Concentration of homovanillic acid and 5-hydroxyindoleacetic acid in the ventricular cerebrospinal fluid of patients with obstructive hydrocephalus

K. KMIĘCIAK-KOLADA, H. MAJCHRZAK, AND Z. S. HERMAN

From the Department of Pharmacology, Silesian School of Medicine, Katowice, and the Division of Neurosurgery, Central Mining Hospital, Bytom, Poland

SUMMARY In 12 patients with different posterior fossa tumours the concentrations of homovanillic acid (HVA) and of 5-hydroxyindoleacetic acid (5-HIAA) were measured in cerebrospinal fluid from the lateral ventricles. All patients had obstructive hydrocephalus. Patients with a clear increase of 5-HIAA/HVA ratio in the ventricular CSF have died subsequently. This feature may have a diagnostic value, and indicates the prevalence of serotonergic neurones in patients with obstructive hydrocephalus with fatal course after surgery.

Homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) are the main metabolites of putative central neurotransmitters, dopamine (DA) and 5-hydroxytryptamine (5-HT) respectively. The level of these metabolites in cerebrospinal fluid (CSF) reflects the concentration of DA or 5-HT in the central nervous system (Moir *et al.*, 1970) and the activity of DA or 5-HT secreting neurones (Sjöström *et al.*, 1975). On the other hand, there are many uncertainties in relating CSF amine metabolite concentrations to the DA and 5-HT in the brain. Garelis *et al.* (1974) indicate that the origin of 5-HIAA in lumbar CSF is uncertain. They suggest that the brain can contribute 5-HIAA to lumbar CSF under some circumstances. The concentration of this metabolite in lumbar CSF can be of clinical value if the changes are general throughout the central nervous system. Recently Wilk and Stanley (1978) have shown that HVA is the major DA metabolite in human brain and that the levels of this metabolite in CSF reflect the HVA levels in brain. Homovanillic acid and 5-HIAA released from the brain tissue into the CSF of lateral and third ventricles are reabsorbed into the blood mainly in the choroid plexus of the

fourth ventricle. Therefore, the level of these metabolites in the CSF of lateral ventricles is three times higher than in the CSF of the subarachnoid space (Gerbode and Bowers, 1968; Sjöström *et al.* 1975). In experimental hydrocephalus in rats and dogs the 5-HIAA level in the CSF of lateral ventricles of the brain was found by Andersson (1968) to be increased. In rabbits with experimental hydrocephalus there is a transient increase of brain noradrenaline level and long-term decrease of brain DA level (Edvinsson *et al.*, 1971).

Andersson and Ross (1966) have observed an increased level of 5-HIAA in the CSF of children with hydrocephalus, and have suggested that it is a diagnostic feature of the early phase of hydrocephalus. Maira *et al.* (1975) have described decreased concentration of HVA in CSF of the spinal subarachnoid space of patients with the Hakim syndrome in which in the presence of hydrocephalus a normal CSF pressure was reported. At present the view predominates that for purposes of diagnosis of acute traumatic brain syndromes it is more important to calculate the HIAA/HVA ratio, than to observe separately the levels of these metabolites (Porta *et al.*, 1975).

In this paper we report the levels of HVA and HIAA, and the ratio of these metabolites in the ventricular CSF of patients with tumours of the posterior fossa.

Address for correspondence and reprint requests: Professor Z. S. Herman, Department of Pharmacology, Marksa 38, 41-808 Zabrze, Poland.

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Patients and methods

Observations were carried out on 12 patients, six men aged 20–62 years and six women aged 24–48 years. They had normal blood pressure and normal consciousness. The CSF was taken from a brain ventricle during ventriculography performed under local anaesthesia (1% lidocaine). The ventriculography was carried out between 9 and 12 am after a night's rest. Immediately after the ventricular puncture the pressure of CSF was measured by an open-ended glass manometer. To examine the extent of hydrocephalus the indices of Schiersmann (1942) and Evans (1942) were calculated. Then 5 ml of CSF was taken and immediately acidified to pH 3 with 0.1 M HCl and kept frozen at -20°C until assayed. The CSF was deproteinised and metabolites were extracted from CSF according to Gerbode and Bowers (1968) with the modification of Ashcroft *et al.* (1975) and measured spectrofluorimetrically using an Aminco-Bowman spectrometer. The HVA concentration was measured according to Anden *et al.* (1963) as modified by Ashcroft *et al.* (1975) and Moir *et al.* (1970), with duplicate samples and internal standards for each assay. Concentration of 5-HIAA was estimated by the method of Miller and Cox (1970).

