Abstract

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Plasma glucose and thiocyanate responses to different mixed cassava meals in non-diabetic Nigerians.

Akanji AO, Adeyefa I, Charles-Davies M, Osotimehin BO.

Source

Department of Chemical Pathology, College of Medicine, Unversity College Hospital, Ibadan, Nigeria.

Abstract

We measured plasma glucose and thiocyanate levels before and up to 4 h after feeding 11 overnight fasted healthy non-diabetic volunteers randomly on three occasions each with three locally consumed cassava meals: (i) gari as eba 50 g; (ii) lafun 50 g and (iii) parboiled cassava flakes 76 g. Each of these meals contained 175 kcal (0.7 MJ) and was consumed with a sauce to a total caloric value of 300 kcal (1.26 MJ). On the fourth visit, each volunteer consumed 75 g glucose. While the peak and 2-h glucose values were greatest with oral glucose (P less than 0.01), they were similar with the three cassava meals, although tended to be lowest with lafun. Similarly, areas (incremental and total) under the glucose/time curves were highest with oral glucose (P less than 0.05), but while eba and cassava flakes were similar, lafun had the lowest values (P less than 0.05). Plasma thiocyanate levels were unchanged after ingestion of oral glucose and eba, but increased to peak values (P less than 0.05) by 14 per cent on cassava flakes and by 23 per cent on lafun. We conclude that post-prandial glycaemia and plasma thiocyanate levels after cassava meals depend on the mode of preparation of the meal and that lafun showed the least glycaemic response of the three cassava meals tested although it caused the greatest increase in plasma thiocyanate levels. These findings suggest that a cyanogenetic potential does not always reflect a tendency to hyperglycaemia.

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Plasma glucose and thiocyanate responses to different mixed cassava meals in non-diabetic nigerians

Abayomi O. Akanji*, Iyabo Adeyefa†, Mabel Charles-Davies and Babatunde O. Osotimehin.

Endocrine-Metabolic Unit, Departments of Chemical Pathology and Human Nutrition†, College of Medicine, University College Hospital, Ibadan. Nigeria.

We measured plasma glucose and thiocyanate levels before and up to 4 h after feeding in 11 overnight fasted healthy non-diabetic volunteers randomly on three occasions each with three locally consumed cassava meals: (i) *gari* as eba 50 g; (ii) *lafun* 50 g and (iii) parboiled cassava flakes 76 g. Each of these meals contained 175 kcal (0.7 MJ) and was consumed with a sauce to a total caloric value of 300 kcal (1.26 MJ). On a fourth visit, each volunteer consumed 75 g glucose. While the peak and 2-h glucose values were greatest with oral glucose ($P < 0.01$), they were similar with the three cassava meals, although tended to be lowest with *lafun*. Similarly, areas (incremental and total) under the glucose-time curves were highest with oral glucose ($P < 0.05$), but while *eba* and cassava flakes were similar, *lafun* had the lowest values ($P < 0.05$). Plasma thiocyanate levels were unchanged after ingestion of oral glucose and *eba*, but increased to peak values ($P < 0.05$) by 14 per cent on cassava flakes and by 23 per cent on *lafun*. We conclude that post-prandial glycaemia and plasma thiocyanate levels after cassava meals depend on the mode of preparation of the meal and that *lafun* showed the least glycaemic response of the three cassava meals tested although it caused the greatest increase in plasma thiocyanate levels. These findings suggest that a cyanogenetic potential does not always reflect a tendency to hyperglycaemia.

Malnutrition-related diabetes mellitus (MRDM) was recognized as a separate subclass of primary diabetes by the WHO Expert Committee on Diabetes Mellitus in its 1985 report. This syndrome is believed to result from a combination of protein malnutrition (especially deficiency of the sulphur-containing amino acids) and endemic cassava consumption (McMillan & Geevarghese, 1979; Vannasaeng *et al.*, 1982; Bajaj, 1985). The latter probably acts *via* its cyanide content which has been shown to be potentially toxic to pancreatic islet cells (McMillan & Geevarghese, 1979; Vannasaeng *et al.*, 1982; Bajaj, 1985). Although MRDM is said to account for 30-40 per cent of juvenile diabetes in India (WHO Expert Committee on Diabetes Mellitus, 1985; Bajaj, 1985), it may not be that common in other tropical countries even when protein malnutrition and/or cassava consumption are rife (Lester, 1984; Teuscher *et al.*, 1987). For instance, less than 2 per cent of juvenile subjects attending a diabetic clinic had MRDM in Ethiopia where malnutrition is endemic (Lester, 1984) and none of 1028 inhabitants of a rural West African village consuming cassava root daily without adequate protein supplementation had diabetes (Teuscher *et al.*, 1987). Only 5 per cent of juvenile subjects attending a Nigerian diabetic clinic fitted into the established criteria for MRDM (Akanji, 1989).

