High prevalence of undiagnosed diabetes and high risk for diabetes using HbA1c criteria in middle-aged patients undergoing cataract surgery

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Received 28 October 2012; accepted 29 October 2012

Abstract

Aim. – This study assessed the prevalence of undiagnosed diabetes and a high risk for diabetes using glycated haemoglobin (HbA1c) values in middle-aged patients undergoing cataract surgery.

Methods. – The study comprised 137 consecutive patients, aged 40 to 65 years, with no known diabetes undergoing cataract surgery at a French national eye centre. Fasting glucose, obesity parameters, and vascular and ocular cataract risk factors were recorded. HbA1c was measured on the day of cataract surgery. Prevalence of undiagnosed diabetes (HbA1c ≥ 6.5%) and a high risk of diabetes (≥ 6.0% but < 6.5%) in the study population was compared with recently published estimates from general French, Dutch and US populations.

Results. – In the study population, undiagnosed diabetes was found in 12 patients (9%; 95% CI: 4–14%) and a high risk for diabetes in 47 (34%; 95% CI: 26–42%). These prevalences were four to 11 times higher than the corresponding population-based estimates, whereas obesity parameters recorded in the general populations and in our study population were similar according to HbA1c subcategories. Of the 125 patients with HbA1c less than 6.5%, values were higher in patients without ocular cataract risk factors (n = 73; 58%) than in those with cataract risk factors (n = 52; 42%) at 5.92 ± 0.30% and 5.57 ± 0.29%, respectively (P < 0.001), thereby suggesting a significant role for blood glucose levels in cataractogenesis.

Conclusion. – Middle-aged patients undergoing cataract surgery showed a high prevalence of diabetes and a high risk for diabetes not recognized before surgery, suggesting that this patient population should be targeted for diabetes screening and prevention.

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Keywords: Diabetes; Prediabetes; Cataract; Screening; HbA1c

Résumé

Prévalence élevée de diabète méconnu ou haut risque de diabète par la mesure de l’HbA1c chez des patients opérés de la cataracte avant l’âge de 65 ans.

Objectif. – Évaluer la prévalence du diabète et du haut risque de diabète par le taux d’hémoglobine glyquée (HbA1c) dans une population de patients opérés de la cataracte avant l’âge de 65 ans.

Méthodes. – L’étude a inclus 137 patients consécutifs âgés de 40 à 65 ans sans diabète connu, opérés de la cataracte dans un centre national français d’ophtalmologie. Les paramètres métaboliques (indice de masse corporelle, périmètre abdominal, glycémie à jeun) ainsi que les facteurs de risque vasculaire et de cataracte étaient enregistrés. L’HbA1c a été mesurée le jour de l’intervention. La prévalence de diabète méconnu (HbA1c ≥ 6,5 %) et de haut risque de diabète (≥ 6,0 % mais < 6,5 %) a été comparée à celle rapportée dans trois études récentes de populations françaises, hollandaise et nord-américaine.

Résultats. – Dans la population étudiée, 12 patients (9%, IC à 95% 4–14%) avaient un diabète méconnu et 47 (34%, IC à 95% 26–42) un haut risque de diabète, soit une fréquence quatre à 11 fois plus élevée que dans les populations générales, pour des paramètres morphologiques par catégorie d’HbA1c similaires. Parmi les 125 patients avec HbA1c inférieure à 6,5%, ceux qui ne présentaient pas de facteurs de risque de cataracte (n = 73; 58%) avaient une HbA1c plus élevée que ceux avec facteurs de risque (n = 52; 42%), respectivement 5,92 ± 0,30% et 5,57 ± 0,29% (P < 0,001), ce qui suggère un rôle propre du niveau glyquémique dans la genèse de la cataracte.

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1262-3636/S – see front matter © 2012 Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.diabet.2012.10.009
Conclusion. – Les patients opérés de la cataracte avant l’âge de 65 ans ont une prévalence très élevée de diabète et de haut risque de diabète non reconnus avant chirurgie, ce qui en fait une population cible importante pour le dépistage et la prévention du diabète à l’occasion de la chirurgie ophthalmologique.

