A TYPE 2 DIABETES SCREENING PROGRAM BY GENERAL PRACTIONERS IN A BELGIAN AT RISK POPULATION

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SUMMARY
Objective: This study was designed to set up in Belgium a national screening program in order to evaluate the prevalence of undiagnosed impaired glucose tolerance and type 2 diabetes in a general population with at least one risk factor.

Material and Methods: 10,201 individuals were screened by 1,466 general practitioners between 1995 and 1998 (age: 57 ± 16 years; BMI: 28 ± 5 kg/m²; mean ± 1SD). A three step diagnosis protocol was followed (blood glucose at random; fasting plasma glucose and, if needed, a 75 g oral glucose tolerance test). WHO criteria were used for diagnosis.

Results: Impaired glucose tolerance was found in 3% of individuals, while 11% had diabetes. Patients with abnormal glucose metabolism were older (P < 0.001) and had an higher BMI (P < 0.001) than non-diabetic subjects. The prevalence of undiagnosed diabetes was slightly higher (14 vs. 11%) when using a fasting plasma glucose threshold of 126 mg/dl (instead of 140 mg/dl) as recommended by the ADA experts.

Conclusion: Undiagnosed abnormal glucose metabolism, in particular diabetes, is particularly frequent in a Belgian at risk population.

Key-words: type 2 diabetes, undiagnosed, screening, risk factors, general practice, Belgium.

RE´SUMÉ - Dépistage par les médecins généralistes des cas méconus de diabète de type 2 dans une population belge à risque.

Objectif : Le but de notre étude a été d’analyser la prévalence dans une population belge à risque de cas méconnus d’intolérance glucidique ou de diabète sucré.

Matériel et Méthodes : 1468 médecins généralistes ont effectué entre 1995 et 1998 un dépistage chez 1468 individus possédant au moins un facteur de risque d’anomalies du métabolisme glucidique. Leur âge était de 57 ± 16 ans (moyenne ± 1DS) et leur index de poids corporel de 28 ± 5 kg/m². Nous avons suivi un algorithme de diagnostic en trois temps : (1) glycémie au hasard ; (2) glycémie plasmatique à jeun et, si nécessaire (3), une épreuve d’hyperglycémie par voie orale (75 g). Les critères de diagnostic ont été ceux de l’Organisation Mondiale de la Santé.

Résultats : Dans ces conditions, nous avons dépisté une intolérance glucidique (sur la base de l’épreuve d’hyperglycémie) chez 3 % des patients et un diabète sucré (sur la base de la glycémie à jeun ou de l’épreuve d’hyperglycémie) chez 11 % des sujets ayant participé à l’étude. Les patients avec intolérance glucidique ou diabète sucré étaient plus âgés (P<0,001) et leur index de poids corporel plus élevé (P < 0,001). Lorsque nous avons considéré, en fonction des recommandations de l’American Diabetes Association, le diagnostic de diabète à partir d’un seuil glycémique à 126 mg/dl, la prévalence du diabète était légèrement plus élevée (14 vs. 11 %).

Conclusion : Dans une population belge à risque, cette étude de dépistage, menée par des médecins généralistes, a permis de diagnostiquer une intolérance glucidique et un diabète sucré respectivement dans 3 et 11 % des cas.

Mots-clés : diabète de type 2, méconnaissance, dépistage, facteurs de risque, médecine générale, Belgique.

Type 2 (non insulin dependent) diabetes, caused by both decreased insulin sensitivity and impaired insulin secretion, has been reported to affect more than 3% of the adult population in developed countries [1]. Its prevalence increases sharply with age. Thus, in individuals above the age of 65 years, it is higher than 10%, in particular when some risk factors such as obesity are present [1-4]. In addition to type 2 diabetes, impaired glucose tolerance (IGT) is, quantitatively, another major problem, with a prevalence between 3 and 10% in Europe [5, 6].

Poor glycaemic control in type 2 diabetes is associated with chronic neurological and vascular complications, especially cardiovascular disease which accounts for 70-75% of total mortality [7, 8]. The importance of lowering blood glucose concentrations in order to reduce the development of these complications is now firmly established [9, 10].

Therefore, early diagnosis as well as adequate (pre- nocuous) treatment are now considered as key stones in taking good care of these patients. However, type 2 diabetes can remain asymptomatic for many years, leading to a (possible) delay before it is detected [11, 12]. As a consequence, major degenerative complications can already be present at the time of (delayed) diagnosis [13]. This clearly emphasizes the need for screening, in particular in at risk populations.

The present study was designed to set up a national screening program in Belgium in order to evaluate the prevalence of undiagnosed IGT and type 2 diabetes in a general “healthy” population, followed by general practitioners (GPs), with one or more risk factors for abnormal glucose metabolism.

