Dietary fibre and ketone bodies: reduced urinary 3-hydroxybutyrate excretion in diabetics on guar

Dietary fibre is known to modify carbohydrate absorption and metabolism in both normal and diabetic individuals.¹⁻³ Except for reports on the action of certain forms of fibre in reducing serum cholesterol concentrations,³ however, no attention has been given to other changes in lipid metabolism.

Since urine testing for ketone bodies is still a major part of the clinical assessment of the diabetic, we have looked at the effect of guar gum on the output of 3-hydroxybutyric acid (3-OHB) in diabetic volunteers. If both 3-OHB and glucose outputs were reduced at the same time then this would suggest a general improvement in diabetic control rather than carbohydrate malabsorption.

Patients, methods, and results

Nine diabetics (4 men, 5 women aged $42 \pm (\text{SE of mean})$ 5 years) were studied. Their blood and urinary glucose data have been reported²; two were taking oral hypoglycaemic agents and seven insulin 36 ± 6 U/day. Their mean weight was $106 \pm 5\%$ of desirable weight.

Seven patients were studied in hospital on metabolically controlled diets: identical two-day rotating menus were provided over both consecutive test and control five-day periods (the order being randomised and separated in five studies by a weekend). Two were studied as outpatients and kept the same meal plans throughout. During the control period patients took between 14 and 26 slices of crispbread per day with meals, and during the test period they took guar crispbread of the same composition except that it also contained 1 g guar/slice. Serum was obtained on the last day of each period and complete 24-hour urine collections were made throughout for analysis of creatinine (Technicon, SMA 12/60).⁴ Urinary 3-OHB, the ketone body least likely to be affected by storage, was estimated by an enzymatic technique modified for use with the Guildford 3500 enzyme analyser.⁵ The significance of differences was calculated using Student's *t* test for paired data.

The mean 3-OHB and glucose outputs over the last two days on guar were much lower than during the control period (see table). Calculated as

Percentage change in 24-hour urinary glucose and 3-OHB outputs for last two days on guar compared with control period

Case no	Last two control days		% Change on guar	
	3-OHB (mmol/24h)	Glucose (mmol/24h)	3-OHB	Glucose
1	1.33	394	-55	-26
2	1.16	1681	-71	-72
3	0.19	327	+6	-19
4	1.46	477	-61	-60
5	1.15	433	-6	+5
6	0.90	688	-44	-46
7	0.73	298	-58	-62
8	15.68	799	-66	-21
9	0.17	178	-5	-38
Mean $\pm$ SE of mean	2.53 ± 1.65	583 ± 150	-40 ± 10 ($P < 0.01$)	-38 ± 8 ($P < 0.002$)

Conversion: SI to traditional units—3-OHB: 1 mmol/l $\approx$ 104 mg/l. Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

the mean percentage difference, 3-OHB excretion was reduced by 36% ($P < 0.02$) on day 4 and by 33% ($P < 0.05$) on day 5. The overall mean reduction for the last two days was 40% ($P < 0.01$) for 3-OHB compared with 38% ($P < 0.002$) for glucose. Because of the differences in mean control daily outputs between individuals (0.17-15.68 mmol/24 h (17.7-1630 mg/24 h)), the large absolute differences in 3-OHB output between the mean values for test and control days were not significant.

Mean 24-hour creatinine outputs over the two periods ranged from 10.7 to 12.6 mmol/24 h (1.2-1.4 g/24 h) and showed no trend, while the mean creatinine clearance on the last day of each period was identical ($95 \pm (\text{SE of mean})$ 11 ml/min for the control period and 95 ± 12 ml/min for the test period). The differences in 3-OHB excretion were therefore unlikely to have been due to incomplete urine collections or changes in renal function.

Comment

Although the percentage changes in urinary glucose and 3-OHB loss were of the same magnitude, a significant correlation was not seen. Nevertheless, the lower 3-OHB output may indicate a reduction in fat metabolism and contribute to the reduced insulin requirement seen in diabetics on high-fibre diets.^{1,2}

The effect of guar on 3-OHB excretion further emphasises that its effect in reducing glucose loss is likely to be due to improved diabetic control rather than secondary to malabsorption of food and therefore reduced caloric intake. If this were not so, increased ketone-body excretion would be expected on a metabolic diet.

We conclude therefore that the observed reduction in 3-OHB excretion adds valuable independent support to the idea that certain types of dietary fibre may be useful in the treatment of diabetics.

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Taste loss associated with oral captopril treatment

Captopril (SQ 14225) is an orally active converting enzyme inhibitor which is an effective antihypertensive agent in man.¹ A study has recently been completed in our unit² comparing the antihypertensive properties of captopril with those of hydrochlorothiazide and examining the value of combining captopril with a diuretic in the management of moderate hypertension. During this study three out of 16 patients treated with captopril developed a definite disturbance of taste.

Case reports

Case 1—A 55-year-old woman was treated with captopril in doses increased at weekly intervals from 75 to 150, 300, and 450 mg/day. During the fifth week hydrochlorothiazide was also prescribed. At this time she complained that sweet foods tasted salty and that she had a persistently bitter taste in the mouth. After this she progressively lost taste discrimination. On testing she could recognise salt applied directly to the tongue and distinguish it from sugar, but after 20 seconds the sugar tasted bitter. Biochemical and haematological values were normal. Captopril (450 mg/day) and hydrochlorothiazide were continued for the next eight weeks but the disturbance of taste persisted. The captopril was replaced by methyldopa and two weeks later her taste had returned to normal.

