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Antiepileptic drugs reduce serum uric acid

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Uric acid examination in 554 epileptic out-patients under long-term anticonvulsant medication revealed significantly lower serum concentrations compared to a group of normal controls. In patients taking enzyme-inducing drugs, uric acid levels were found to be lower than in those under valproate sodium. In addition, uric acid concentrations showed a negative correlation with duration of therapy in epileptic males. At this time, we can only speculate on the mechanism involved in the reduction of uric acid by enzyme-inducing anticonvulsants as well as on the possible implication of this finding in the treatment of hyperuricemia.

INTRODUCTION

Investigations on the possible influence of long-term anticonvulsant medication on the serum concentration of uric acid have scarcely been done. In their survey of side-effects of anticonvulsants Meinardi and Stoel[2] only mention the possibility of hyperuricemia under carbamazepine therapy.

PATIENTS AND METHODS

We examined 554 epileptic out-patients (326 males, 228 females, aged 20–40) treated with anticonvulsants for more than 1 year. Uric acid in serum was measured by applying a standard colorimetric method using phosphotungsten (Autoanalyzer System SMA 12/60). The Wilcoxon test served to compare the concentrations obtained to those of a normal population (787 males, 748 females) of the same age and living in the Heidelberg area, that had been examined with the same method by one of us (B.S.)[1]. Uric acid concentrations of patients under monotherapy with phenytoin, carbamazepine, primidone, or valproate sodium for at least 1 year before examination were compared using the Kruskal–Wallis test. Subsequently, the uric acid levels of the epileptics were correlated (Spearman's rank correlation coefficient) with duration of therapy according to sex.

RESULTS

Mean values and standard deviations were 4.7 ± 1.4 mg/dl in epileptic males and 3.5 ± 1.1 in epileptic females, both differing ($P < 0.0001$) in Wilcoxon test from those of the control group (6.4 ± 1.1 in males and 4.5 ± 0.8 in females). The frequency distributions are given in Figs. 1 and 2. In the group under valproate sodium uric acid concentrations were higher (mean ± S.D., 5.7 ± 1.3 mg/dl in males (n = 25), 4.2 ± 1.5 in females (n = 14)) than in the groups taking phenytoin (4.4 ± 1.1 in males (n = 28), 3.4 ± 1.1 in females (n = 23)), primidone (5.1 ± 1.2 in males (n = 50), 3.4 ± 0.8 in females (n = 29)), or carbamazepine (4.1 ± 1.3 in males

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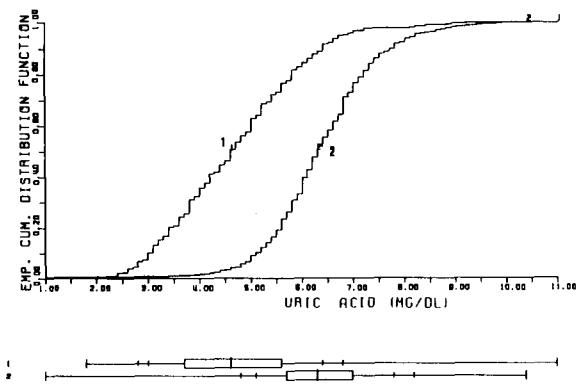

Fig. 1. Frequency distribution of uric acid in serum of epileptic males (1) and male controls (2).

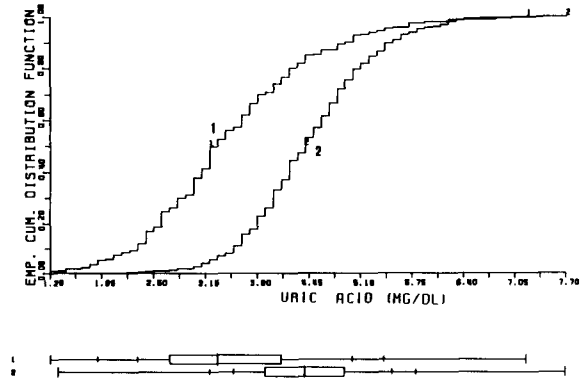

Fig. 2. Frequency distribution of uric acid in serum of epileptic females (1) and female controls (2).

(n = 24), 3.1 ± 0.9 in females (n = 30)) (Fig. 3). According to the Kruskal–Wallis test, the differences between the epileptics under valproate sodium and those under other anticonvulsants were significant for both sexes ($P = 0.0001$ in males and $P = 0.0389$ in females). The uric acid serum levels in male epileptics showed a negative correlation with duration of therapy ($P < 0.01$).

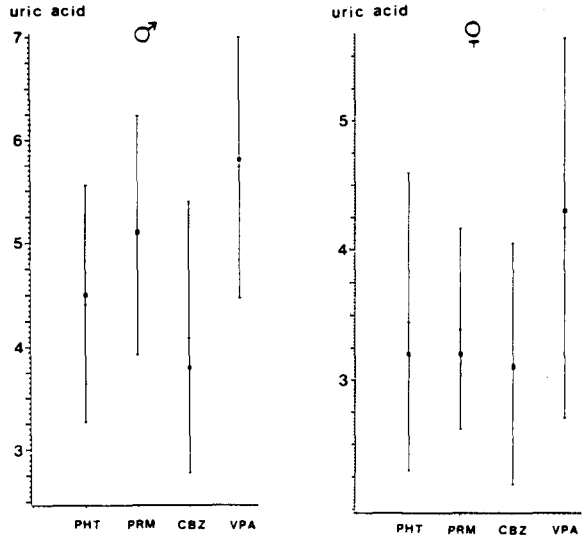

Fig. 3. Uric acid in serum (mg/dl) of male and female epileptics under monotherapy with phenytoin (PHT), primidone (PRM), carbamazepine (CBZ), or valproate sodium (VPA) (mean ± S.D., □ = median).

DISCUSSION

Our findings suggest that long-term antiepileptic medication has an influence on serum uric acid, resulting in lower concentrations. The pathogenic mechanism is not clear; but our data show that especially antiepileptic drugs with enzyme-inducing properties (phenytoin, carbamazepine, primidone)[3] are effective, as has been reported for bilirubin reduction[4]. Thus, we postulate that acceleration of protein synthesis, caused by enzyme-inducing properties of anticonvulsants, may lead to lower uric acid serum levels. The possible influence of anticonvulsants on uric acid could be of value in the treatment of hyperuricemia.

REFERENCES

1 Arab, L., Schellenberg, B. and Schlierf, G., Nutrition and health. A survey of young men and women in Heidelberg, *Ann. Nutr. Metab.*, 26, Suppl. 1 (1982) 1–244.

2 Meinardi, H. and Stoel, L.M.K., Side-effects of antiepileptic drugs. In: P.J. Vinken and G.W. Bruyn (Eds.), *Handbook of Clinical Neurology, Vol. 15,* North-Holland Publ., Amsterdam, 1974, pp. 705–738.

3 Richens, A., Liver enzyme induction by antiepileptic drugs: its clinical significance. In: A. Richens and F.P. Woodford (Eds.), *Anticonvulsant Drugs and Enzyme Induction,* Elsevier, Amsterdam, 1976, pp. 3–12.

4 Yeung, C.Y., Tam, L.S., Chan, A. and Lee, K.H., Phenobarbitone prophylaxis for neonatal hyperbilirubinaemia, *Pediatrics,* 48 (1971) 372–376.