SHORT COMMUNICATION

The effect of high animal protein intake on the risk of calcium stone-formation in the urinary tract

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(Received 22 January 1979; accepted 24 May 1979)

Summary

1. Studies were carried out on six normal male subjects to determine the short-term effect of increasing the dietary consumption of animal protein on the urinary risk factors for stone-formation, namely, volume, pH, calcium, oxalate, uric acid and glycosaminoglycans.

2. An increase of 34 g/day of animal protein in the diet significantly increased urinary calcium (23%) and oxalate (24%). Total urinary nitrogen increased by an average of 368 mmol/day. The accompanying increase in dietary purine (11 mmol of purine nitrogen/day) caused a 48% increase in the excretion of uric acid.

3. The overall relative probability of forming stones, calculated from a combination of the risk factors, was markedly increased (250%) throughout the period of high animal protein ingestion.

Key words: dietary proteins, urinary calcium, urinary calculi, urinary oxalate, urinary uric acid.

Introduction

It has been suggested that calcium stone-formation in the upper urinary tract is essentially a disease of the affluent society (Andersen, 1973; Blacklock, 1976). In support of this hypothesis, it would appear that hospitalization for stones has been increasing in the Western world during the last 30 years (Andersen, 1973; Hodgkinson & Marshall, 1975; Sierakowski, Finlayson, Landes, Finlayson & Sierakowski, 1978; Robertson, Peacock & Hodgkinson, 1979b). Recently it has been shown that there is a strong correlation between the occurrence of stones in the population and the level of affluence, as defined by the expenditure on food (Robertson, Peacock, Heyburn, Speed & Hanes, 1979a). The only dietary factor which correlated consistently with expenditure on food was the intake of animal protein. These observations are thus compatible with the hypothesis that the risk of calcium stone-formation in a given population is related to the consumption of animal protein.

The object of this study has been to determine the effects of increasing dietary animal protein on the composition of urine and the risk of forming calcium-containing stones.

Materials and methods

The subjects studied were six normal male volunteers aged between 22 and 40 years. They were studied on a ‘free diet’ at home but were given dietary advice on maintaining a constant intake of calcium, protein and fluid throughout the 12 days of the study.

The first 3 days formed a control period, during which the subjects consumed about 50 g of animal protein/day. From day 4 to day 12, they ingested 150 g of skipjack tuna fish extra in their diet each day. This added 34 g of animal protein/day, 0.25
mmol of calcium/day, 9·2 mmol of inorganic phosphorus/day, 1·7 mmol of magnesium/day, 27 mmol of sodium/day, 377 mmol of total nitrogen/day and 11 mmol of purine nitrogen/day. Dietary histories were kept to assess the intake of animal protein during the control and test periods.

Twenty-four hour urine samples were collected with 5 ml of 20% hibitane as preservative on each day and analysed for the main risk factors of calcium stone-formation, namely volume, pH, calcium, oxalate, uric acid and glycosaminoglycans. The methods of analysis and the relative probability of forming stones, calculated from these six measurements, were determined as described by Robertson, Peacock, Heyburn, Marshall & Clark (1978).

To monitor the compliance of the subjects with the high animal protein diet, total urinary nitrogen was estimated from the combined measurements of urinary creatinine, uric acid, urea and ammonia (Chaney & Marbach, 1962).

Results

The mean value for each urinary risk factor during the three control days was calculated for each individual. From this the change in each risk factor was calculated for each day of the study. The group mean (±SEM) changes in the risk factors are shown in Fig. 1 for each of the 12 days. The significances of the changes on each day were estimated by comparing the daily group mean changes with the over-all mean value during the control period.

Fig. 1 also shows the mean (±SEM) values for the overall relative probability of forming stones. During the period of high animal protein consumption there were significant increases in urinary calcium (23%), oxalate (24%) and uric acid (48%). The increases in urinary oxalate and uric acid were observed in all subjects, but one (an Asian) failed to show a significant increase in urinary calcium. There was a small but non-significant increase in urinary volume of 200 ml/day. The net effect of these changes, including the increase in urinary volume, was to increase the mean relative probability of forming stones by about 250%, most of the values exceeding the upper limit of normal.

The total urinary excretion of nitrogen increased by an average (±SEM) of 368 ± 16 mmol/day between days 2 and 9 of the high animal protein diet. Dietary nitrogen increased by an average of 377 mmol/day during the same period.

Discussion

The 34 g/day of additional dietary animal protein given in this study is sufficient to raise the consumption of animal protein of the average Briton (~45–50 g/day) to that of the average American (75–80 g/day). It was given in the form of tuna fish partly for convenience of handling and partly because this is very low in calcium and oxalate, two of the risk factors under study. Although dietary sodium, magnesium and phosphate were also increased, previous analysis has shown that none of these ions appears to be a significant risk factor in the genesis of calcium stones (Robertson et al., 1978). Therefore the urine analysis of these ions has not been included in this report.

The constant increase in total urinary nitrogen excretion of 368 mmol/day from day 2 to day 9 of the high animal protein dietary period is almost equal to the calculated increase in nitrogen consumption, indicating that the subjects were adhering to their high animal protein diet.

This study confirms reports that a high protein intake increases the urinary excretion of calcium (Sherman, 1920; McCance, Widdowson & Lehmann, 1942; Anand & Linkswiler, 1974; Margen, Chu, Kaufmann & Calloway, 1974; Adams, Gray & Lemann, 1978). This additional calcium may come from bone resorption, since recent studies indicate that individuals on a high protein intake appear to be in negative calcium balance (Linkswiler, Joyce & Anand, 1974; Chu, Margen & Costa, 1975; Adams et al., 1978).

The increase in urinary oxalate on a high animal protein diet has not previously been reported. It may derive from the increased endogenous production of oxalate from the metabolism of phenylalanine, tyrosine and tryptophan (Gershoff & Prien, 1960; Gambardella & Richardson, 1977), which are present in relatively high proportions in animal protein compared with vegetable protein (Paul & Southgate, 1978). This relationship between oxalate excretion and dietary animal protein estimated from diet histories has also been noted in our idiopathic calcium stone-formers (W. G. Robertson, P. J. Heyburn, M. Peacock, F. A. Hanes & R. Swaminathan, unpublished results).

The increase of 1·7 mmol/day in the excretion of uric acid, resulting from 11 mmol of additional purine nitrogen in the diet, is consistent with that found by other workers giving the same purine load (Zöllner & Griebisch, 1973; Coe, Moran & Kavalich, 1976).
A high animal protein diet therefore adversely affects three of the six urinary risk factors for the disease. These increases are slightly offset by the small increase in urinary volume which presumably arises from the increase in sodium load. However, even taking this into account, the calculated overall risk of forming stones increases markedly, most of the values moving into the region where there is a high probability of forming calcium oxalate stones (Robertson et al., 1978). The small fall in the risk of stones at the end of the study is entirely the result of the small increase in urinary volume, since the increases in urinary calcium, oxalate and uric acid are all sustained during the period of study.

These observations are consistent with our suggestion, from epidemiological studies, that an increase in the dietary consumption of animal protein increases the risk of stone-formation in the population (Robertson et al., 1979a,b).

References


FIG. 1. Mean (±SEM) changes from the basal diet in the risk factors for calcium stone-formation and the mean (±SEM) relative probability of forming stones during the period of high animal protein consumption. *P < 0.05; **P < 0.01; ***P < 0.001.


