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Low glycaemic index diet in patients prescribed clozapine: pilot study

AIMS AND METHOD

This study aimed to investigate the potential benefits of a low glycaemic index diet in patients with schizophrenia taking clozapine. Seven patients consented to participate in a 5-week pilot study. Measurements were taken of body weight, random blood glucose and cholesterol levels.

RESULTS

The mean weight loss per patient was 2.9 kg in 4 weeks. Random blood glucose levels reduced from a mean of 5.3 mmol/l at the beginning of the study to 4.7 mmol/l at the end.

CLINICAL IMPLICATIONS

A low glycaemic index diet may possibly reduce the substantial cardiovascular risk in patients receiving antipsychotic medication.

Atypical antipsychotic agents have been reported to have a deleterious effect on glucose metabolism. Koller *et al* (2001) described a causal relationship between clozapine use and diabetes. Mir & Taylor (2000) described the hyperglycaemic effects of conventional and atypical antipsychotic drugs, and recommended blood glucose monitoring for patients prescribed clozapine and olanzapine. There have also been reports that antipsychotics have an effect on cholesterol levels (Lindermayer *et al*, 2003). The concomitant use of sodium valproate with clozapine has been reported by Hendenmalm *et al* (2002) to increase the risk of developing glucose intolerance. The risk of developing diabetes mellitus is increased in people who are obese. Antipsychotic drugs are known to cause weight gain in some patients, adding to the risk of glucose metabolism problems. If this is added to the independent risk factor of people with a diagnosis of schizophrenia being more likely to develop diabetes mellitus, and the number of people with mental health problems who smoke, the future cardiovascular health of these patients has the potential to be very bleak.

The American and Australian Diabetic Associations are now recommending that people with diabetes follow a diet comprising foods with a low glycaemic index (Kunar, 2002), which has the effect of steadying blood glucose levels. There is also debate about the use of this diet in obese patients (Palwak *et al*, 2002): the low-fat diets traditionally recommended were by their nature a higher glycaemic index diet. The rise and fall in blood glucose levels stimulated appetite in some patients, making it more difficult for them to lose weight.

The glycaemic index (GI), put simply, is a number indicating how quickly and by how much a person's blood glucose concentration increases after eating a certain food, and is calculated using the following equation:

$$\mathrm{GI} = \frac{\text{curve to 50 g carbohydrate from test food}}{\text{incremental area under the glucose response curve to 50 g carbohydrate standard}} \times 100$$

The aim of the diet is to try and consume foods that have a lower glycaemic index (GI). A table giving the glycaemic index values of a range of foods is available on request from the author. A GI value below 50 is considered low; a value above 70 is high, and patients should be encouraged to avoid such foods. A GI value below 70 but above 50 is considered to be intermediate, and such foods should be eaten sparingly or mixed with a low GI food if possible.

The aim of our study was two-fold: to investigate the feasibility of a low GI diet in a group of patients with schizophrenia undergoing compulsory treatment with clozapine, and to study the effect of this diet on weight, body mass index (BMI), and random blood glucose and serum cholesterol levels.

Method

The study population were in-patients in the Tayside low-security forensic psychiatry service. All the patients had a diagnosis of schizophrenia or schizoaffective disorder, and had been prescribed clozapine; exclusion criteria were a previous diagnosis of diabetes or other metabolic disorder, or of a malabsorption syndrome, including coeliac disease. All participants gave informed consent to the study.

The study was 5 weeks long. Before it began, there was a presentation to the nursing staff in the wards to educate them about the diet principles and the study design. Posters were put up in the patients' wards, showing the diet in pictorial form, as an aid to compliance. At the end of each week, the patients were weighed. Week 1 was a control week during which the patients were asked to follow their normal diet. During this week, blood samples were collected for random plasma glucose and cholesterol testing. The samples were taken in the morning after breakfast as the normal ward routine dictated, and were sent to the local laboratory for analysis. The assays were monitored to meet internal laboratory standards and tested by the UK National External Quality Assessment scheme. The patients were asked to keep a simple food diary for this first week, and their hospital menu cards were also collected. Also during this week the patients were given an explanation individually of the nature of the study diet, together with a diet reminder sheet.