■ RESEARCH DESIGN AND METHODS

A representative sample of 1466 GPs all over Belgium (about 17% of active practitioners) was involved in this survey, which was conducted between 1995 and 1998. The study was planned to include data on the screening of 10,000 subjects at risk of having an undiagnosed IGT or type 2 diabetes.

The GPs were asked to screen consecutively outpatients willing to participate (in the absence of diabetes symptoms) on the basis of a six item check list of risk factors of type 2 diabetes: age over 60 years, positive family medical history, overweight or obesity (as defined by a body mass index between 25 and 30 or higher than 30 kg/m², respectively), unexplained tiredness, recurrent infections, as well as signs and/or symptoms which may be secondary to chronic complications of diabetes (macrovascular disease, neuropathy, retinopathy, nephropathy, hypertension).

Subjects identified as being at risk on the basis of the presence of one or several of these factors were invited to take part. They supplied a finger prick capillary blood sample which was tested for random glucose level using a blood-glucose measuring device (One Touch Basic System [Lifescan]; Sensor Electrodes Plus [Medisense]) (step 1). At the time of screening, the patient’s main demographic data (gender, age, height, weight) were recorded.

The results of blood glucose value (BG) were interpreted by the GPs according to the World Health Organization (WHO) criteria indicative of the diagnosis of IGT or type 2 diabetes, which represented the guidelines at the time the study was set up [14]. Briefly, if the random BG was less than 100 mg/dl, abnormal glucose metabolism was considered as being improbable and these subjects were not further investigated. In contrast, if the random BG specimen was between 100 and 200 mg/dl, or higher than 200 mg/dl, an abnormal glucose metabolism was suspected and a confirmatory test (fasting venous plasma glucose measurement (FPG) by a glucose oxidase method) was carried out at a local laboratory (step 2). Thus, patients were considered as normal if their FPG was below 100 mg/dl. A diagnosis of type 2 diabetes was considered if FPG was ≥ 140 mg/dl. If FPG was between 100 and 140 mg/dl, an oral glucose tolerance test (75 g) (OGTT) was performed (step 3). If glycaemia observed at 120’ of the test was between 140 and 200 mg/dl, the patient was classified as having IGT. Diabetes was considered for a 2 h post challenge glucose value ≥ 200 mg/dl.

In addition to this interpretation, as the diagnostic criteria for diabetes were recently revised by the American Diabetes Association (ADA) [15], we retrospectively analysed the prevalence of diabetes in this population according to the ADA recommendations (FPG ≥ 126 mg/dl instead of ≥ 140 mg/dl). We also looked secondarily for the prevalence of Impaired Fasting Glycaemia (IFG) (≥ 110 < 126 mg/dl).

Participating GPs were asked to send copies of the completed questionnaires to the study data monitoring center (Laboratoires Servier) for analysis.

The GPs who participated in the study attended regularly workshops with endocrinologists.

■ STATISTICS

After double data counting into a computersided database, the analysis was carried out using the SPSS Statistical Program. Data listings were prepared and descriptive statistics were calculated for all variables recorded on the questionnaires. Statistical tests used were Chi-Square, Mantzel-Haenszel for linear association, Pearson and Kruskal-Wallis. Analysis of variance was performed for detecting main effects and interactions of risk factor(s). Data are presented as mean ± 1SD.

P values of < 0.05 were considered statistically significant.
RESULTS

We analysed 10,201 data sheets. They were correctly completed for 9,340 subjects. 53% of them were female. The age was 57 ± 16 years and BMI 28 ± 5 kg/m² (mean ± ISD). The distribution by age is shown in Table I. 17% of subjects were under the age of 40 and 50% over 60 years. Table I also shows that obesity was found in 25% of individuals.

The incentives for screening were age over 60 years (in 44% of patients), overweight or obesity (47%), a positive family medical history of diabetes (33%), tiredness (27%), recurrent infections (10%) and/or suspected chronic complication(s) of diabetes (3%).

Random BG (step 1) was lower than 100 mg/dl in 44% of the subjects (n = 4,145) who were no longer investigated. In contrast, abnormal glucose metabolism was suspected in 56% of subjects (n = 5,195): 48% (n = 4,498) had random BG values between 100 and 200 mg/dl while 8% (n = 697) had levels above 200 mg/dl.

Confirmatory FPG (step 2) was normal in another cohort of 30% of subjects (n = 2,779), while 10% (n = 982) had values higher than 140 mg/dl and were considered as being diabetics. An OGTT was performed in 1,434 patients (16% of the total group) with FPG levels between 100 and 140 mg/dl. 12% (n = 1,123) had a BG value at 120 lower than 140 mg/dl and were therefore considered as normal. One per cent (n = 85) was diagnosed as having diabetes on the basis of a BG higher than 200 mg/dl while 3% of subjects (n = 226) had IGT.

