Original article

Dietary cassava, \(\beta\)-cell function and hyperbolic product loss rate in type 2 diabetes patients from South Kivu

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Abstract

Objective. – Cassava, a major carbohydrate source in Africa, contains potentially diabetogenic chemicals, although its consumption is not associated with incident diabetes. As it is not known whether cassava intake impairs residual \(\beta\)-cell function in patients with type 2 diabetes (T2D), our study compared the metabolic phenotypes of diet- and/or oral antidiabetic drug (OAD)-treated T2D patients in South Kivu (Democratic Republic of the Congo) with \([\text{Cassava (+)}; n = 147]\) and without \([\text{Cassava (–)}; n = 46]\) self-reported cassava consumption.

Design & methods. – A total of 193 patients [male:female (%) 37:63; mean \(\pm\) 1 SD age: 56 \(\pm\) 11 years] were interviewed to determine the frequency and distribution of eight major dietary carbohydrate (CHO) sources (cassava, plantain, rice, maize, bread, sorghum, potatoes and legumes). Fasting glucose, insulin and lipid levels were obtained after an overnight fast and OAD discontinuation. Cassava (+) and Cassava (–) groups were compared for HOMA indices of insulin sensitivity (S), beta-cell function (B), hyperbolic product (B \(\times\) S) and B \(\times\) S loss rate (B \(\times\) S LR).

Results. – Diabetes duration was 6 \(\pm\) 7 years, age at diabetes diagnosis was 51 \(\pm\) 11 years and BMI was 25 \(\pm\) 5 kg/m\(^2\). Cassava intake was reported by 76% of patients, and amounted to 29 \(\pm\) 11% of their daily CHO intake. The Cassava (–) group ate more plantain, maize, bread and potatoes, and less sorghum. Age, gender and age at diabetes diagnosis did not differ between Cassava (+) and (–) patients, nor did BMI, fat mass, waist circumference, lipid profile and metabolic syndrome prevalence. HOMA indices of S, B, B \(\times\) S and B \(\times\) S LR did not differ significantly between groups – Cassava (+) vs (–): S, 114 \(\pm\) 56% vs 114 \(\pm\) 60%; B, 34 \(\pm\) 30% vs 39 \(\pm\) 32%; B \(\times\) S, 38 \(\pm\) 35% vs 40 \(\pm\) 31%; and B \(\times\) S LR, 1.19 \(\pm\) 0.84% vs 1.09 \(\pm\) 0.65% per year–nor did the glucose-lowering modalities.

Conclusion. – Cassava consumption in South Kivu is not associated with changes in T2D phenotype or in the glucose homoeostasis determinants S, B, B \(\times\) S and B \(\times\) S LR. Cassava consumption does not accelerate \(\beta\)-cell function loss in such a population, whose markedly compromised glucose homoeostasis renders them vulnerable to environmentally acquired \(\beta\)-cell impairment.

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Keywords: Cassava; \(\beta\)-cell function; Type 2 diabetes; Sub-Saharan Africa

Résumé

Consommation de manioc, fonction sécrétoire \(\beta\) et perte du produit hyperbolique chez des patients diabétiques de type 2 du Sud-Kivu.

Introduction. – Le manioc, source majeure de glucides en Afrique noire, contient des composés chimiques potentiellement diabétogènes, bien qu’un rapport entre consommation de manioc et incidence du diabète n’ait pas ét été formellement démontré. Il n’y a pas de données sur la consommation de manioc en tant que toxique environnemental susceptible d’altérer la fonction sécrétoire \(\beta\) résiduelle dans le diabète de type 2, ou d’accélérer le taux de perte de celle-ci.

Objectifs. – Comparer des diabétiques de type 2 vivant au Sud-Kivu (RDC) traités par régime seul ou antidiabétiques oraux (ADO), selon la consommation anamnestique de manioc comme source de glucides (manioc (+) : \(n = 147\); non consommateurs de manioc (manioc (–) : \(n = 46\)).

Sujets étudiés et méthodes. – Cent quatre-vingt-treize patients (M:F (%) 37:63; âges de 56 \(\pm\) 11 ans (m \(\pm\) DS) ont été soumis à un questionnaire de fréquence de consommation et de distribution de huit sources régionales majeures de glucides (manioc, plantain, riz, maïs, pain, sorgho, pommes

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de terre et légumineuses). La glycémie, l’insulinémie et les composants lipidiques du sérum ont été dosés à jeun après interruption des ADO. Le modèle informatisé HOMA a été utilisé pour comparer les sujets manioc (+) et manioc (–) en termes de sensibilité à l’insuline (S), de fonction β (B), de produit hyperbolique [B × S], et de taux de perte progressive de B × S [TP B × S].