Futhermore, epidemiological studies suggested that (a) many African and Asian communities traditionally consume large amounts of cassava and yet have a low preva-

* To whom all correspondence should be addressed).

lence of MRDM (Abu-Bakare *et al.*, 1986; Teuscher *et al.*, 1987) and (b) certain communities in India do not consume large amounts of cassava yet have a high prevalence of MRDM (Abu-Bakare *et al.*, 1986). These observations led to doubts on the role of cassava intake in the development of MRDM. It may however be that the source and mode of preparation of the cassava influence how much cyanide is made available in the diet. Different cassava mealsd might thus present different amounts of cyanide to the pancreatic islets.

The metabolic product of cyanide in mammals is thiocyante (SCN), *via* a reaction catalysed by the enzyme thiosulphate cyanide sulphur transferase (rhodanase), and plasma SCN levels rise when cassava meals are consumed (Osuntokun, 1969 1970). Measurement of plasma SCN levels could therefore indicate the cyanognetic potential of a cassava meal if the hepatic pool of free amino acids (especially the sulphur-containing amino acids) is adequate to supply the required thiol groups. It could also be reasoned that, if cyanide damages the pancreatic B-cells, foodstuffs with a high cyanide content (as reflected in post-prandial plasma SCN levels) should impair glucose tolerance whether taken as single meals (acutely) or as part of a regular diet.

As a preliminary step in investigating these hypotheses, we fed overnight fasted healthy male Nigerian adults on four occasions in random order with 75 g glucose and one or other of three different cassava meals derived from fresh cassava root processed differently. Each of the three diets was isoenergetic with 75 g glucose. We then assessed post-prandial plasma glucose and SCN levels after these cassava meals and related these parameters to changes observed when oral glucose was taken. Our results should offer further information on the glycaemic responses to different cassava meals and might be a basis for offering dietary advice to diabetics in tropical populations with endemic cassava consumption.

Subjects and methods

Subjects

Eleven health male medical students aged 23.1 ± (s.d.)1.2 years with body mass index 20.2 ± 1.4 kg/m^2 were recruited into the study after voluntary informed consent. They were non-diabetic with screening pre-recruitment 2-h post-prandial whole-blood glucose values of 3.4 ± 0.9 mmol/l. None had a family history of diabetes and none was regularly on any medication known to influence glucose metabolism. These subjects consumed a typical Nigerian diet containing 10–15 per cent protein, 10–20 per cent fat and 65–70 per cent carbohydrate to a total daily energy intake of about 2000 kcal (Republic of Nigeria Nutrition Survey, 1968). They usually consumed cassava in one form or the other at least once daily. They were studied on four mornings (from 09.00 h) after an overnight 10-h fast (with water *ad libitum*). The four meals (Table 1) were taken in random order.

Meals

On each study morning, each volunteer consumed one of the following meals (Table 1): (i) oral glucose 75 g dissolved in 250–300 ml water; (ii) *eba* made from *gari* 50 g. *Gari* is produced from fresh cassava tubers after some processing: the fresh tubers are peeled and washed before being grated and soaked in water for about 24 h; the moist grated cassava is then packed into sacks and allowed to ferment for 3–5 d before being fried with or without palm-oil. The final product is *gari* which can be consumed as such or made into *eba*, the latter by adding the *gari* into boiling water and stirring until a thick paste forms. *Eba* is usually consumed with a vegetable sauce. Fresh cassava tuber contains 52.3 mg HCN/100 g dry matter and this is reduced to

Table 1. Composition of the four meals.

