Increased exposure to hepatitis B virus by other than the sexual route may be expected in prostitutes. Transmission by the parenteral route as a result of drug addiction may be more common in prostitutes. None in our sample had a history of parenteral drug abuse, which is very rare in Greece (Adjutantis, 1973). Treatment for syphilis, gonorrhea, and other infections may be other vehicles for parenteral transmission, but evidence of hepatitis B infection was no greater among the prostitutes with syphilis in our sample. Thus these factors do not seem to explain the great difference in prevalence rates between the prostitutes and controls in our study. We believe that the distribution of evidence of hepatitis B virus infection in the prostitutes in our study is compatible with a venereal mode of transmission. Other carefully controlled studies would, we hope, confirm our findings and provide further support for our belief.

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References

- Adjutantis, G. (1973). *Minerva Medica Greca*, 1, 119.
 Blumberg, B. S., Sutnick, A. T., and London, T. (1969). *Journal of the American Medical Association*, 207, 1895.
 Cossart, Y. (1971). *Journal of Clinical Pathology*, 24, 394.
 Fulford, K. W., Dane, D. S., Catterall, R. D., Woof, R., and Denning, J. V. (1973). *Lancet*, 1, 1470.
 General Register Office. (1951). *Classification of Occupations*, 1950. London, H.M.S.O.
 Heathcote, J., and Sherlock, S. (1973). *Lancet*, 1, 1468.
 Hersh, T., Melnick, J., Goyal, R. K., and Hollinger, F. B. (1971). *New England Journal of Medicine*, 285, 1363.
 Jeffries, D. J., James, W. H., Jefferiss, F. J. G., Macleod, K. G., and Willcox, R. R. (1973). *British Medical Journal*, 2, 455.
 Papaevangelou, G., Kourea, T., and Tsoukas, S. (1971). *Pathologia et Microbiologia*, 37, 361.
 Papaevangelou, G., Trichopoulos, D., Papoutsakis, G., Kremastinou, T., and Pavlides, E. (1973). Ninth International Congress on Tropical Medicine and Malaria. *Abstracts*, 2, 166.
 Pesendorfer, F., Krassnitzky, O., and Wewalka, F. (1970). *Klinische Wochenschrift*, 48, 58.
 Prince, A. M. (1968). *Proceedings of the National Academy of Sciences of the United States of America*, 60, 814.
 Prince, A. M., et al. (1970). *New England Journal of Medicine*, 282, 987.
 Reitman, S., and Frankel, S. (1957). *American Journal of Clinical Pathology*, 20, 56.
 Szmunes, W., Prince, M., Brotman, B., and Hirsch, R. (1973). *Journal of Infectious Diseases*, 127, 17.
 Vahrman, J. (1973). *Lancet*, 2, 157.
 Vyas, G. N., and Shulman, N. R. (1970). *Science*, 170, 332.

PRELIMINARY COMMUNICATIONS

"Anticonvulsant Action" of Vitamin D in Epileptic Patients? A Controlled Pilot Study

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Summary

The frequency of epileptic seizures was observed in a controlled therapeutic trial on 23 epileptic inpatients before and after treatment with vitamin D, or placebo in addition to anticonvulsant drugs. The number of seizures was reduced during treatment with vitamin D, but not with placebo. The effect was unrelated to changes in serum calcium or magnesium. The results may support the concept that epileptics should be treated prophylactically with vitamin D.

Introduction

Minor degrees of hypocalcaemia (Richens and Rowe, 1970; Christiansen *et al.*, 1973) and hypomagnesaemia (Christiansen *et al.*, 1974) are known to occur in epileptics on anticonvulsant therapy. As a lowering of the concentration of these ions in extracellular fluid would tend to increase neuromuscular irritability it is conceivable that the effect of anticonvulsants could be partially counteracted. These biochemical changes are part of an osteomalacic state in such patients, and since small doses of vitamin D can increase the bone mineral content

(Christiansen *et al.*, 1973) it is possible that vitamin D might also influence the number of epileptic fits. For practical purposes the problem might be reformulated in the following way: Does vitamin D reduce the number of seizures in epileptic patients on anticonvulsant therapy? We report here the results of a controlled pilot study which seem to indicate that this may be the case.

Patients and Methods

Altogether 23 epileptic inpatients who had relatively frequent fits were selected for the study (table I). All the patients originally had typical grand mal or focal motor attacks and several of them also had other types of seizure. Since they were receiving various combinations of phenytoin, phenobarbitone, and primidone, for the purpose of analysis dosage (table 1) was calculated according to the data of Richens and Rowe (1970).

The number and type of seizures were recorded by experienced nurses who were unaware whether the patient was receiving vitamin D or placebo. Grand mal, abortive forms of grand mal as seen in patients on anticonvulsant treatment, and focal motor seizures were recorded.

TABLE I—Details of Patients and Dose and Duration of Anticonvulsant Treatment. Patients were divided into Two Treatment Groups (see text)

Group	No. of Patients	Sex		Age (Years)		Daily Dose of Anticonvulsant (Units*)		Duration of Anticonvulsant Treatment (Years)	
		M.	F.	Mean	Range	Mean	Range	Mean	Range
A	9	4	5	15	9-27	6.9	2-11	11	3-23
B	14	11	3	13	6-25	6.0	3-12	11	5-17

*Dose calculated in units according to data of Richens and Rowe (1970).

Blood samples were drawn for the determination of serum calcium, serum magnesium, and serum alkaline phosphatase. These determinations, all in duplicate, were performed as previously reported (Christiansen *et al.*, 1973, 1974).

