Cerebrospinal Fluid Concentration and Urinary Excretion of Cyclic Adenosine-3', 5'-Monophosphate in Various Diseases of Children

A Preliminary Study

V. V. Myllylä, E. R. Heikkinen, S. Similä, E. Hokkanen, and H. Vapaatalo

Departments of Neurology and Pediatrics, University Central Hospital of Oulu and Department of Pharmacology, University of Oulu, SF-90220 Oulu 22

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Abstract. Cerebrospinal fluid (CSF) concentration and urinary excretion of cyclic adenosine-3',5'-monophosphate (cAMP) were measured in children aged from 3 days to 15 years by the protein-binding method of Gilman (1970).

The mean CSF cAMP concentration (22.4 ± 0.6 (S.E.) nmol/l) of 24 "healthy" children tended to be lower (P < 0.2) than that of adult patients who revealed no pathological findings on clinical examination. No difference in the results was found between the sexes. High cAMP concentrations were found in CSF of children suffering from cerebellar glioma, hypothalamic precocious puberty, bacterial meningitis, or Cushing's disease.

The urinary excretion of cAMP varied from 0.2 to 5.3 in "healthy" and from 1.3 to 7.6 µmol/24 hrs in diseased children. Two children with pheochromocytoma showed a striking decrease in the rate of urinary excretion of the nucleotide after surgical treatment.

Key words: Cyclic adenosine-3',5'-monophosphate — Cerebrospinal fluid — Urinary excretion — Diseases of children.

Zusammenfassung. Die Konzentration des cyclischen Adenosin-3',5'-Monophosphat (cAMP) im Liquor cerebrospinalis und seine Ausscheidung im Urin wurden bei Kindern im Alter von 3 Tagen bis 15 Jahren gemessen.

Der Mittelwert von cAMP im Liquor cerebrospinalis (22.4 ± 0.6 nmol/l) der 24 gesunden Kinder war etwas niedriger als der 13 Erwachsener ohne pathologische klinische Befunde (P < 0.2). Es gab keinen Unterschied zwischen Mädchen und Jungen. Hohe cAMP-Werte wurden im Liquor cerebrospinalis der Kinder, die an einem cerebellaren Gliom, einer vorzeitigen hypothalamischen Pubertät, einer bakteriellen Meningitis oder einem Cushing-Syndrom litten, gemessen.

Die Ausscheidung des cAMP war 0.2—5.3 bei gesunden Kindern und 1.3—7.6 µmol/24 Std bei kranken Kindern. 2 Patienten, erkrankt an Phäochromocytom, zeigten eine starke Verminderung der Ausscheidung von cAMP nach der Operation.

Introduction

Cyclic adenosine-3',5'-monophosphate (cAMP) has been found in all mammalian tissues studied. It is well known that cAMP is involved in the regulation of metabolism and in other functions of many tissues.
(for review, see Greengard and Costa, 1970). An important role of cAMP in nervous system was envisaged when it was found that the enzymes synthesizing and degrading cAMP are more abundant in brain than other tissues (Sutherland et al., 1962; Klainer et al., 1962; Butcher et al., 1962; for review, see Breckenridge, 1972).

There are reports on cAMP concentration in cerebrospinal fluid (CSF) and the possible functions of this nucleotide within the central nervous system (CNS) (Robison et al., 1970; Cramer and Lindl, 1972; Cramer et al., 1972a; Cramer et al., 1972b; Cramer et al., 1973; Heikkinen et al., 1974a and b). Studies of Cramer and coworkers (1972a) suggest that the turnover of cAMP in brain is increased in mania and decreased in depression. Recently we described elevated cAMP values in CSF of patients shortly after an epileptic attack and in patients suffering from active or rapidly progressive damage of CNS (Heikkinen et al., 1974b; Myllylä et al., 1974a and b).

In some disease states the urinary excretion and plasma concentration of cAMP have been shown to differ from those of healthy people (Sutherland et al., 1968; Abdulla and Hamadah, 1970; Murad et al., 1972; Williams et al., 1973; Heikkinen et al., 1974a).

Earlier we studied the differences of cAMP in CSF in various age groups of adults (Heikkinen et al., 1974a). The aim of this study was to obtain information about the CSF concentration and urinary excretion of cAMP in "healthy" (i.e. just cured from purulent meningitis) and some diseased children.

**Patients and Methods**

The investigation was carried out on 34 inpatients at the Department of Pediatrics, University Central Hospital of Oulu. The mean age of the patients was 7 years; they ranged from 3 days to 15 years old. There were 13 females and 21 males.

A CSF sample of 3—6 ml was taken for diagnostic purposes by routine lumbar puncture in a sitting or supine position. The punctures were made at 10 to 13 hours to avoid possible diurnal variations.

For the measurement of the cAMP concentration 1 ml of fresh CSF was taken from the samples. Proteins were precipitated by adding 1 ml of 0.6 M perchloric acid. The samples were stored at $-20^\circ C$ for 1—3 weeks before determination.

The cAMP concentrations were measured by the protein-binding method of Gilman (1970). The values were expressed as nmoles/l of CSF. The cAMP concentrations in CSF were compared with those of 13 adult patients with myalgic headache who revealed no pathological findings on clinical examination.

The 24 hrs urine was collected from 15 patients. CSF concentration of cAMP was also measured in 10 of these patients. The urine was stored at $+4^\circ C$ during collection, and then the samples were stored at $-20^\circ C$ for 1—3 weeks before the determination of cAMP. The same method for determination of cAMP was used as for the CSF cAMP. The urinary excretion of cAMP was expressed as μmoles in 24 hrs urine.

The Student's t test was used for statistical treatment of the results.