Meal	*g*	*kJ**
glucose	75	1260
gari/eba	50	735
lafun	50	735
cassava flakes	76	735

Each of the cassava meals was eaten with a sauce containing 20 g lean meat (193 kJ), 10 g spinach (34 kJ), 5 g each of tomatoes (4 kJ), onion (8 kJ) and pepper (11 kJ) and 8 g of palm oil (275 kJ) with salt to taste, which contributed 525 kJ to the energy content of the meal.

*Calculated from standard food tables.

Table 2. Plasma glucose and thiocyanate concentrations and areas under the 4 hour glucose/time curves.
(MEANS (SD))

	oral glucose	*eba*	*lafun*	*cassava flakes*
fasting plasma glucose (mmol/l)	3.7(0.7)	3.6(0.6)	3.5(0.4)*	3.2(0.5)*
peak plasma glucose (mmol/l)	5.7(0.5)	5.5(0.7)*	5.1(1.3)	5.4(0.9)
2-h plasma glucose (mmol/l)	4.8(0.8)	4.2(0.6)*	4.0(0.5)*	4.0(0.5)*
total area under glucose/time curves (mmol.4 h/l)	21.7(2.7)	19.8(2.2)*	18.4(2.1)*†	19.0(2.6)*
incremental area (Y) (mmol.4 h/l)	5.2(2.4)	3.8(2.6)*	2.5(2.4)*†	4.3(2.8)
Ymeal/ Yglucose	1	0.72(0.41)*	0.53(0.37)†*	0.82(0.49)*
fasting plasma SNC (mmol/l)	0.102 (0.036)	0.120 (0.040)	0.096 (0.040)	0.104 (0.040)
peak plasma SCN (mmol/l)	0.109 (0.033)	0.118 (0.040)	0.118 (0.050)¶	0.119 (0.050)¶
increase to peak plasma SCN (mmol/l)	0.006 (0.029)	−0.001 (0.019)	0.028 (0.018)¶	0.017 (0.019)

*$P < 0.05$ compared to oral glucose,
†$P < 0.05$ compared to *eba* and cassava flakes;
§$P < 0.05$ compared to *eba*;
¶$P < 0.05$ compared to fasting values

lafun and greatest with *eba*, although the differences between them were not statistically significant (Figure, Table 2).

The total areas under the glucose/time curves were lower with the cassava meals compared with oral glucose (all $P < 0.05$) (Table 2), a pattern which was also observed for the incremental areas (which corrected for the difference in fasting glucose concentrations). The respective total and incremental areas for the different cassava meals were lowest for *lafun* (Table 2). The ratio of the incremental area for each meal to that for oral glucose (Ymeal/Yglucose in Table 2) gives an index of post-prandial glycaemia and might be taken as an indication of the tendency to hyperglycaemia after each meal. This ratio was again lowest for *lafun* ($P < 0.05$) (Table

1.1 mg HCN/100 g dry matter by the processes involved in the preparation of *gari* (Tewe, 1975); (iii) *lafun* (50 g) prepared from cassava tuber by initial washing and peeling of the fresh tuber followed by slicing to thin flat pieces which are then soaked in water to ferment for about 24–36 h; the pieces are subsequently sun-dried and milled to produce to flour from which *lafun* is made by pouring into boiling water and stirring with a ladle to produce a smooth, thick past. *Lafun* is also consumed with a vegetable sauce. Cassava flour typically contains 6.5 mg HCN/100 g dry matter (Tewe, 1975); (iv) parboiled cassava flakes (76 g). This meal is made from the sweet cassava (*manioc palmata*) variety after an intial washing and peeling of the tuber followed by cutting into thin slices which are then soaked overnight in water before being sun-dried. The dried flakes are prepared for consumption by boiling in water, and again eaten with a vegetable sauce. Dried sweet cassava contains about 3.2 mg HCN/100 g dry matter (Tewe, 1975).

While *gari* and *lafun* each contain about 97 per cent carbohydrate (dry weight), cassava flakes contain about 60 per cent (Tewe, 1975). *Gari* and *lafun* are usually made from the bitter cassava (*manioc utilissima*) variety. While *gari* involves a heat-frying stage, *lafun* and cassava flakes are not oven-fried but instead sun-dried. Ultimately, each is boiled in water for consumption by man. Each cassava meal taken contained about 0.7 MJ as energy in cassava. The composition of the vegetable-and-meat sauce used (0.52 MJ) is also indicated in Table 1.

