- Preliminary Note -

Amine metabolites in the ventricular cerebrospinal fluid of patients with ventricular dilatation
HPLC and clinical application (IV)

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In recent years, considerable interest has been directed towards the role of neurotransmitters in various types of brain dysfunctions, including cerebral ischemia, brain tumor and hydrocephalus. There are increasing experimental and clinical evidences that disturbances in the metabolism of central monoamines play an important role in the pathogenesis of hydrocephalus, but the clinical diagnostic and therapeutic implications from the viewpoint of neurotransmitters remain to be established.

A damage of the periventricular structures has been described in the hydrocephalic brains of experimental animals. The damage of the brain tissue can be estimated in terms of alterations in certain biochemical parameters. Among these, ventricular CSF amine metabolites: homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5 HIAA) and 3-methoxy-4-hydroxyphenylethylene glycol (MHPG); the major metabolite of dopamine, serotonin and norepinephrine, have aroused great interest since they are thought to reflect the brain function and the CSF dynamics.

In this work, we tried to analyze and accumulate data about patients with ventricular dilatation which were studied from the viewpoint of the metabolic changes of ventricular CSF amine metabolites.

Twenty five patients with ventricular dilatation which was evaluated by the bifrontal cranioventricular index (CVI) were studied. The data reported by West and Chase was available for control group. CVI was calculated as the ratio of the width of the frontal horns of the lateral ventricles and the distance between inner table of the skull of both sides on a CT scan taken parallel to the OM-line. CVI over 0.40 was interpreted as ventricular dilatation. On the basis of the clinical and neuroradiological evaluation, these patients were divided into three groups; 16 patients with obstructive hydrocephalus (O group), 5 patients with the acute stage of congenital hydrocephalus (C group) and 4 patients with secondary normal pressure hydrocephalus after subarachnoid hemorrhage (N group).

Ventricular CSF samples were obtained through the shunt tube or the drainage tube inserted into the lateral ventricle. In this biochemical analysis, the high performance liquid chromatography systems (HPLC) consisted of a YANACO L-2000 pump with a loop injector.

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The electrochemical detector was a YANACO VMD-101. The column packed with octadyslfurane was 4 mm in diameter by 250 mm in length. The flow rate was 1.0 ml/min, and the working electrode potential was set at +0.9 V vs Ag/AgCl. A mobile phase was citrate (Na)–citrate buffer (pH 4.5) containing 12% acetic acid, 10% methanol and 1% tetrahydrofuran. The estimation of MHPG levels was performed in a special laboratory.

A chromatogram of 5-HIAA, HVA and 5-hydroxytryptamine (5-HT) after extraction procedure is shown in Fig. 1. 5-HT, 5-HIAA and HVA appeared within 8 minutes after injection of standard sample.

The mean values (± standard error of the mean) for HVA, 5-HIAA and MHPG levels in O group were 320±115, 147±61 and 10.4±2.8 (ng/ml) respectively. In C group: HVA 264±82, 5-HIAA 194±58, MHPG 10.9±6.4 (ng/ml). In N group: HVA 114±17, 5-HIAA 75±14, MHPG 11.1±4.2 (ng/ml). HVA and 5-HIAA levels were significantly higher in O group and C group than in N group (p<0.05). MHPG levels did not differ among three groups. HVA levels were significantly higher in O group than in control group (p<0.02), while HVA levels were significantly lower in N group than in control group (p<0.02). 5-HIAA levels were significantly higher in O group and C group than in control group (p<0.05). HVA levels in O group with marked ventricular dilatation (CVI>0.50) were over 300 ng/ml. No relationship was found between HVA levels and CVI in C group, while there was the opposite relationship in N group (Fig. 2).

Reabsorption of amine metabolites is considered to take place in the region of the fourth ventricle (choroid plexus) by active transport. In the acute stage of congenital hydrocephalus increased ventricular fluid pressure can induce the hypofunction of choroid plexus in the fourth ventricle. Consequently elevated HVA and 5-HIAA levels are considered to be due to impaired reabsorption of these metabolites from the CSF. Edvinsson et al. reported that in spite of the normalization of ventricular fluid pressure, both dopamine and HVA levels in brain showed a progressive decrease in a month in kaolin-induced hydrocephalus. In the so-called human normal pressure hydrocephalus, lower amine metabolites may indicate a decreased production of biogenic amines.

These data might be of diagnostic and prognostic value and of importance in the evaluation of the treatment of this pathological state. However, we have not had enough
cases, so we have to accumulate more data. It is also necessary to discuss this pathogenesis from the view point of metabolic analysis, besides CT scan and CT-cisternography.

References


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