Original article

Five-year predictive factors of type 2 diabetes in men with impaired fasting glucose


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Abstract

Aim. – The outcome of 743 French men (age 20–60) with impaired fasting glucose (IFG) [blood glucose 6.1–6.9 mmol/l] at T1 was evaluated 5 years later, at T2.

Methods. – Personal and family medical history, smoking, nutritional habits, physical activity, blood pressure, body mass index (BMI) and waist girth, fasting biological data were collected at T1 and T2. Predictive factors for developing diabetes were compared between those who returned to normal fasting glucose and those who had diabetes, before and after adjustment for age, BMI, glucose and triglyceride (TG) levels.

Results. – At T2, 44%, 39%, 17% were classified as normal fasting plasma glucose (FPG), IFG or diabetic, respectively. Odd ratios for diabetes were 4.2 for men with a family history of diabetes (FHD), 3.4 if BMI $\geq$ 25 kg/m$^2$, 2.9 if waist girth $\geq$ 90 cm, 2.8 if TG $\geq$ 2 mmol/l and 1.9 if no daily dairy products were eaten. Still significant after adjustment for age, BMI, glucose and TG levels were: FHD ($P = 0.001$), no daily dairy products ($P = 0.001$), high alcohol intake ($P = 0.02$) and low physical activity ($P = 0.02$).

Conclusion. – No daily dairy products, high alcohol intake and low physical activity were independent predictive factors of a 5-year onset of diabetes after adjusting for BMI, FHD, triglyceride and glucose levels at baseline. For a better prevention of diabetes, these findings give clues for behaviour modifications as soon as IFG is detected.

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Résumé

Facteurs prédictifs de la conversion de l’hyperglycémie modérée à jeun en diabète de type 2, avec un suivi de cinq ans.

Objectif. – Les facteurs de risque de développer un diabète chez 743 hommes d’âge moyen (20 à 60 ans) présentant une hyperglycémie modérée à jeun (HMJ : glycémie [6,1–6,9 mmol/l]) à T1 ont été étudiés cinq ans plus tard, à T2.

Méthodes. – Les antécédents familiaux (AF) et personnels, le mode de vie (tabagisme, habitudes alimentaires, activité physique), les données biométriques (indice de masse corporelle (IMC), tour de taille, pression artérielle) ainsi que les données biologiques à jeun ont été recueillies à T1 et T2. Les données des sujets dont la glycémie a été normalisée et celles des sujets qui ont évolué vers le diabète ont été comparées. Les facteurs prédictifs de devenir diabétique ont été comparés à ceux des sujets redevenus normoglycémiques avant et après ajustement sur l’âge, l’IMC, la glycémie et les triglycérides (TG).

Résultats. – À T2, 44 % étaient revenus en normoglycémie, 39 % restaient HMJ et 17 % étaient devenus diabétiques. Les odd-ratios étaient respectivement : AF de diabète (4,2), surpoids (3,4), tour de taille (2,9), TG $\geq$ 2 mmol/l (2,8) et absence de consommation de laitages (1,9). Après ajustement sur âge, IMC, glycémie, TG, les variables suivantes restaient significativement différentes : AF de diabète ($P = 0,001$), absence de consommation de laitages ($P = 0,001$), consommation élevée d’alcool ($P = 0,02$), et activité physique faible ($P = 0,02$).

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Conclusion. – Après ajustement sur âge, IMC, valeurs de glycéémie et de triglycérides à jeun, les antécédents familiaux de diabète, la forte consommation d’alcool, la faible consommation de produits laitiers, le faible niveau d’activité physique sont les principaux facteurs prédictifs d’une évolution de l’hyperglycémie modérée vers le diabète. Ces résultats donnent une orientation sur les comportements à modifier pour prévenir le diabète chez les sujets qui présentent une hyperglycémie modérée à jeun.