Case 2—A 65-year-old man complained of taste loss during his third week of captopril treatment. The dose at the time was 150 mg/day. No other drugs were prescribed. He also complained of a persistent salty taste in his mouth. Captopril was stopped and his taste recovered after about 10 days. The drug was then restarted at the same dose and five days later the disturbance of taste recurred. Biochemical and haematological values

were normal and his serum zinc value was 11 mmol/l (72 mg/100 ml) (normal 11-19 mmol/l (72-124 mg/100 ml)). He gave no response to oral zinc supplements. When the captopril was stopped on the second occasion his taste recovered within three days.

Case 3—A 43-year-old woman had received treatment with hydrochlorothiazide 100 mg/day for eight weeks and captopril (in increasing doses to 300 mg) for four weeks. She then noticed a disturbance of taste affecting all types of food and accompanied on occasions by slight nausea. All biochemical and haematological values were normal and her plasma zinc concentration was 13 mmol/l (85 mg/100 ml). The dose of captopril was reduced stepwise over the subsequent three weeks but the disturbance did not clear until about two days after the drug was withdrawn. Oral zinc supplements were used during the withdrawal phase without apparent effect.

Comment

Three out of 16 patients treated with the angiotensin-converting enzyme inhibitor captopril (SQ 14225) developed a loss of taste which persisted until the drug was withdrawn. A persistent abnormal taste in the mouth accompanied the disturbance in two patients and nausea was present in one. This side effect has been the most prominent adverse reaction to captopril in our experience with the drug.

The explanation for the development of this problem is not clear. Several other drugs, including griseofulvin, lincomycin, penicillamine, and thiamazole, are reported to cause a similar disturbance, and in the case of thiamazole and penicillamine it has been suggested that the problem results from the complexing of zinc by these drugs.³ Zinc depletion in humans after treatment with D-penicillamine or histidine or after burns, liver damage, or malabsorption is commonly associated with decreased taste acuity that may respond to zinc supplements.⁴

Captopril binds to zinc ions present at the active centre of the converting enzyme⁵ and might be expected to reduce tissue zinc levels. The normal plasma zinc concentrations and the failure of zinc supplementation to relieve the disturbance in two cases do not, however, support this suggestion.

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Screening for hypertension: a hospital-based home-visiting programme

Hypertension remains a common and dangerous disease for which effective treatment is available. Attempts have been made to screen populations considered to be at risk with varying success.^{1,2} A large hospital-based pilot study was undertaken to assess the feasibility of screening for hypertension by visiting at home the patients of an urban group practice. An excellent contact rate and follow-up attendance rate was achieved.

Population, methods, and results

The survey was conducted in Hove, Sussex, an urban English town. From the family practitioner committee records 7544 names and addresses of patients aged from 15 to 75 years inclusive on the lists of four general

practitioners of a group practice were obtained. Inaccuracy of records owing to changes of address or doctor or death reduced this to a total of 4993 possible contacts. These each received a letter explaining the purpose of the survey, and subsequently one or more home visits were made by a nurse. At the first visit a brief questionnaire was completed recording relevant medical history, drug therapy, and smoking habits. Blood pressure readings were taken on the right arm, in the sitting position, using a standard mercury sphygmomanometer (Korotoff V). Limits for "normal" blood pressures related to age were based on figures published by the New York Metropolitan Life Insurance Company³ and the Framingham study.⁴ Patients with a raised blood pressure were visited a second time at home. If the blood pressure was still raised they were referred to the hypertension clinic at the hospital. They were classified as hypertensive only when two further measurements at the clinic exceeded our normal range. Patients with a single raised reading were classified as labile and are being followed up only, whereas those persistently hypertensive were offered treatment.

The table summarises the results of the survey. Of all possible contacts, 92% (4545) were interviewed. The survey found 631 hypertensives, of whom 329 were already known to their doctors and 302 were previously undetected. Of the former group, less than 50% were judged to be adequately controlled by our criteria. All those who were requested to attend the follow-up clinic complied. In the group of newly discovered hypertensives 24% were under 45 years of age. The greatest number of hypertensive men occurred in the 45-54 age group and in the women in the 55-64 age group. The prevalence of hypertension, as defined by the age-related criteria, was found to be 14.2% of the population studied.

Summary of results of survey of hypertension in a population aged 15-75 years

Total population registered with practice	..	..	..	..	..	7544
Inaccurate records	..	..	..	..	..	2551
Remaining possible contacts	..	..	..	..	..	4993
Declined to co-operate	..	..	..	..	..	172
Uncontactable	..	..	..	..	..	398
Total willing to participate	..	..	..	..	..	4423
"Normal" blood pressure	..	..	..	..	..	3756
Total number of hypertensives	..	..	..	..	..	631
Previously known hypertensives	..	..	..	..	..	329
Previously undetected hypertensives	..	..	..	..	..	302
Classified as "labile" hypertensives	..	..	..	..	..	216

Comment

There is a relatively high prevalence of hypertension in the community. The major problem of a screening programme is contacting the target population and then achieving a high follow-up rate. We believe that our direct combined approach of an initial explanatory letter followed by at least two home visits by nurses was responsible for the high level of co-operation and the 100% follow-up rate at the hospital clinic. The high prevalence, asymptomatic nature, serious consequences, and efficacy of treatment of hypertension should justify the effort expended in screening the population. The cost of uncovering each new hypertensive patient was estimated in this survey to be about £100. This is not excessive when considering the age distribution and consequences of the disease and the costs of its morbidity and mortality. Our study shows the effectiveness of combined home visiting and hospital referral in detecting hypertension in a community without undue burden on general practitioner services.

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