Résultats. – La durée connue du diabète était de 6 ± 7 ans, l’âge au diagnostic de 51 ± 11 ans, et l’indice de masse corporelle (IMC) de 25 ± 5 kg/m². La consommation de manioc était rapportée par 76 % des sujets, et évaluée à 29 ± 11 % des apports journaliers en glucides. Les sujets manioc (–) avaient une consommation accrue en plantain, mais, pain, pommes de terre, et moindre en sorgho. Il n’y avait pas de différences significatives entre sujets manioc (+) et (–) concernant l’âge, le sexe, l’âge au diagnostic de diabète, l’IMC, la masse grasse, le périmètre abdominal, les composants lipidiques du sérum et la prévalence du syndrome métabolique. Les modalités thérapeutiques du traitement antidiabétique ne différaient pas entre les deux groupes. Les indices HOMA-dérivés (S, B, [B × S] et [TP B × S] n’étaient pas significativement différents entre les groupes manioc (+) et (–) : S : 114 ± 56 vs. 114 ± 60 %; B : 34 ± 30 vs. 39 ± 32 %; [B × S] : 38 ± 35 vs. 40 ± 31 %, et [TP B × S] : 1,19 ± 0,84 vs. 1,09 ± 0,65 %/an.

Conclusions. – La consommation de manioc dans cette population du Sud-Kivu n’est pas associée à une altération supplémentaire des déterminants de l’homéostasie glucidique du diabète de type 2. Elle n’est pas associée à une accélération de la perte progressive de fonction β au sein de cette population avec homéostasie glucidique compromise et vulnérable à des facteurs environnementaux diabétogènes.

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Mots clés : Manioc ; Fonction sécrétoire β ; Diabète de type 2 ; Afrique sub-saharienne

1. Introduction

Type 2 diabetes (T2D) is characterized by progressive and unrelenting β-cell function loss in both patients treated solely with lifestyle changes and those receiving glucose-lowering pharmacotherapy. The pace and extent of β-cell function loss largely determine the progressive requirements for multiple glucose-lowering therapies, including exogenous insulin. With the more common form of T2D, numerous studies have previously demonstrated that, subsequent to diabetes diagnosis and regardless of the degree of insulin resistance, β-cell function loss is poorly modifiable and linear over time, although the steepness of the slope varies across patients, genders and ethnogeographical groups. Such variations in steepness are most likely determined by both genetic and environmental (intrauterine and postnatal) factors, including dietary ones [1–5].

Cassava (Manihot esculenta), an important source of starch in Sub-Saharan Africa, contains various amounts of cyanogenic glucosides that can be converted by linamarase to cyanide, a controversial causal factor in tropical diabetes. Although cassava contains potentially diabetogenic chemicals, it is not clear whether or not its chronic consumption is associated with incident T2D. In a rodent model, a cassava-enriched diet, while not diabeticogenic, worsened the severity of diabetes [6]. It is not known, however, whether or not cassava intake can impair residual β-cell function in patients already diagnosed with T2D. A seasonal, non-progressive, spastic paraparesis — known locally as ’konzo’ — has been found to be causally related to insufficient soaking of these bitter roots as part of its dietary processing. Also, a relationship between cassava marketing, processing and dietary cyanide risk showed that acceleration of its marketing combined with defective processing methods can result in preferential dietary cyanide exposure in rural sellers compared with urban buyers [7–10].

For this reason, the aim of the present study was to compare diet- and/or oral antidiabetic drug (OAD)-treated T2D patients in three localities in South Kivu (rural, semi-rural and urban) with [Cassava (+)] and without [Cassava (–)] self-reported cassava consumption as a dietary staple or co-staple. The cassava (+) and (–) groups were compared according to computer-based homoeostatic model assessment (HOMA) indices of insulin sensitivity (HOMA-S), beta-cell function (HOMA-B), hyperbolic product (B × S) and B × S loss rate (B × S LR).