Results

Obstructive hydrocephalus was found in all patients. The Schiersmann index was 3.5 in two patients and lower in the others. The Evans index exceeded 0.3 in all patients. The CSF pressure in three patients was zero, and in the others ranged between 240–500 mm H₂O. The range of HVA levels was 104.18–871.0 ng/ml, average 365.99 ± 65.00 ng/ml. The highest level of HVA was observed in ventricular CSF of patients with astrocytoma and ependymoma, the lowest in patients with meningioma. The range of 5-HIAA levels was 47.02–245.5 ng/ml, average 129.75 ± 35.72 ng/ml. The 5-HIAA/HVA ratio ranged between 0.028 and 1.06. This ratio was highest in patients who subsequently died after operation. However no significant correlation was found between the CSF pressure, Schiersmann or Evans index, and HVA or 5-HIAA levels (Tables 1 and 2).

Discussion

The mean level of 5-HIAA observed in the CSF of our patients is comparable with values reported in patients with supratentorial or subtentorial tumours (Chase and Gordon, 1973; Maira *et al.*, 1975; Porta *et al.*, 1975). However, we have observed higher

Table 1 Concentration of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in the ventricular CSF of patients with posterior fossa tumours

Case number	Age (yr)	Sex	Pressure of cerebrospinal fluid (mm H ₂ O)	Schiersmann index	Evans index	HVA (ng/ml)	5-HIAA (ng/ml)	5-HIAA/HVA ratio	Histopathological diagnosis
1	24	F	280	2.8	0.39	311	—	—	Glioblastoma multiforme
2	41	M	240	3.2	0.39	287	—	—	Glioblastoma multiforme
3	46	F	240	2.8	0.36	—	48	—	Neurinoma
4	55	F	370	2.5	0.40	342	57	0.16	Neurinoma
5	40	F	240	2.9	0.36	331	47	0.14	Haemangioblastoma
6	22	M	500	3.0	0.39	871	245	0.28	Astrocytoma
7	20	M	0	3.5	0.31	536	105	0.19	Ependymoma
8	58	F	0	3.5	0.33	337	—	—	Tumor trunci cerebri

Table 2 Concentration of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in the ventricular CSF of patients with posterior fossa tumours who subsequently died

Case number	Age (yr)	Sex	Survival time after measurement (days)	Pressure of cerebrospinal fluid (mm H ₂ O)	Schiersmann index	Evans index	HVA (ng/ml)	5-HIAA (ng/ml)	5-HIAA/HVA ratio	Histopathological diagnosis
1	54	F	14	350	2.8	0.37	104	54	0.52	Meningioma
2	62	M	5	60	3.2	0.36	271	281	1.03	Arachnoiditis of cisterna magna
3	50	M	3	0	3.1	0.35	—	46	—	Metastatic cerebellar carcinoma
4	40	M	2	500	3.0	0.34	268	283	1.06	Glioblastoma multiforme

values of HVA level in the CSF than West *et al.* (1972) in patients with posterior fossa tumours. No significant correlation was found between the CSF pressure and the levels of HVA and 5-HIAA in our patients, in agreement with Porta *et al.* (1975). We have not examined the levels of these metabolites in ventricular CSF of normal human subjects for ethical reasons. Therefore, we cannot state the real difference from normal of the concentration of both metabolites in our patients. However, evident differences were found depending upon the type of the tumour which caused the hydrocephalus. In experimental hydrocephalus of rats and dogs Andersson (1968) has observed a clear increase of 5-HIAA in ventricular CSF. We have not found in the literature clinical investigations reporting normal values of HVA and 5-HIAA in human ventricular CSF. A significant observation we have made is that patients with significant increase of the ventricular 5-HIAA/HVA ratio have died after surgery (Table 3), suggesting that this feature may be of prognostic value and indicate the prevalence of 5-hydroxytryptaminergic neurones and imbalance with neurones producing DA. This is supported by the finding that 5-HT is an important factor in hydrocephalus and constriction of brain blood vessels (Osterholm *et al.*, 1969; Welch *et al.*, 1973). The second supporting fact is the finding of Porta *et al.* (1975) that a high HIAA/HVA ratio was present after cranial trauma in patients who later died or became demented.

Table 3 Ratio of 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) in patients with cranial tumours related to mortality

Outcome	5-HIAA/HVA ratio
Died	0.87 ± 0.30
Survived	0.19 ± 0.06 P < 0.01

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