Keywords: Impaired fasting glucose; Type 2 diabetes; Men; Longitudinal study; Epidemiology

Mots clés : Hyperglycémie modérée à jeun ; Diabète de type 2 ; Hommes ; Étude longitudinale ; Épidémiologie

1. Introduction

Impaired fasting glucose (IFG) was defined in 1997 as fasting plasma glucose (FPG) levels ranging from 6.1 to 6.9 mmol/l [1]. We have previously reported the prevalence of IFG (9.5%) in a group of 28,663 French men diagnosed with a single fasting blood glucose value and we have described their cardiovascular and behavioural risk factors [2]. The prevalence of IFG in different male populations aged 40–59 is highly variable (from 7.5% in the Chinese and Japanese [3] to 16% in Mexican-Americans [4]). The prevalence of IFG increases with age, as shown for example in Bangladesh (from 10% to 13%) [5]. Important variations have also been observed in Europe (6.0–13.1% according to age in the DECODE Study analysing data from 13 European cohorts in nine countries [6]). Prevalence of 25.2% [7] and 27.1% [8] has been reported in high-risk populations of both sexes in Spain and Germany, respectively. In France, the MONICA Study [9] gave figures for three different towns with an IFG percentage of 11.8% in men aged 35–64 (8.3% in North of France, 10.1% in East and 16.8% in South).

The outcome of subjects with impaired glucose tolerance (IGT), i.e. 2-hour glucose during oral tolerance test (OGTT): 7.8–11.0 mmol/l, has been more extensively studied. The performance of IGT to predict type 2 diabetes at 5 years is 33% in a North American population [10] and 39% in six prospective studies analysing very different ethnic populations of various ages such as Pima, Nauruan, Hispanic, Mexican-American and Caucasian populations with a mean follow-up of 7 years [11]. One workshop reported comparisons between IFG and IGT: only half the people or fewer with IFG have IGT, while a lower proportion (20–30%) of subjects with IGT also have IFG [12]. IFG depends primarily on early defective insulin secretion and IGT on insulin resistance [13] but contradictory results have also been claimed, with a major role of insulin secretion deficiency in IGT [14]. It has been demonstrated in some studies (but never in France) that the sensitivity of IFG to predict diabetes was lower than IGT in most populations [12, 15–17]. A recent study involving Chinese subjects with diabetic risk factors (history of gestational diabetes or family history of diabetes [FHD]) showed that IFG status is an independent factor for progression to diabetes [18]. Therefore, as the FPG measure is easier to perform than OGTT in large scale populations, more information is necessary to define the predictive value of IFG for diabetes in order to better design prevention programs.

In this study, we reassessed 5 years later male subjects with IFG. Our goals were: (i) To evaluate the percentage of subjects who became diabetics within 5 years. (ii) To identify the predictive factors in IFG subjects leading to diabetes versus normalisation of fasting glucose.

2. Subjects and methods

2.1. Population

We studied the 5-year outcome of IFG subjects recruited from medical check-ups provided by the French social security system in the nine preventive health centres of IRSA. This health care exam is covered by the French social security every 5 years. So each subject affiliated to the National Health System can volunteer to benefit from this exam. Subjects were classified as IFG if they had FPG level of 6.1–6.9 mmol/l, no personal history of diabetes and no hypoglycaemic drug treatment. During the period 1995–1997 (T1), 4532 out of 56,650 men were classified as IFG (8%). We compared the 743 subjects who had a second check-up within 5 years ± 6 months (T2) to those who had not (N = 3789). Then we studied the T1 biological, clinical and behavioural data of the 743 IFG men according to their glycaemia status at T2: FPG < 6.1 mmol/l (N = 324), IFG (N = 292) or FPG > 6.9 mmol/l (N = 127).

2.2. Data collection

All subjects were interviewed at both examinations by a trained nurse who collected information about current treatments and smoking habits. She evaluated daily physical activity in three classes (low, medium, high) on the basis of information given by subjects on duration and regularity of daily physical activity at home, at work and during leisure time; she also noted down if no sports activity was practiced. Current smokers included all active chronic cigarette or cigar smokers, without quantitative detail. Weight and height were measured on bare-foot, lightly clad subjects, and the body mass index (BMI) was calculated.

Nutritional profile was assessed by a previously validated self-administered 18-item questionnaire [19] which asked about quantity and frequency of usual intake of meat, fish, eggs, delicatessen meats, fried food, butter, cheese, dairy products (yoghurt, cottage cheese, ice-cream, cream, milk), bread, sweet desserts, sugar, sweetened beverages and water. Alcohol...
consumption was estimated by three questions concerning daily intake of wine, beer and cider, in six classes (nothing, < 0.5, < 1, < 2, < 3, ≥ 3 l), and weekly intake of cocktails/spirits in number of glasses. Alcohol intake was estimated high if more than 0.5 l wine/beer/cider a day or more than 3 cocktails/spirits a week were consumed. Low or moderate alcohol consumption was assessed if less or equal to 0.5 l wine/beer a day and less than 4 cocktails/spirits a week were declared.