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The low GI diet began on week 2 of the study and continued for a further 3 weeks. During the last week of the study, patients were again asked to complete a food diary and their menus were collected. At the end of the 5-week period blood samples were again taken for glucose and cholesterol testing and sent to the laboratory. The patients completed a questionnaire concerning the diet.

Results

Twelve patients were asked to take part in the study, seven of whom gave informed consent. The patients were in two wards: an 8-bed admission ward and a 17-bed rehabilitation ward. These wards were chosen because nursing staff were on hand to offer advice to the patients. The patients who refused were either unable to give informed consent because of the severity of their illness at that time, or were already on a diet and did not wish to change. Six of the patients had a diagnosis of schizophrenia and the remaining patient had a diagnosis of schizoaffective disorder. All of them were taking clozapine: the mean daily dosage was 553.57 mg per patient, and this did not change throughout the study.

The mean body weight at the start of the study was 105.2 kg (range 86.6–120) and the mean BMI was 30.3 kg/m^2 (range 23.5–36.9). This compared with end-of-study values of mean weight 102.8 kg (range 82–122) and mean BMI 29.6 kg/m^2 (range 22.9–37.6). For weight, the 95% confidence interval was −0.3 to 5.0 (P=0.07) and for BMI it was −0.2 to 1.5 (P=0.09). The changes in BMI for each patient are given in Table 1.

Table 1. Change in body mass index (BMI) for each patient at the beginning and end of the study

Patient	Start BMI (kg/m^2)	Finish BMI (kg/m^2)
1	34.8	34.5
2	30.8	29.1
3	28.3	28.0
4	36.9	37.5
5	27.3	26.9
6	23.5	22.9
7	31.1	29.0

Six of the patients lost weight, but the seventh gained 2 kg. The mean weight lost in 4 weeks was 2.9 kg, and the maximum weight loss was 7.1 kg. The mean random plasma glucose concentration was 5.4 mmol/l at the start of the study and 4.7 mmol/l at the end of the study (95% CI −0.3 to 1.2; P=0.2). The mean blood cholesterol level at the beginning of the study was 5.8 mmol/l; at the end of the diet it was 5.5 mmol/l. One patient was excluded from this analysis because of an initial cholesterol level greater than 10 mmol/l, and this patient was prescribed simvastatin.

Only six patients completed their questionnaires at the end of the study. None reported any side-effects from the diet. Three patients felt that the diet satisfied their hunger most of the time. All the patients stated that they understood the general principles of the diet and that it had been well explained to them. The comments on the questionnaire referred only to the lack of suitable choice on the hospital menu.

Discussion

In this pilot study a low glycaemic index diet resulted in weight reduction, a reduction in mean random plasma glucose levels and reduced blood cholesterol concentration in the majority of the seven patients with schizophrenia treated with clozapine. Although the study failed to show statistical significance, probably because of the small sample size, this is an important (albeit preliminary) finding, given the potential morbidity associated with antipsychotic treatment-emergent obesity. We also demonstrated that even severely ill detained patients are able to understand aspects of the diet and make appropriate dietary changes.

The patient group was initially selected as it was hoped that the 24-hour nurse presence would encourage compliance with the diet. In practice, this was counter-balanced by the severity of the patients' illness. The main problem with the diet was not – as expected – in enabling the patients to understand the diet, but in access to the foodstuff required. Unfortunately, the patients were unable to complete even a simple food diary, and they did on occasion eat food that was not provided by the hospital kitchen and therefore was not recorded on the hospital menus that were collected by nursing staff.

It was encouraging that six of the patients managed to lose weight in the 4-week period, although a longer study would provide more information as to the capacity of this diet to aid in weight loss or prevention of weight gain in these patients. It was of interest that the random blood glucose and cholesterol levels were also reduced in the study group, but again, this was only during a 4-week period, and would require further study to assess its clinical significance. We were unable to find any other reported studies on this topic to compare our results against.

We hope to undertake a much larger study of this dietary intervention in an out-patient setting and over a longer time frame to assess whether the changes in weight and blood glucose level are maintained. We also plan to develop a patient information leaflet to improve compliance with the diet, given the concentration and memory problems associated with schizophrenic illness. We hope to prove that the benefit of this diet in patients receiving antipsychotic medication is clinical and not just theoretical.

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