebral circulation and metabolism has been confirmed here. But, as shown above, the fact that the cerebral circulation and metabolism are generally more severely disturbed in the cases of essential hypertension with retinal changes, cardiac or renal disturbances than in those free of such complications is worthy of clinical attention.

4. *Anemia and cerebral circulation and metabolism*

According to Heyman and others¹³⁾ in cases with chronic anemia CBF is increased, but no such a fact has been reported as observed among the patients with essential hypertension. In the present study it has been observed that some tendency of increased CBF may be found among the patients of essential hypertension with lowered hemoglobin content, as seen in Fig. 7, where relation between the arterial hemoglobin content and CBF is graphically shown.

Fig. 7. Relation between hemoglobin content in arterial blood and CBF.

This seems to represent a kind of homeostasis against the hazard of oxygen deficiency in the brain due to anemia. Thus, anemia too seems to require notice as an important factor changing CBF in essential hypertension.

SUMMARY

On 51 cases of essential hypertension the relations between the clinical findings and the cerebral circulation and metabolism measured by N_2O method have been investigated and the following facts elucidated:

1. With the advance of the retinal findings according to Keith-Wagener's classification, cerebral blood flow (CBF) and cerebral oxygen consumption ($CMRO_2$) tend further to decrease and cerebral vascular resistance (CVR) to increase. The latter has a particularly close parallel-

lism with the retinal findings.

2. In the group showing the hypertrophy of the left ventricle on the roentgenogram or the group, in which the left ventricular hypertrophy, coronary insufficiency or myocardial damage is suggested by the electrocardiographical findings, the disturbances in the cerebral circulation and metabolism are found the severer than in the groups without such finding. Similar relation in the group with prolonged circulation time may be confirmed.

3. No close parallelism is established between CBF and renal blood flow (RBF), while some correlation is found between CVR and renal vascular resistance (RVR), also, between the renal function, as tested with P.S.P. excretion, on the one hand and CBF and CVR on the other.

4. In the cases with lowered hemoglobin content of the blood, CBF is to some extent augmented.

The expense of this study was in part defrayed by a Grant in Aid for Medical Research, Welfare Ministry. The author wishes to express his thanks to Dr. S. Sato, chief doctor of our Medical Clinic for co-operation in carrying out this investigation.

References

- 1) Tateyama, Tohoku J. Exp. Med., 1959, **70**, 115.
 - 2) Matsuoka, Kaigun Gunikai Zasshi (Jap.), 1944, **33**, 1064.
 - 3) Shigiya, Nisshin Igaku (Jap.), 1949, **36**, 452.
 - 4) Aizawa, Rinsho to Kenkyu (Jap.), 1956, **33**, 810.
 - 5) Kato and Yasui, Sogo Igaku (Jap.), 1956, **13**, 781.
 - 6) Leopold *et al.*, Am. J. Ophthalmol., 1949, **32**, 365.
 - 7) Hafkenshiel, J. Clin. Invest., 1954, **33**, 63.
 - 8) Bernsmeier *et al.*, Klin. Wschr., 1954, **32**, 971.
 - 9) Okinaka, Cerebral Damage of Vascular Origin (Jap.), Tokyo, 1955.
 - 10) Yokomatsu, Keio Igaku (Jap.), 1956, **33**, 306.
 - 11) Aizawa *et al.*, Nihon Junkankigaku Shi (Jap.), 1958, **22**, 55.
 - 12) Atarashi *et al.*, *Ibid.*, 1958, **22**, 239.
 - 13) Heyman *et al.*, J. Clin. Invest., 1952, **31**, 824.
-