A physician asked subjects about their family and personal medical history. He measured waist girth (smallest horizontal circumference between costal margin and iliac crests) and systolic and diastolic blood pressure in subjects who had been lying down for at least 5 min.

3. Biological tests

Venous blood samples were taken after overnight fasting. FPG was assayed by the glucose-oxidase method on a fluorooxalated plasma sample on a RA1000 (Bayer Diagnostics, Puteaux, France) with an intra-assay variation coefficient of 1.7%. Classification of subjects at both T1 and T2 was established on a single fasting blood glucose measurement.

Normal FPG was defined as FPG < 6.1 mmol/l, with no personal history of diabetes and no hypoglycaemic treatment.

IFG was defined as FPG 6.1–6.9 mmol/l, with no personal history of diabetes and no hypoglycaemic treatment.

Diabetes mellitus was defined as FPG ≥ 7 mmol/l or hyperglycaemic treatment or personal history of diabetes.

Serum cholesterol, triglyceride, gamma-glutamyl transferase (GGT) and blood creatinine levels were measured on a DAX 24 (Bayer Diagnostics, Puteaux). Creatinine clearance (ml/mn) was calculated using the Cockroft-Gault formula: 1.23 × (140-age) × weight (kg)/blood creatinine (μmol/l) and then adjusted to an average body surface of 1.73 m², divided by the body surface area of the subject calculated using the Dubois formula (surface area (m²) = weight (kg)⁰.⁴²⁵ × height (cm)⁰.⁷²⁵ ÷ 0.007184). Haematocrit, haemoglobin, red blood cell (RBC) and white blood cell (WBC) count were assayed on a Technicon H⁺ analyser (Bayer Diagnostics, Puteaux). The criteria used to define the metabolic syndrome were: waist ≥ 90 cm and triglyceride levels ≥ 2 mmol/l, the so-called “hypertriglyceremic waist” according to Després’ group [20].

4. Statistical methods

Results were expressed as mean ± standard deviations (S.D.s) and percentages. Because distributions were not normal, GGT and triglyceride levels were log-transformed. For expected risk factors, odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated for men with diabetes and compared to those without diabetes at the second check-up as a reference.

To determine the risk factors for developing diabetes 5 years after an IFG was detected compared to a normalisation (FPG < 6.1 mmol/l) of a hyperglycaemia, qualitative parameters were compared using a χ² test or logistic regression and quantitative parameters with analysis of variance and GLM ANOVA as appropriate. Three models were used: a model with adjustment on age and BMI, a model with adjustment on age, BMI and triglycerides and a model with adjustment on age, BMI, triglyceride and glucose levels.

In addition, a logistic regression was performed to assess the independent role of behavioural data to predict a 5 year diabetes onset in IFG subjects after adjustment on biometrical and biological data (age, BMI, glucose, triglycerides).

All statistical tests were considered significant at P < 5%. NCSS (Number Cruncher Statistical Systems, Dr Hintze, Kaysville, UT, USA), version 2000 was used.

5. Results

The 3789 hyperglycaemic men who did not have a second check-up at T2 were not different from those who did, mostly for FPG (P = 0.64), BMI (P = 0.19), FHD (P = 0.07) and level of education (P = 0.55) but they were 2.7 years older (P < 0.0001) (Table 1).

The main characteristics of the 743 subjects who were studied are summarised in Table 1 (mean age, 44.5 years; BMI, 26 kg/m²; waist girth, 92 cm). Within 5 years, 127/743 men (17%) with IFG became diabetic patients, 39% were still classified as IFG and 44% returned to normal FPG. The 5-year incidence of diabetes at T2 (T1+ 5 years) according to FPG at T1 is presented in Fig. 1.

