is hoped that in the future a solution which is as effective as saline, but which can be injected intravenously or intraperitoneally without danger to the patient, will be found.

We wish to thank Professor S. G. Clayton, Mr. J. M. Brudenell, and Mr. R. M. Feroze for their encouragement and for allowing us to include their patients in this series. We are also grateful to the medical and nursing staff of H₂ Ward, Dulwich Hospital, and Fergusson Ward, King's College Hospital, for their kind help and co-operation.

Requests for reprints should be sent to Dr. J. R. Friend.

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Effect of Frusemide Administration on Calcium Excretion

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British Medical Journal, 1971, 1, 437-438

Summary

Each of eight adipose but otherwise normal patients on a reducing diet received daily oral doses of frusemide for four days; the degree of hypercalciuria was found to be significant during the first three days, but on day four the calcium excretion in the urine had become normal though frusemide was still being given. The rates of excretion of sodium and calcium in the urine were closely correlated.

Introduction

Thiazide diuretics are known to reduce the excretion of calcium in the urine (Lamberg and Kuhlback, 1959), and these drugs have been used in the treatment of idiopathic hypercalciuria (Yendt, Gagne, and Cohan, 1966). Tambyah and Lim (1969) found a significant increase in the urine excretion of calcium throughout an eight-hour interval after oral administration of a single dose of 80 mg frusemide. They suggested that frusemide might be of value in the treatment of hypercalcaemia provoked by malignant diseases. As we have observed the development of hypocalcaemia in a patient with cardiac insufficiency treated with frusemide (Toft and Roin, 1971) we found it of interest to examine the effect of continuous frusemide therapy on the daily excretion of calcium in normal subjects, because this aspect had apparently not been studied.

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Patients and Methods

Eight adipose but otherwise normal patients took part in the experiment. Urine was collected on seven consecutive days, beginning at 8 a.m. and ending at 8 a.m. On days 4, 5, 6, and 7 oral doses of 80 mg of frusemide were given at 8 a.m. The calcium level in serum was determined on the first and seventh days at 12 noon. Levels of calcium in serum and urine and the level of sodium in the urine were determined by spectrophotometry. The patients were on reducing diets but had free access to fluid intake. The calcium content of the diets was estimated at less than 800 mg daily.

Results

The effect of frusemide on the daily excretion of calcium in the urine is shown in the Table. Rates of excretion did not deviate significantly during the three 24-hour control periods. The types of deviation to be expected because of the variations observed during the control period of three days were analysed, and on the basis of this analysis the excretion of calcium during treatment was calculated. The excretion of calcium was found to be increased during the first, second, and

Excretion of Calcium in Urine before and during Treatment with Daily Doses of 80 mg of Frusemide

Case No.	Total 24 hour Excretion of Calcium in Urine (mg)							
	No Frusemide (Control)				During Frusemide Therapy			
	Periods of 24 Hours			Average of Periods 1, 2, 3	Periods of 24 Hours			
	1st	2nd	3rd		4th	5th	6th	7th
1	223	181	175	193	225	204	209	211
2	162	179	179	173	230*	285‡	290‡	223
3	142	168	113	141	223†	144	102	122
4	179	180	204	188	240*	172	204	195
5	191	183	237	204	237	220	232	133†
6	279	335	305	306	338	304	293	264
7	278	279	275	277	298	292	244	205†
8	139	133	157	143	249‡	229†	211*	184
Mean	199.1	204.8	205.6	203.1	255‡	231.3†	223.1*	192.1
Standard deviation	55.9	66.9	63.5	59.5	41.2	58.4	60.0	46.5

Deviations from the mean figure obtained during the control period are calculated (t test) on the basis of the daily variations during the control period.

* P<0.05. † P<0.01. ‡ P<0.001.

third 24-hour periods of treatment, but comparison of the mean values obtained during the control periods and those obtained during treatment showed that the increase in excretion of calcium was highly significant only during the first 24-hour period ($P<0.001$). On day 4, when doses of frusemide were still being administered, the excretion of calcium was not significantly higher in any of the patients than it had been during the period of control.

The average excretions of sodium and calcium in the urine were closely correlated ($r=0.94$; $P<0.001$). No significant changes in levels of calcium in serum were observed during treatment with frusemide.

Discussion

Excretion of calcium in the urine depends on the ratio of volumes filtered in the glomeruli to degree of absorption in tubules. Under normal conditions 98% of the filtered load of calcium will be reabsorbed. Walser (1961) showed in experiments on dogs that there was a positive correlation between clearances of calcium and sodium. Later, this fact was found to apply also to man (Kleeman *et al.*, 1964). Our findings support the observation by Tambyah and Lim (1969) of an increased excretion of calcium in the urine after administration of a single dose of frusemide. According to those authors the excretion of calcium was more than

redoubled throughout an eight-hour interval after oral administration of 80 mg of frusemide. The daily excretion observed in our series was only slightly increased, and only for a short period; the excretion became normal within a few days despite continued daily administrations of frusemide. The action of frusemide on the renal excretion of calcium is apparently tied up with its natriuretic property, and since the excretion of sodium is increased only during the initial stages of frusemide therapy, the rise in the excretion of calcium in the urine will be only of transient nature.

Our findings suggest that frusemide can hardly be considered suitable as a permanent treatment of hypercalcaemia, whereas it may be of value as an adjunct to sodium infusions in the treatment of hypercalcaemic crises, in which cases the effects are intensified and the hazards of acute cardiac arrest reduced.

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PRELIMINARY COMMUNICATIONS

Association between Psychopathic Disorder and Serum Antibody to Herpes Simplex Virus (Type 1)

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British Medical Journal, 1971, 1, 438-439

Summary

The sera of a small series of patients has been examined for herpes simplex virus antibody. Three clinically-defined groups of patients were compared: (a) aggressive psychopaths, (b) psychiatric controls, and (c) general hospital patients. The first group had an unusually high average kinetic neutralization constant against type 1 herpes simplex virus.

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Introduction

We wish to report some preliminary results which indicate an association between antibody to herpes simplex virus (type 1) and psychopathic disorder. As a working hypothesis we postulate a virus infection during childhood (either inapparent or at least unrecognized) which damages those areas of the brain related to personality. This concept is in accordance with the ideas put forward by Knobloch and Pasamanick (1958).

Several papers have suggested that herpes simplex virus infection may be associated with psychiatric disorder—for example, Drachman and Adams (1962) and Shearer and Finch (1964). Rimon and Halonen (1969) reported that 28 psychotic depressives (mean age 47 years) showed higher complement fixation titres against herpes simplex virus than did other psychiatric patients and non-psychiatric persons. It is well known that herpes infections can persist through life, giving recurrent lesions in some individuals and in others no apparent illness at any time. Indeed, Scott (1957) estimated that clinical illness was observed in only 10 to 15% of primary infections. Herpes simplex virus may therefore cause minimal brain damage.

Subjects and Methods

We have examined the sera of 13 aggressive psychopaths, 14 non-aggressive psychiatric cases, and 13 non-psychiatric controls for neutralizing antibody to herpes simplex virus type 1 and type 2. All subjects gave consent after the purpose of the investigation had been explained to them. The aggressive psychopaths were selected on the following criteria: (1) a history of severe and/or persistent violence against the person—that is, self-injury or bodily harm to others; and