2. Patients and methods

The present study design was cross-sectional and included 193 consecutive adult outpatients (> 18 years) with T2D, defined according to the Expert Committee on the Diagnosis and Classification of Diabetes [11], and not treated with insulin. Gender distribution (male-to-female, M:F) was 37:63% and the mean ± 1 SD age was 62 ± 11 years. Known diabetes duration was 12 ± 7 years, with an age at diabetes diagnosis of 51 ± 11 years. Mean body mass index (BMI) was 25 ± 5 kg/m². All patients were assessed for sources and distribution of carbohydrate (CHO) intake, using a semi-quantitative questionnaire that included the major regional dietary CHO sources (cassava, plantain, rice, maize, bread, sorghum, potatoes and legumes). The two groups were analyzed in parallel as cassava non-consumers [Cassava (–); n = 46] and consumers [Cassava (+); n = 147].

The following sociodemographic and clinical variables were also recorded: achieved educational level (’low’ vs ‘high’, defined as no, or primary or secondary, education vs higher education and university, respectively); positive family history of diabetes; current OAD use; waist circumference; and total body fat (electrical bioimpedancemetry, Body Fat Analyzer, Omron BF 300). Hypertension prevalence was defined by a blood pressure (BP) ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic, and/or current treatment with BP-lowering drug(s) prescribed for high BP.

In addition, the following biological variables were recorded in the fasting state: glucose; specific insulin; and serum lipids (total cholesterol (C), high-density lipoprotein cholesterol (HDL-C); triglycerides; low-density lipoprotein cholesterol (LDL-C), calculated using Friedewald’s formula, non-HDL-C by subtracting HDL-C from total C; and microalbuminuria (urinary albumin concentration > 20 mg/L and < 200 mg/L, or
2.1. Statistical analysis

Results are presented as means ± 1 SD. The significance of differences between means was assessed by Student’s t test or, alternatively, by Welch’s test for datasets with non-Gaussian distribution, and by Fisher’s exact test for differences in proportions. Results were considered significant or non-significant (NS) for values of P < 0.05 or ≥ 0.05, respectively.

3. Results

There were 46 patients in the Cassava (−) group and 147 in the Cassava (+) group. Glucose-lowering therapies included diet and lifestyle as the sole therapy (9%), phyto- and ethnobotany (3%), metformin (18%) and/or sulphonylurea (82%). All patients taking sulphonylurea were treated with glibenclamide, the only β-cell stimulant locally affordable and/or available. OAD as monotherapy was taken by 70%, and a combined sulphonylurea–metformin regimen by 15%. No patients were treated with glitazones or glinides.

The anamnestic frequencies of dietary CHO sources in the two groups (Fig. 1) reveal significant differences between groups in bread, sorghum and potato consumption. The major CHO source in Cassava (−) patients was plantain (31%), followed by sorghum (19%). Cassava represented 29% of acknowledged CHO intake in Cassava (+) patients, followed by sorghum (24%) (Table 1).

The study patients’ characteristics (Table 2) show no significant differences in age, diabetes family history, age at diabetes diagnosis and (known) diabetes duration [10 ± 6 years in Cassava (−) vs 11 ± 8 years in Cassava (+)], socioeducational levels, smoking history and habitual ethanol intake. Metformin and sulphonylurea were taken by 15 and 83%, respectively, of Cassava (−) patients, and by 18 and 82%, respectively, of Cassava (+) patients (NS). Also, 76% and 11% in the Cassava (−) group were using OADs as monotherapy or in combination, respec-

![Fig. 1. Anamnestic carbohydrate source frequencies in non-cassava-consuming (n = 46; white bars) compared with cassava-consuming (n = 147; black bars) type 2 diabetes patients. P = 0.0165 (bread), P = 0.0001 (sorghum) and P = 0.0162 (potatoes) for between-group differences.](image)

![Table 1. Carbohydrate sources and distribution.](image)

<table>
<thead>
<tr>
<th>CHO Source</th>
<th>Cassava (−)</th>
<th>Cassava (+)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassava (%)</td>
<td>~ 29 (11)</td>
<td>~ 29 (11)</td>
<td>~</td>
</tr>
<tr>
<td>Plantain (%)</td>
<td>31 (27)</td>
<td>18 (13)</td>
<td>0.0027</td>
</tr>
<tr>
<td>Rice (%)</td>
<td>10 (14)</td>
<td>8 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Maize (%)</td>
<td>14 (21)</td>
<td>8 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Bread (%)</td>
<td>14 (17)</td>
<td>6 (10)</td>
<td>0.0037</td>
</tr>
<tr>
<td>Sorghum (%)</td>
<td>19 (21)</td>
<td>24 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Potatoes (%)</td>
<td>8 (16)</td>
<td>2 (6)</td>
<td>0.0162</td>
</tr>
<tr>
<td>Legumes (%)</td>
<td>4 (11)</td>
<td>4 (9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results are expressed as means (1 SD). Differences between means were assessed by z or t test for unmatched samples, and considered statistically significant at P values < 0.05. Cassava (+) and (−) denote patients with or without anamnestic cassava consumption.