Table 1 Characteristics of 4532 men with IFG (glycaemia: 6.1–6.9 mmol/l) and no personal history of diabetes nor hypoglycaemic treatment at T1: those submitted to a single check-up and those who benefited from a second one 5 years later (T2)

<table>
<thead>
<tr>
<th>Variable</th>
<th>One exam (T1)</th>
<th>Two exams (T1 and T2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.2 (9.9)</td>
<td>44.5 (7.5)</td>
</tr>
<tr>
<td>University graduate (%)</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>FHD (%)</td>
<td>1.7</td>
<td>2.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.9 (4.4)</td>
<td>26.4 (3.6)</td>
</tr>
<tr>
<td>Waist girth (cm)</td>
<td>91.1 (11.8)</td>
<td>92.2 (9.9)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>137 (16)</td>
<td>135 (13)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>82 (10)</td>
<td>81 (10)</td>
</tr>
<tr>
<td>Systolic/diastolic blood pressure ≥ 140/90 mmHg (%)</td>
<td>51</td>
<td>49</td>
</tr>
<tr>
<td>FPG (mmol/l)</td>
<td>6.37 (0.23)</td>
<td>6.36 (0.22)</td>
</tr>
<tr>
<td>FPG [6.4–6.9] mmol/l (%)</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>FPG [6.7–6.9] mmol/l (%)</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.54 (1.25)</td>
<td>1.54 (1.07)</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>5.96 (1.07)</td>
<td>5.86 (1.01)</td>
</tr>
<tr>
<td>GGT (IU/l)</td>
<td>43.1 (59.3)</td>
<td>45.4 (48.7)</td>
</tr>
<tr>
<td>Creatinine clearance (μmol/l)</td>
<td>100.2 (20.9)</td>
<td>98.7 (15.1)</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>149 (11)</td>
<td>153 (9)</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>45.0 (3.3)</td>
<td>46.0 (2.6)</td>
</tr>
<tr>
<td>RBCs (10¹² per l)</td>
<td>4.93 (0.39)</td>
<td>5.07 (0.33)</td>
</tr>
<tr>
<td>WBCs (10⁹ per l)</td>
<td>7.06 (1.93)</td>
<td>6.97 (1.91)</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>22</td>
<td>23</td>
</tr>
</tbody>
</table>

*a Cockroft–Gault formula adjusted to body surface area (Dubois formula).
levels ≥ 2 mmol/l gave the next significant OR (OR: 3.2).
Among behavioural variables, an OR of 1.7 was observed for no daily dairy products intake, 1.6 for a low physical activity and 0.6 for low or moderate alcohol intake.

Table 3 shows medical history, biometrical and biological data at T1 for the three groups defined as normal FPG, IFG and diabetes groups at T2. Comparisons between normal FPG and diabetes group parameters are given in terms of crude data and after adjustment for age, BMI, triglyceride and glucose levels. A FHD (P = 0.001), BMI (P = 0.0002), FPG (P = 0.0001) and triglyceride levels (P = 0.0002) remained significant after adjustment. Some haematological levels were higher at T1 in those who became diabetic at T2 when baseline data were adjusted on age, BMI and triglycerides: haemoglobin (P = 0.08) and haematocrit (P = 0.05). When glucose was added as a covariate, the difference was no longer observed.

Table 4 summarises behavioural variables at T1 and comparisons between normal FPG, IFG and diabetes groups at T2. No daily dairy products (P = 0.001), high alcohol intake (P = 0.02), low or moderate alcohol intake (P = 0.03), low levels of daily physical activity (P = 0.02) were linked to the occurrence of diabetes in IFG subjects when data were adjusted on age, BMI and triglycerides and glucose. Current smoking was significant when data were adjusted on age and BMI but was no longer significant when triglycerides and glucose were added in the model.

No daily dairy products, low or moderate alcohol intake and low physical activity to a lesser extent were independent predictive factors of a 5 year onset of diabetes after adjusting for BMI, FHD, triglycerides and glucose at baseline (Table 5).

6. Discussion

Our study using data drawn from those collected in periodic prevention exams was not based on a designed cohort. Due to voluntary attendance, not all IFG men who benefited from the first exam attended the second at T2 within T1 + 5 years ± 6 months (Table 1). Before undertaking the study, we checked that there was no difference between IFG subjects who benefited from the second check-up and those who did not. No differences were noted between the baseline data of the two groups excepted for age (2.7 years), making the recruitment bias unlikely. The only effect might be a small decrease in diabetes incidence observed due to lower age.