Thus, 86% of the screened subjects (n = 8,047) were considered as having normal glucose tolerance (group I) while 3% (n = 226) had IGT (group II) and 11% (n = 1,067) diabetes (group III).

Distribution of age and BMI of patients with diabetes are shown in Table I. The BG values and main demographic characteristics of the subjects of the three groups are indicated in Table II. Table III reports the proportion of subjects with normal status, IGT and diabetes according to combined or isolated risk factor(s). Tiredness as risk factor was not included in the analysis since its prevalence was comparable in the three groups (in 27, 23 and 28% of subjects respectively, P = 0.299, Chi Square, NS). Similarly, the contribution of suspected chronic complications in the diagnosis of IGT or diabetes was not reported due to the low number of cases. Thus, when the other incentives for screening were considered, overweight and obesity (combined or single) was significantly the most contributive risk factor for the diagnosis of type 2 diabetes (P < 0.001). Moreover, we also observed a significative difference between the contribution of combined or isolated risk factor(s) in the proportion of patients with normal or abnormal glucose metabolism (P < 0.001 by Kruskal-Wallis test).

When using ADA fasting criteria for diabetes (FPG ≥ 126 mg/dl), we found that 1,267 patients (instead of 982 in the WHO definition) had diabetes (Table IV). Among the subgroup of 645 individuals with IFG in whom an OGTT was carried out, 479 had a BG value at 120 lower than 140 mg/dl, while another 123 had IGT. 43 subjects with a BG value above 200 mg/dl should be considered as diabetics. Thus, the overall prevalence of diabetes (on the basis of fasting and OGTT values) was of 14% (n = 1,310).

DISCUSSION AND CONCLUSIONS

Recent studies showed an increasing worldwide prevalence of type 2 diabetes [2, 3]. The third National Health and Nutrition Examination Survey (NHANES) also indicated that the overall prevalence of diabetes in US adults between 40 and 74 years of age increased from 8.9% in the period 1976-1980 to 12.3% by 1988-1994 [4]. It is of interest to mention that epidemiological projections even suggest a doubling of this number by the year 2010, mainly due to sedentary lifestyles (physical inactivity and/or diet) and obesity [2, 3].

A major difficulty in a prevention policy is that the disease is frequently totally free of symptoms. Thus, there are now thought to be at least 60 million known cases of type 2 diabetes worldwide but also 60 million unreported cases [2]. Harris et al. found that as many as 50% of the people with the disease in the USA (or about 8 million individuals) are undiagnosed [6] while

Table I. Age and Body Mass Index distribution (BMI) in the total cohort and in the group of patients with diabetes*.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total cohort [n = 9,340]</th>
<th>Diabetic patients [n = 1,067]</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>30-39</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>40-49</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>50-59</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>60-69</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>24</td>
<td>29</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>25-30</td>
<td>46</td>
<td>48</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>25</td>
<td>38</td>
</tr>
</tbody>
</table>

* in % of subjects.
### Table III. Proportion of patients with normal glycaemic status, IGT and diabetes according to risk factor(s) *

<table>
<thead>
<tr>
<th>Four risk factors</th>
<th>Group I (normal)</th>
<th>Group II (IGT)**</th>
<th>Group III (diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>overweight/history/age/infections</td>
<td>62</td>
<td>15</td>
<td>24</td>
</tr>
<tr>
<td><strong>Three risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overweight/history/infections</td>
<td>65</td>
<td>9</td>
<td>26</td>
</tr>
<tr>
<td>overweight/age/infections</td>
<td>71</td>
<td>3</td>
<td>26</td>
</tr>
<tr>
<td>overweight/age/history</td>
<td>72</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>history/age/infections</td>
<td>83</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td><strong>Two risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overweight/infections</td>
<td>75</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>overweight/age</td>
<td>81</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>overweight/history</td>
<td>81</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>age/infections</td>
<td>84</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>age/history</td>
<td>85</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>infections/history</td>
<td>93</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>One risk factor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overweight</td>
<td>86</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>history</td>
<td>92</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>age</td>
<td>93</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>infections</td>
<td>94</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>

* expressed in % of screened subjects.
** IGT for Impaired Glucose Tolerance.
*** OGTT: Oral Glucose Tolerance Test, in 1434 subjects with FPG ≥ 100 < 140 mg/dl.

Tamayo-Marco et al. observed a comparable percentage in Spain [16] and Stolk et al. in the Rotterdam Study [17].