![Table 2. Patients’ characteristics.](image)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cassava (−)</th>
<th>Cassava (+)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64 (11)</td>
<td>62 (11)</td>
<td>NS</td>
</tr>
<tr>
<td>Age at diabetes diagnosis (years)</td>
<td>53 (11)</td>
<td>50 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex ratio (M:F) (%)</td>
<td>46:54</td>
<td>35:65</td>
<td>NS</td>
</tr>
<tr>
<td>Education (%)</td>
<td>65:35</td>
<td>79:21</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking*</td>
<td>96:4</td>
<td>97:3</td>
<td>NS</td>
</tr>
<tr>
<td>Ethanol (U week−1)</td>
<td>11 (34)</td>
<td>9 (23)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg m−2)</td>
<td>25 (6)</td>
<td>25 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>90 (13)</td>
<td>88 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Fat mass (relative) (%)</td>
<td>32 (7)</td>
<td>33 (8)</td>
<td>NS</td>
</tr>
<tr>
<td>Fat mass (absolute) (kg)</td>
<td>21 (9)</td>
<td>21 (9)</td>
<td>NS</td>
</tr>
<tr>
<td>Metabolic syndrome (%)</td>
<td>60</td>
<td>68</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>64</td>
<td>69</td>
<td>NS</td>
</tr>
<tr>
<td>eGFR (ml min−1 1.73 m2)</td>
<td>77 (32)</td>
<td>78 (28)</td>
<td>NS</td>
</tr>
<tr>
<td>Microalbuminuria (%)</td>
<td>59</td>
<td>47</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results are expressed as means (1 SD) or proportions (%). Differences between means were assessed by z or t test for unmatched samples, and between proportions by Fisher’s exact test. Differences were considered statistically significant at P values < 0.05. *: never vs. former/current smokers; §: lower- vs. higher education levels; BMP: body mass (Quetelet’s) index; BP: blood pressure; eGFR: estimated glomerular filtration rate; M:F: male: female; NS: non-significant.
are not significant.

± vs 114

B, %), hyperbolic product (B × S) and hyperbolic product lifetime loss rate (B × S LR, %/year) in non-cassava-consuming (n = 46; white bars) compared with cassava-consuming (n = 147; black bars) type 2 diabetes patients. The B × S loss rate values were multiplied by 50 for clarity. All between-group differences are not significant.

Fasting plasma glucose obtained by HOMA after OAD discontinuation was 10.0 ± 4.9 mmol L⁻¹ vs 10.7 ± 5.6 mmol L⁻¹ in Cassava (–) and Cassava (+) patients, respectively (NS). Insulin sensitivity (HOMA-S) was 114 ± 60% in Cassava (–) vs 114 ± 56% in Cassava (+) (NS). Unadjusted β-cell function (HOMA-B) was 39 ± 32% in Cassava (–) vs 34 ± 30% in Cassava (+) (NS). The HOMA hyperbolic product B × S was 40 ± 31% in Cassava (–) vs 38 ± 35% in Cassava (+) (NS), and B × S LR was 1.09 ± 0.65% per year in Cassava (–) vs 1.19 ± 0.84% per year in Cassava (+) (NS; Fig. 2). We observed no relevant or significant differences in any glucose homeostasis indices across the patient subgroups from the three localities studied.

Hypertension prevalence was 64% in Cassava (–) vs 69% in Cassava (+) (P = 0.5328). Current systolic and diastolic BP levels were 142–87 ± 26–12 mmHg in Cassava (–) vs 143–89 ± 27–15 mmHg in Cassava (+) (NS). The proportion of patients achieving BP targets (< 130 mmHg systolic and < 80 mmHg diastolic) with or without BP-lowering drugs reached 30% in Cassava (–) vs 29% in Cassava (+) (NS). The eGFR was 77 ± 32 mL/min per 1.73 m² in Cassava (–) vs 78 ± 28 mL/min per 1.73 m² in Cassava (+) (NS). Microalbuminuria was 40 ± 34 mg/dL in Cassava (–) vs 33 ± 29 mg/dL in Cassava (+) (NS).