Within 5 years 17% of men with IFG at T1 became diabetic patients and 39% maintained their IFG status, while 44% returned to normal FPG (< 6.1 mmol/l) at T2. In an earlier study [2], the prevalence of IFG was nearly threefold lower in women than in men; we have therefore limited the present study to men with IFG. Similarly, a recent publication indicated that among subjects with normal plasma glucose at baseline, men were more likely to develop IFG than women [21].

The high proportion of subjects in whom FPG returned to the normal range at T2 could be explained by the intra-individual variability of FPG and/or regression to the mean effect. Moreover one can speculate that medical check-ups
including repeated advice on one hand and initialisation of the National Program for Nutrition and Health (PNNS) [22] on the other might have had a beneficial effect on fasting glucose. We found only one publication dealing with the becoming of IFG subjects in a Chinese population from Taiwan [23]. In this study (half men and half women, mean age 57.4 years), 9.6% of subjects with IFG progressed to diabetes within 3 years. Unfortunately, we cannot extrapolate these previous results to ours because the genetic backgrounds are different, the duration of survey is shorter and data for both sexes are mixed in ours because the genetic backgrounds are different, the duration of survey is shorter and data for both sexes are mixed.

The next significant ORs (Table 2) were BMI (3.4), waist girth (2.9) and triglyceride levels (2.8). Triglyceride levels remained significant after adjustment for age, BMI and glucose (Table 3). This high incidence is mainly explained by the inclusion of both sexes. The Hoorn study in the Netherlands reported a cumulative incidence of 38% diabetes during 10-year follow-up (22/142). Although the follow-up was twice as long as in the present study and three times longer than the Taiwan study, this low figure is explained by the inclusion of both sexes. The Hoorn study in the Netherlands reported a cumulative incidence of 38% diabetes over a period of 6.4 years in a population with IFG at baseline. This high incidence is mainly explained by higher age (50–75 years at baseline) [16]. In a Mauritian population with a high prevalence of diabetes, 28.9% of subjects aged 25–70 with IFG developed diabetes during a 5-year follow-up [17] and 38% after an 11-year follow-up [21].

Among the predictive factors increasing the risk of having diabetes within 5 years (Table 2), the strongest ORs were observed for FHD (4.2), then for fasting blood glucose: the higher the FPG at T1, from 6.1 to 6.9 mmol/l, the greater the chance of becoming diabetic 5 years later, with an exponential evolution from 7% to 56% according to FPG levels (Fig. 1). The next significant ORs (Table 2) were BMI (3.4), waist girth (2.9) and triglyceride levels (2.8). Triglyceride levels remained significant after adjustment for age, BMI and glucose (Table 3). The combination of waist circumference ≥90 cm and triglyceride levels ≥2 mmol/l, the so-called “hypertriglyceridemic waist” [20,25], increased the OR of each parameter taken alone (3.2) (Table 2). Waist–hip ratio and triglyceride levels were also found to be significant predictive factors for progression to diabetes in the Taiwan study [23].

The ORs for high haematomatrit (1.8) and haemoglobin (1.3) values were also significant (Table 2) and mean levels between groups still differed after adjustment for age, BMI and triglycerides (P = 0.05 and P = 0.08, respectively) (Table 3). This was previously reported by Facchini et al. [26] in healthy men and women, i.e. that insulin resistance and plasma insulin response to oral glucose are consistently positively associated with haemoglobin and haematomatrit levels. He hypothesises
Table 4
Smoking, physical activity and nutritional habits at T1 in the normal FPG, IFG and diabetic subject groups at T2. Tests between normal FPG and diabetic subject groups on crude data and after adjustment for age, BMI, triglycerides and glucose