Our own data in Belgium, based on a simple methodology successfully used by GPs in at risk patients, are in accordance with - and extend the previous observations. Thus, we showed that in a cohort of 9,340 outpatients with one or more risk factors for diabetes, only 86% of individuals had normal glucose tolerance, while 3 and 11% respectively were characterized by undiagnosed IGT (on the basis of OGTT) or diabetes (on the basis of FPG or OGTT). Our prevalences are high when compared with other reports [18, 19], but in accordance in Europe with data published by Kohler et al. [20] and by Papazoglou et al. [21]. Comparable prevalence of undiagnosed diabetes have also been observed in Canada [22] and in other parts of the world [23].

The (secondary) use of ADA criteria for diabetes (i.e. FPG ≥ 126 mg/dl) even increases the prevalence of diabetes up to 14% of the total population, as also reported by the recent study of Kohler et al. in Germany [20]. Lasfargues et al. also observed an higher prevalence of diabetes in France when considering a glycaemic threshold of 126 instead of 140 mg/dl [24]. It is of interest to note that in the subgroup of 645 patients with IFG (according to the ADA definition), only 123 had confirmed IGT while 479 and 43 subjects respectively had to be considered as “normal” or “diabetic” on the basis of OGTT. These observations are in agreement with recent reports, which stress the equivocal of the ADA recommendations concerning the place of OGTT in the diagnosis of diabetes [25].

Our selection criteria for screening could account for the high prevalence of abnormal glucose metabolism, in particular type 2 diabetes. It cannot be excluded that additional screening parameters (such as a history of gestational diabetes, ethnic predisposition, abdominal fat distribution and/or hyperlipaemia) could even contribute to increase this frequency of disease.

As expected, the diabetic patients in our cohort were older when compared with non-diabetic individuals and had also an higher BMI. The latter data in Belgian subjects extend previous observations, especially when emphasizing the role of overweight and/or obesity in the genesis of type 2 diabetes [2, 26, 27]. In our study, we also observed that overweight and obesity were the most contributive screening risk factors for a diagnosis of type 2 diabetes.

Chronic poor glycemic control in type 2 diabetes leads to the development of neurological and vascular complications [7-9, 28-30]. Undiagnosed diabetes is therefore a serious condition [31] in particular when considering high risk populations. On the other hand, it has been shown that antihyperglycaemic oral drugs are very effective in the management of newly-diagnosed type 2 diabetic individuals. Thus, in 5,772 patients, recruited through GPs in France (Diadem Study), FPG, postprandial blood glucose as well as HbA1c improved significantly during a 2 years gli-clazide treatment [32]. Moreover, the UKPDS has unequivocally demonstrated in recently diagnosed type 2 diabetic patients that tight glycaemic control obtained with insulin or antihyperglycaemic oral drugs such as sulfonylureas or biguanides (and optimized blood pressure levels) reduced the rate of these complications [9, 10]. Therefore, due to both the high prevalence of (undiagnosed) diabetes as well as the risk of development of chronic complications – which can be prevented by adequate management - a policy

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**TABLE IV. Distribution of patients according to WHO/ADA definition for diabetes (n)**

<table>
<thead>
<tr>
<th>Group</th>
<th>WHO definition</th>
<th>ADA definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 100</td>
<td>2,779 (54%)*</td>
<td>3,283 (63%)*</td>
</tr>
<tr>
<td>100 ≤ FPG &lt; 140</td>
<td>1,434 (27%)*</td>
<td>645 (13%)*</td>
</tr>
<tr>
<td>140 ≤ FPG &lt; 200</td>
<td>982 (19%)*</td>
<td>1,267 (24%)*</td>
</tr>
<tr>
<td>200 ≤ FPG &lt; 260</td>
<td>1,726 (32%)*</td>
<td>542 (10%)*</td>
</tr>
</tbody>
</table>

* n=5,195 had a fasting plasma glucose (FPG) determination
* in % to the 5,195 subjects
* in % of patients with FPG between ≥ 100 < 140 (WHO) or ≥ 110 < 126 mg/dl (ADA)
of screening appears now as essential, in particular when targeted to at-risk populations.

In conclusion, this survey by GPs (the first in Belgium) shows that in our country (undiagnosed) glucose intolerance or type 2 diabetes were present in 3 and 11% of at risk cases, respectively. As expected, the use of ADA criteria seems even to increase its prevalence. Systematic screening of abnormal glucose metabolism by primary care network, using simple and reliable methods of diagnosis, seems of interest and should be recommended, in particular when risk factor(s) are present.

Acknowledgments – The authors thank Mrs S. Meerkens for excellent secretarial assistance as well as the Company Medis- trat (Brussels) for statistical analysis. They also thank all the general practitioners who participated to the study.

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