Serum total C was 166 ± 51 mg/dL in Cassava (–) vs 176 ± 44 mg/dL in Cassava (+) (NS). LDL-C was 106 ± 43 mg/dL in Cassava (–) vs 110 ± 36 mg/dL in Cassava (+) (NS), while HDL-C was 39 ± 13 mg/dL in Cassava (–) vs 43 ± 13 mg/dL in Cassava (+) (NS). Triglycerides (TG) were 120 ± 105 mg/dL in Cassava (–) vs 114 ± 54 mg/dL in Cassava (+) (NS). Non-HDL-C was 127 ± 44 mg/dL in Cassava (–) vs 132 ± 38 mg/dL in Cassava (+) (NS), and total C/HDL-C was 4.58 ± 1.83 mg/dL in Cassava (–) vs 4.26 ± 1.12 mg/dL in Cassava (+) (NS).

4. Discussion

This is the first study to address the influence of dietary cassava as part of the staple diet on β-cell function indices in T2D patients in South Kivu (RDC). To the best of our knowledge, there are no published data on such interactions between models of insulin secretion or β-cell function loss rate and dietary cassava as a potential amplifying factor in the natural history of T2D. Although dietary cassava does not appear to be associated with incident T2D, a possible detrimental effect on residual β-cell secretion cannot be excluded in those with compromised insulin secretion as a result of established T2D [7–10].

The mathematical analyses of the relationship between insulin secretion and insulin sensitivity show a hyperbolic function to the extent that the product of the two variables is a constant (also known as the ‘disposition index’). Thus, measurement of β-cell function and insulin sensitivity can only be interpreted properly when both results are available. As our group and others have previously reported, the hyperbolic product $B \times S$ represents the true underlying β-cell function adjusted for an individual’s insulin sensitivity, and supports the requirement for successive glucose-lowering therapies in patients with diabetes [17–27], including those in Sub-Saharan Africa [28].

HOMA was designed to assess both insulin sensitivity and β-cell function, and both variables have been independently validated by reference tests. A HOMA-based approach is advantageous over other methods, which provide only one such measure, and is a simple, low-cost and noninvasive way to obtain the disposition index $B \times S$ in states of abnormal glucose homeostasis, including T2D. Determining $B \times S$ also allows derivation of an estimate of lifetime β-cell loss rate by standardizing the $B \times S$ deficit to age at the time of assessment [24]. Using such an approach, we observed that the $B \times S$ LR did not differ between consumers and non-consumers of cassava, which rules out any long-term detrimental effect of this CHO source on residual β-cell function in adults with T2D. This observation is also of practical economic significance, as cassava is a cheap staple with a low glycaemic index that can be cultivated on nutrient-poor soils, making it widely available to many low-income populations in (sub)tropical regions [29–32]. Other potential biases within cassava consumers are between-subject variability in starch-processing and the influence of different cultivars on the contents of potential diabetogenic compounds.

There were significant differences between groups in bread, sorghum and potato consumption. These alternative CHO sources in cassava non-consumers are often more expensive, suggesting a relatively greater affluence in this group. We could find no differences in education levels between groups, although...
the present survey did not specifically address socioeconomic status. As a whole, the patients’ characteristics between groups were remarkably similar, including demographics and anthropometric indices, and this similarity between groups may somehow underlie the lack of differences in insulin sensitivity, lipid values and albuminuria.

The present study also has the usual limitations of a cross-sectional study design, including an inability to establish directionality for the observed associations. Another study limitation is the absence of HbA1c measurement, which precludes the assessment of either a beneficial or detrimental effect of any specific CHO source and intake (including cassava) on post-prandial glycaemic excursions and overall diabetes control. The glycaemic index score and load of processed cassava starch was reported to be 46 and 65, respectively, vs glucose and bread (with scores of 100) [31]. Our study groups also did not differ in fasting plasma glucose (both were around 10.0 mmol L\(^{-1}\)) on the HOMA day. Such a measure, given that most patients were taking an OAD as monotherapy, suggests that had HbA1c been measured, many patients would most likely have been considered poorly controlled.

In conclusion, cassava consumption in T2D patients in South Kivu is not associated with any changes in diabetic phenotype or in glucose homeostasis determinants, as assessed by HOMA-S, HOMA-B, B × S and B × S LR. Cassava consumption does not accelerate β-cell function loss in this population, despite their markedly compromised glucose homeostasis and, as a result, their high vulnerability to environmentally acquired β-cell impairment. This absence of any detrimental effect of cassava consumption may be the result of either (i) a lack of significant amounts of cyanide-(un)related diabetogenic compounds in the regional cassava cultivars or (ii) appropriate food processing, or (iii) both of these factors.

Conflict of interest

The authors do not report any conflict of interests.

References