<table>
<thead>
<tr>
<th>Nutritional habits</th>
<th>Normal FPG, N = 324</th>
<th>IFG, N = 292</th>
<th>Diabetes, N = 127</th>
<th>ORs 95% CI</th>
<th>P</th>
<th>Age, BMI adjusted</th>
<th>Age, BMI triglycerides adjusted</th>
<th>Age, BMI triglycerides, glucose adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>No daily breakfast</td>
<td>27%</td>
<td>29%</td>
<td>33%</td>
<td>0.22</td>
<td>0.14</td>
<td>0.14</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>No daily dairy products</td>
<td>34%</td>
<td>39%</td>
<td>50%</td>
<td>0.002</td>
<td>0.007</td>
<td>0.004</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Meat more than 200 g a day</td>
<td>6%</td>
<td>7%</td>
<td>10%</td>
<td>0.14</td>
<td>0.14</td>
<td>0.20</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>Fish less than twice a week</td>
<td>82%</td>
<td>76%</td>
<td>77%</td>
<td>0.19</td>
<td>0.17</td>
<td>0.20</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Eggs more than 7 a week</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>0.83</td>
<td>0.70</td>
<td>0.85</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>Delicatessen meats more than four times a week</td>
<td>17%</td>
<td>15%</td>
<td>18%</td>
<td>0.92</td>
<td>0.41</td>
<td>0.81</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Fried food more than four times a week</td>
<td>1%</td>
<td>0%</td>
<td>2%</td>
<td>0.34</td>
<td>0.17</td>
<td>0.17</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Butter more than twice a day</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
<td>0.12</td>
<td>0.22</td>
<td>0.21</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Sweet desserts more than four times a week</td>
<td>13%</td>
<td>12%</td>
<td>10%</td>
<td>0.33</td>
<td>0.26</td>
<td>0.23</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>Pieces of sugar more than 4 a day</td>
<td>12%</td>
<td>7%</td>
<td>9%</td>
<td>0.45</td>
<td>0.81</td>
<td>0.72</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>Sweet drinks more than 0.5 l a day</td>
<td>9%</td>
<td>6%</td>
<td>11%</td>
<td>0.54</td>
<td>0.30</td>
<td>0.29</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>High alcohol intake b</td>
<td>29%</td>
<td>34%</td>
<td>41%</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Low or moderate alcohol intake a</td>
<td>60%</td>
<td>55%</td>
<td>47%</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>No alcohol intake</td>
<td>11%</td>
<td>11%</td>
<td>13%</td>
<td>0.86</td>
<td>0.82</td>
<td>0.82</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Water less than 0.5 l a day</td>
<td>23%</td>
<td>23%</td>
<td>20%</td>
<td>0.54</td>
<td>0.76</td>
<td>0.65</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low physical activity b</td>
<td>11%</td>
<td>17%</td>
<td>21%</td>
<td>0.01</td>
<td>0.05</td>
<td>0.05</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>No sporting activity</td>
<td>25%</td>
<td>26%</td>
<td>29%</td>
<td>0.31</td>
<td>0.37</td>
<td>0.50</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>Tobacco</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>21%</td>
<td>22%</td>
<td>28%</td>
<td>0.10</td>
<td>0.01</td>
<td>0.06</td>
<td>0.50</td>
<td></td>
</tr>
</tbody>
</table>

P. Lecomte et al. / Diabetes & Metabolism 33 (2007) 140–147

Table 5
ORs for the 5-year incidence of diabetes according to baseline behaviourlal data after adjustment for FHD, BMI, triglycerides and glucose at baseline

<table>
<thead>
<tr>
<th>ORs</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No daily dairy products</td>
<td>1.86</td>
<td>1.21–2.86</td>
</tr>
<tr>
<td>Low or moderate alcohol intake a</td>
<td>0.66</td>
<td>0.43–1.00</td>
</tr>
<tr>
<td>Low alcohol intake b</td>
<td>1.70</td>
<td>0.98–2.95</td>
</tr>
</tbody>
</table>

a Alcohol consumption less or equal to 0.5 l wine/beef a day and less than 4 cocktails/spirits a week.

b Nurse’s estimation of low daily physical activity at home, at work or during leisure time (duration and regularity).

Insulin promotion to increase the synthesis of RBC. Similar findings were recently published in an elderly non smoking non-diabetic Korean population [27]: a correlation was found between insulin resistance, haemoglobin and WBC. This suggests that increased erythropoiesis and subclinical inflammation could be part of the metabolic syndrome [28], and depends to some extend upon glycaemia. Indeed, it was previously shown that insulin stimulates the growth of human erythroid progenitors in vitro [29]. Haematoctrit and haemoglobin levels were no longer significant when glucose level was added in the model: this agrees with the previous hypothesis.