Procedure.—The patients were allocated to two treatment groups (A and B, see table I) by means of random sampling numbers (Bradford Hill, 1967). The duration of the trial was 84 days and it was divided into three periods of 28 days. The

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first period (T_1) was an observation period. In periods T_2 and T_3 , the patients received 500 mg calcium daily (Calcium-Sandoz) plus either vitamin D_2 or placebo. In group A the patients received 4,000 and 16,000 IU vitamin D_2 daily in periods T_2 and T_3 , respectively. The group B patients were given placebo during period T_2 and 8,000 IU vitamin D_2 daily during period T_3 . Throughout the study the dose of anticonvulsants was kept constant. The blood samples were drawn at the end of each period.

Results

The numbers of seizures in the two groups of patients in each of the three periods are shown in table II. The mean frequency is of the seizures (expressed as a percentage of the T_1 values) are shown in the chart. With the use of Wilcoxon's test the pair differences between the observation period (T_1) and periods T_2 and T_3 were evaluated from the raw data given in table II and also from the percentage values. A reduction in the number of seizures was observed when the patients received vitamin D_2 ($P < 0.1$ to < 0.01), whereas this did not occur with placebo treatment ($P > 0.1$) (table III).

Within each group the biochemical measurements were virtually unchanged during the trial (table IV).

Discussion

These results show a reduction in the number of seizures in epileptic patients treated with vitamin D_2 . This action was not

TABLE II—Number of Epileptic Seizures recorded in Periods T_1 , T_2 , and T_3 in the Two Groups of Patients

Case No.	T_1	T_2	T_3
Group A			
1	5	4	3
2	3	1	4
3	5	1	3
4	5	3	4
5	5	4	1
6	15	12	8
7	33	19	14
8	18	23	19
9	9	7	8
Group B			
10	3	2	1
11	7	6	7
12	20	21	13
13	2	2	1
14	2	3	3
15	16	17	8
16	16	3	7
17	57	34	9
18	5	2	4
19	10	6	9
20	13	30	4
21	69	53	63
22	19	4	8
23	10	16	10

TABLE III—Statistical Evaluation of Frequency of Epileptic Seizures (Data from Table II) using Wilcoxon's Test for Pair Differences

Group	Difference between observation period (T_1) and period on:	Values calculated from:	
		Raw Data	Percentage Values
A	4,000 IU vitamin D_2 daily (T_2)	$P < 0.1$	$P < 0.05$
	16,000 IU vitamin D_2 daily (T_3)	$P < 0.05$	$P < 0.05$
B	Placebo (T_2)	$P > 0.1$	$P > 0.1$
	8,000 IU vitamin D_2 daily (T_3)	$P < 0.01$	$P < 0.01$

TABLE IV—Mean Serum Calcium, Magnesium, and Alkaline Phosphatase Levels (± 1 S.E. of Mean) in the Two Treatment Groups at End of Each Period

Group	Measurement	End of Period T_1	End of Period T_2	End of Period T_3
A	Serum calcium (mg/l.)	92.6 $\pm$ 1.0	94.7 $\pm$ 1.1	94.1 $\pm$ 1.2
	Serum magnesium (mmol/l.)	0.83 $\pm$ 0.01	0.83 $\pm$ 0.01	0.84 $\pm$ 0.02
	Serum alkaline phosphatase (K.A. units/100 mls.)	17.1 $\pm$ 2.1	17.6 $\pm$ 1.9	17.9 $\pm$ 2.4
B	Serum calcium (mg/l.)	94.7 $\pm$ 0.9	95.4 $\pm$ 1.1	93.4 $\pm$ 0.8
	Serum magnesium (mmol/l.)	0.83 $\pm$ 0.02	0.83 $\pm$ 0.02	0.83 $\pm$ 0.02
	Serum alkaline phosphatase (K.A. units/100 ml.)	19.8 $\pm$ 1.6	19.1 $\pm$ 1.6	18.8 $\pm$ 1.6

Mean frequency of epileptic seizures, expressed as percentage of values in observation period (T_1), and dose of vitamin D_2 .

concomitant with a change in the serum levels of calcium and magnesium. Hypocalcaemia and raised serum alkaline phosphatase levels were found in these patients, as previously reported (Richens and Rowe, 1970; Christiansen *et al.*, 1973). The serum magnesium levels were not significantly lower than the normal values recently reported from our group (Christiansen *et al.*, 1974). Thus the patients did not exhibit anticonvulsant hypomagnesaemia. This may be explained partly by the low age of the patients, since normal children have a slightly higher serum magnesium concentration than do normal adults (Christiansen and Rødbro, 1974).

This pilot study was planned to investigate whether treatment with vitamin D could reduce the number of epileptic fits and, if so, whether this effect was related to a change in the serum concentrations of calcium and magnesium. A beneficial effect on epilepsy was found, though it was unexplained. Thus the results are of interest in the standing debate whether epileptics should receive prophylaxis with vitamin D. This presumably would not be recommended if the only effect was a normalization of a laboratory value, be it bone mineral content or serum calcium. It is unknown whether epileptic patients on anticonvulsant therapy have general symptoms of osteomalacia; it is also unknown whether the iatrogenic lowering of total body calcium (Christiansen *et al.*, 1973) is harmful to the patient. If our results can be confirmed in larger series they would lend further support to the concept that prophylactic vitamin D treatment is advisable for epileptics on anticonvulsant therapy.

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References

- Christiansen, C., Rødbro, P., and Lund, M. (1973). *British Medical Journal*, 4, 695.
- Christiansen, C., and Rødbro, P. (1974). To be published.
- Christiansen, C., Nielsen, S. P., and Rødbro, P. (1974). *British Medical Journal*, 1, 198.
- Hill, A. B. (1967). *Principles of Medical Statistics*, 8th edn. London, Lancet.
- Richens, A., and Rowe, D. J. F. (1970). *British Medical Journal*, 4, 73.