Protocol

Blood samples were taken at cannula insertion (−15 min), at commencement of eating (0 min) and subsequently at 30, 60, 90, 120, 180 and 240 min after starting to eat each meal. Blood was collected from an antecubital vein kept patent by regular flushing with small volumes of sterile (150 mmol/l saline). The fasting concentration was taken as the mean of the −15 and 0 min values. Each study lasted 4 h. Blood was always collected into heparinized tubes (5 ml for plasma SCN) and fluoride oxalate tubes (2 ml for plasma glucose) which were centifuged immediately. Plasma was stored frozen −20°C before estimation within 3 months of specimen collection.

Biochemical estimations

Plasma glucose was measured by a glucose oxidase method using 4-aminophenazone as oxygen acceptor (Trinder, 1969) and plasma thiocyanate was estimated by the ferric nitrate colorimetric method (Bowler, 1944). The latter method gave an intra-assay coefficient of variation (CV) of 2.5 per cent and an inter-assay CV of 5.6 per cent from pooled plasma samples. The recovery of 0.1 mmol/l sodium thiocyanate added to plasma was 104 per cent. The range of fasting plasma SCN levels obtained in our subjects was 0.040–0.180 mmol/l ($n = 44$), which is similar to values reported in healthy control subjects in Nigeria (Osuntokun, 1969) and the West Indies (Bennett *et al.*, 1987).

Statistics

The results are expressed as means ± s.d. The total areas under the 4-h glucose/time curves were calculated by the trapezoidal rule. The differences between glucose concentrations at the same time points, areas under the glucose/time curves for the different meals, fasting and peak as well as increase (from fasting to peak) in plasma SCN levels for the different meals were sought by paired Student's *t*-tests and ANOVA as appropriate. The level of statistical significance was $P < 0.05$.

Results

All our subjects were young adult male Nigerians and none was obese. All had normal plasma albumin levels (38.0 ± 6.0 g/l). The plasma glucose concentrations and areas (total and incremental) under the glucose/time curves over 4 h are indicated on Table 2. The fasting plasma glucose levels were different, but this is probably due only to random variation. The peak plasma glucose levels (usually at 30 min) were lower and the 2 h plasma glucose levels were significantly lower with the three cassava meals than with isoenergetic oral glucose ($P < 0.05$). Of the three cassava meals, those two values (for peak and 2 h plasma glucose) tended to be lowest with

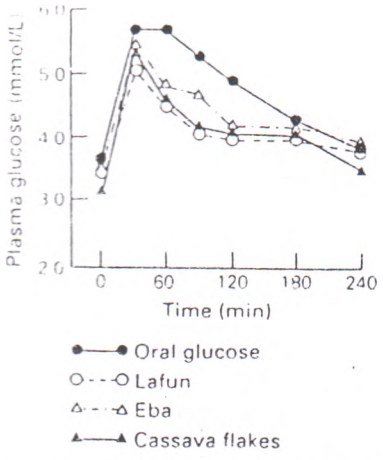

Figure 1. *Mean plasma glucose concentrations during the four different meals in the eleven subjects.*

2), and the three cassava meals had values much lower than for oral glucose.

The fasting and peak post-prandial plasma SCN concentrations for the different meals are also shown on Table 2. Only with *lafun* (23 per cent) and cassava flakes (14 per cent) were there significant differences ($P < 0.05$) between peak and fasting SCN levels. The changes seen with oral glucose (as expected) and *eba* were not statistically significant. Also the mean increase to peak in SCN values appeared highest with *lafun*, although this was different only from values obtained with *eba* ($P < 0.05$) and oral glucose ($P < 0.06$) (Table 2), probably because of the wide scatter of individual responses and the relatively small number of subjects studied. This pattern was also obtained when the fasting SCN levels on the four occasions (that the subjects were studied) were averaged and used as baseline (to correct for intra-individual variability) in computing the differences from peak values (data not indicated on the table). The peak values were attained by 60-90 min after ingestion of each meal.