In this population with diabetes at T2, half of the subjects did not consume dairy products every day (Table 4). This factor is predictive of diabetes after adjustment for age, BMI, triglycerides and glucose (P = 0.001). It suggests that low calcium intake can be a factor leading to diabetes. According to Zemel et al. [30], low calcemia is followed by increased levels of parathormone (PTH) inducing high calcitriol levels with an intracellular Ca2+ increase in adipocytes leading to activation of fatty acid synthase (FAS) and enhanced lipogenesis. Similarly, intracellular Ca2+ increase in β cells stimulates insulin release and inhibition of lipolysis in adipocytes. These results observed in animals have been confirmed in humans. Dairy intake was inversely related to the frequency of metabolic syndrome in men in the DESIR cohort [31]. Similar observations concerning the benefits of high-calcium intake have been reported by Davies et al. [32]: increase in calcium intake in five studies was associated with a significant weight loss. Similarly, Pereira et al. [33] in the CARDIA Study showed an inverse relationship between increased dairy consumption and the occurrence of insulin resistance syndrome (IRS) within 10 years in young (18–30 years) overweight adults. The benefit of a higher calcium intake has recently been emphasised in an interventional study by Zemel et al. [34]: obese adults (N = 32) assigned for 24 weeks to a standard balanced diet (~500 kcal) lost 6.4% of their body weight, 8.6% on a high-calcium diet and 10.9% on a high-dairy diet. Overall fat loss and fat loss from the trunk region were greater with high-calcium intake.

High alcohol intake was more frequent and low or moderate alcohol intake was less frequent in subjects who became diabetic even after adjustment for age, BMI, triglycerides and glucose (respectively, P = 0.02 and P = 0.03). High alcohol intake...
is a factor leading to diabetes whereas low or moderate intake is beneficial [35,36]. Increased insulin sensitivity with moderate alcohol consumption has recently been confirmed [37].

In our findings, the percentage of low physical activity increased linearly for subjects who returned to normal FPG (11%), for those still classified as IFG (17%) and for those who became diabetic subjects (21%) (Table 4). The difference between the two extreme groups was still significant after adjustment for age, BMI, triglycerides and glucose ($P = 0.02$). Moreover, hyperglycaemic subjects at T1 who became diabetic patients at T2 tended to have more often no sports activity than those who returned to normal FPG (29% vs. 25%, not significant) (Table 4). These findings confirmed the stated link between low daily physical activity and diabetes. Two recent studies demonstrated that the most efficient method to prevent the occurrence of diabetes in subjects with IGT is to increase physical activity [38,39]. This provides a key argument for promoting regular physical activity in IFG subjects in preventive interventions.

In this study, active smoking was not more frequent in subjects who became diabetic on crude data. The lower weight of current smokers might explain this. Adjustment for age, BMI and triglycerides revealed a difference close to significance ($P = 0.06$) for active smoking as a risk factor for diabetes. This difference disappeared when glucose was added in the adjustment. This is in agreement with a previous study in which smoking was demonstrated to be a risk factor for diabetes in a population of almost 30,000 subjects attending IRSA preventive health centres [40]. Besides its well-known benefit effect, smoking prevention might reduce the incidence of diabetes. This has been convincingly shown in a large American study [41]: 10 years after men had stopped smoking, the incidence of diabetes returned to the level of those who had never smoked. Smoking was also found to be an independent risk factor for progression to diabetes in the study of Chinese subjects with IFG [23].

7. Conclusion

Although the natural history of type 2 diabetes is still controversial, it is now accepted that IFG appears some years before the onset of diabetes. In this study of middle-aged men, 5 years after IFG was detected, 44% returned to normal FPG, 39% were still classified as IFG and 17% became diabetic patients. FHD, overweight, moderately increased FPG, high triglyceride levels, no daily dairy products intake, high alcohol intake, smoking and low levels of physical activity were the main significant predictors leading from IFG to diabetes. Therefore, the PNNS [22] developed in France since 2000 in the whole population should be fully applied: it favours a reduction of salt, lipids, saccharose and alcohol consumption, lowers blood cholesterol, blood pressure and overweight, with an increase of physical activity and fruit, vegetable, and calcium consumption. Our results suggest that reinforcing the application of the PNNS targeted at IFG subjects would be of considerable benefit to them. Has the time of diabetes prevention based on FPG measurement rung?

Acknowledgments

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References


