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Gas Chromatographic Estimation of Homovanillic Acid in Serum of Normals and Psychotic Patients

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Summary: Homovanillic acid is extracted from 0.5 ml serum with ethyl acetate at acidic pH, and its pentafluoropropionic anhydride and hexafluoroisopropanol derivative injected into a 3% SE-30 column at 140 °C, fitted with an electron capture detector. In a group of normal volunteers (n = 42) a mean value of $62 \pm 45 \mu\text{g/l}$ was found. The distribution of the serum concentrations was found to be bimodal. Using the same procedure for the homovanillic acid estimation in cerebrospinal fluid (CSF), mean values of $73.0 \pm 41 \mu\text{g/l}$ serum and $68 \pm 36 \mu\text{g/l}$ CSF were found for a group of 22 untreated patients with paranoid-hallucinatory syndrome. After treatment with neuroleptics, for 1 week to 1 month, the homovanillic acid concentration increased significantly only in the CSF. By the procedure described, other acidic metabolites of biogenic amines are extracted together with homovanillic acid and can also be estimated in the same sample.

Gaschromatographische Bestimmung von Homovanillins  ure im Serum Gesunder und psychotischer Patienten

Zusammenfassung: Homovanillins  ure wird aus 0.5 ml Serum mit Ethylacetat bei saurem pH extrahiert und nach Derivatisierung mit Pentafluorpropions  ureanhydrid und Hexafluorisopropanol auf einer 3% SE-30 S  ule gaschromatographisch getrennt und mit Elektroneneinfangdetektor bestimmt. F  r eine Gruppe von Normalpersonen (n = 42) wurde ein Mittelwert von $62 \pm 45 \mu\text{g/l}$ Serum ermittelt, und die Verteilung der Konzentrationen war bimodal. Die gleiche Methode kann f  r die Homovanillins  ure Bestimmung im Liquor cerebrospinalis angewandt werden. In einer Gruppe psychotischer Patienten mit paranoid-halluzinatorischem Syndrom (n = 22), unbehandelt, wurden Mittelwerte von $73 \pm 41 \mu\text{g/l}$ Serum und $68 \pm 36 \mu\text{g/l}$ Liquor gefunden. Nach Behandlung mit Neuroleptika kam es zu einer Homovanillins  ure Anstieg nur im Liquor. Die Methode erfafst au  er Homovanillins  ure auch andere saure Metabolite biogener Amine.

Introduction

Homovanillic acid (4-hydroxy-3-methoxyphenylacetic acid) is considered to be the main metabolite of dopamine in the brain. It has been detected in brain tissue and cerebrospinal fluid (CSF) (1-3) and its concentration in CSF may reflect the central dopamine turnover (for review see l.c. (4)).

Dopamine is metabolized by the alternative action of monoamine oxidase and catechol-O-methyltransferase; the O-methylated and oxidatively deaminated product, an aldehyde, is further oxidized to the acid by aldehyde dehydrogenase. The O-methylation can take place at the 4-OH group of dopamine, whereby iso-homovanillic acid is produced. It has been detected in small amounts in CSF (5, 6).

An active transport system, sensitive to probenecid, removes homovanillic acid from the brain to CSF and from CSF to the blood (7). It is localized in the region of the fourth ventricle (8). In CSF, there is a gradient in the homovanillic acid concentration: in man, the concentration falls from $466 \mu\text{g/l}$ in the ventricular CSF to 185 in the cisternal and to $53 \mu\text{g/l}$ in the lumbar CSF (9). In lumbar CSF, the concentration of homovanillic acid depends greatly on the conditions under which the puncture was performed (position of the patient, restriction of movement for several hours before puncture, amount of fluid taken).

Urinary concentrations of homovanillic acid do not correlate with CSF concentrations (10) and it is still unknown which part of urinary homovanillic acid originates from central dopamine turnover. Its estimation