Discussion

The cornerstone in the management of diabetes is the diet which should aim at ensuring normoglycaemia and maintaining ideal body weight (WHO Expert Committee, 1985). Probably the simplest approach to achieving this aim is to emphasize foods with a low glycaemic index (Jenkins *et al.*, 1984). The diets proposed by the British and Canadian Diabetes Associations emphasize low fat (about 20 per cent) and high carbohydrate (about 60 per cent) intake with the latter containing about 90 per cent complex carbohydrates, especially dietary fibre (Mann, 1984). These recommendations were made for Caucasians, and even now are the subject of considerable controversy (Garg *et al.*, 1988; Reaven, 1988). Although the typical African diet easily meets the recommended prescription on percentage dietary composition (Republic of Nigeria Nutrition Survey, 1968), the problem of the diabetes practitioner in African countries is in translating these dietary requirements into the readily available foodstuffs, and at the same time ensuring compliance to the almost invariably unpalatable or expensive meals. This problem is further compounded by the fact that the typical West African diet derives about 70 per cent of total daily energy from cassava (Teuscher *et al.*, 1987), which although a good source of dietary fibre (about 0.5 per cent dry matter) (10), may contribute to the development of MRDM (Vannasaeng *et al.*, 1982; Bajaj, 1985; WHO Expert Committee, 1985).

Our study therefore investigated different cassava meals consumed in Nigeria in relation to post-prandial glycaemia and changes in blood SCN levels. The results obtained indicated that the post-prandial glucose levels were always lower with the cassava meals compared to isoenergetic amounts of oral glucose. The least glycaemia was observed with *lafun*.

There are differences in the cyanide content of the various cassava meals due to the variation in the method by which the derivatives are processed from cassava (Oyenuga & Amizigo, 1957; Tewe, 1975). This fact is indicated by the respective values for the cyanide content of *gari*, *lafun* and cassava flakes (Tewe, 1975). Our results show that plasma SCN levels increased with *lafun* and cassava flakes, which, in the unprepared form, contain the greatest amount of cyanide. The rise in blood SCN therefore appeared to reflect the cyanide content of the cassava derivative. It is

of interest that *lafun* and cassava flakes with the greatest cyanide content of the cassava meals have no applied heat treatment during preparation. One could thus speculate that it is the heat treatment (other than sun-drying) *per se* that contributes to the reduced cyanogenicity of various cassava products (this was particularly obvious with *eba*).

The differing values of post-meal SCN concentrations could not have directly been from the cassava itself (since cassava contains only about 0.34–0.70 mmol SCN/100 g) (Osuntokun & Monekosso, 1969), nor from the vegetable in the sauce used, as only the *Brassica spp* of vegetables such as cabbage have a high SCN content (Osuntokun, 1969) and these were not used in this study. Moreover, the same sauce was used for the three cassava meals.

This study should be considered preliminary. It is essential to assess plasma insulin changes in response to the different cassava preparations for a better understanding of the basis of the glycaemic responses. Also, effects may be modified by chronic cassava feeding during which tolerance may have developed, although the subjects studied here consumed cassava daily as part of their regular diets. Additionally, efforts are currently underway to repeat the studies in different groups of diabetic subjects with varying glycaemic control to assess whether the patterns in glycaemic responses to cassava meals might be different from the pattern established here in the non-diabetic subjects.

This is of particular interest as Nigerian diabetic patients are routinely advised to avoid meals prepared from cassava. Such meals are believed to cause prolonged hyperglycaemia and worsen glycaemic control. Compliance to this dietary advice has always been poor because cassava is the main staple, being relatively cheap and available. Our results, albeit in non-diabetic subjects (and we presently have little reason to suspect that the trend might be different in the diabetics), suggest that cassava could be introduced into the diabetic diet as long as it is in a *lafun* form and in the context of a high-carbohydrate and low-fat diet.

We conclude that: (i) glycaemic responses and post-prandial changes in plasma SCN levels after cassava meals depend on the mode of preparation of the cassava meals; (ii) *lafun* caused the lowest glycaemic response of three popular cassava meals studied and could cautiously be added to the diabetic diet, and (iii) *lafun* caused the greatest increase in plasma SCN levels and also the lowest post-prandial glycaemia suggesting that a cyanogenetic potential does not necessarily correlate with a tendency to hyperglycaemia, contrary to the described theories on the genesis of MRDM.

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