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Mots clés : Diabète ; Prédiabète ; Cataracte ; Dépistage ; HbA1c

1. Introduction

Cataract is a primarily age-related ocular condition that causes significant vision loss in approximately 40 to 80% of people aged above 75 years [1]. Diabetes mellitus is a well-established cataract risk factor that promotes early cataracts [2–4]. Among diabetic patients, increased levels of glycated haemoglobin (HbA1c) have been associated with increased cataract risk in US (Beaver Dam, Wisconsin) [2] and Barbados [3] eye studies. Intensive blood glucose control led to a 24% reduction in cataract extraction in the UK Prospective Diabetes Study (UKPDS), corresponding to a 19% reduction in cataract surgery per 1% decrease in HbA1c level [5]. Consistent with the UKPDS finding, an 11% reduction in cataract extraction was observed with tight glycaemic control in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study [6]. These data suggest a causal role for glycaemia in the pathogenesis of cataract in diabetic patients. However, it remains unclear whether blood glucose levels are associated with cataract in non-diabetic subjects.

HbA1c is the best available marker of overall glycaemic exposure. Beyond its well-established use for monitoring diabetes treatment, its value as a screening and diagnostic test for diabetes has emerged over the past decade. In 2009, an international expert committee recommended a 6.5% HbA1c cut-off point for the diagnosis of diabetes, and HbA1c at 6.0 to 6.4% for identifying individuals with the highest risk of progression to diabetes [7]. A year later, the American Diabetes Association (ADA) recommended the use of HbA1c as a diagnostic test for diabetes with less than 5.7%, 5.7 to 6.4% and greater or equal to 6.5% cut-off points for defining normoglycaemic, prediabetic and diabetic categories of patients, respectively [8].

The hypothesis of the present study was that non-diabetic patients with early cataracts exhibit a high prevalence of abnormal blood glucose levels, thereby making them a relevant target population for diabetes screening. Thus, the prevalence of undiagnosed diabetes and a high risk of diabetes was assessed by HbA1c measurements in middle-aged patients with no known diabetes who were undergoing cataract surgery.

2. Methods

The study was performed in April and May 2009 at a daycare unit of the Quinze-Vingts Hospital in Paris, France. All patients aged 40 to 65 years undergoing cataract extraction were considered for inclusion. Exclusion criteria were congenital cataract, known diabetes and a history of systemic corticosteroid therapy. Fasting blood glucose was measured by systematic preoperative testing. On the day of surgery, HbA1c values were measured, and body mass index (BMI), waist circumference (WC), traditional cardiovascular risk factors and the following cataract risk factors were recorded: previous ocular trauma or inflammation of the affected eye; and high myopia (≥−6.0 diopters and/or axial length ≥26 mm). Diabetes status was defined on the basis of recently recommended HbA1c cut-off points [8]. The prevalence of undiagnosed diabetes (HbA1c ≥ 6.5%) and a high risk of diabetes (HbA1c ≥ 6.0% but < 6.5%) in the study population was compared with those found in recent population-based studies in France [9], the Netherlands [10] and the US [11]. The study had the approval of our institutional review board, and informed consent was obtained in accordance with the Declaration of Helsinki.

Analyses were performed using SPSS software, version 15.0 for Windows (SPSS, Chicago, IL, USA). Descriptive statistics are presented as means ± SD for continuous variables and as percentages (95% confidence interval [CI]) for categorical variables. Significance was considered a P value <0.05.

3. Results

3.1. Description of the study population

During the 2-month study period, 619 outpatients underwent cataract surgery at our daycare unit: 11 of them (2%) were aged less than 40 years (range 4–38 years); 408 (66%) were more than 65 (66–99) years; and 200 (32%) were between 40 and 65 years. From this latter group, eight patients with previous steroid use, one with congenital cataract and 54 with known diabetes were excluded. The remaining 137 patients were included in the study: 83 (61%) had no ocular cataract risk factors; mean age was 57.4 ± 6.0 years; 64 (47%) were male; 44 (32%) had a family history of diabetes; 35 (26%) had a history of smoking; 35 (26%) were taking antihypertensive drugs; and 22 (16%) were taking lipid-lowering drugs. Mean BMI and WC were 25.8 ± 4.3 kg/m² and 93.3 ± 13.0 cm, respectively. Abdominal obesity, defined as a WC greater or equal to 102 cm in men and greater or equal to 88 cm in women, was seen in 63 patients (46%). Mean fasting blood glucose and HbA1c levels were 99 ± 13 mg/dL and 5.88 ± 0.37%, respectively. Sixty-one patients (45%) had a fasting blood glucose greater or equal to 100 mg/dL.

3.2. Prevalence of newly diagnosed diabetes and a high risk for diabetes

Of the 137 study patients, 12 (9%; 95% CI: 4–14%) had newly diagnosed diabetes, 47 (34%; 95% CI: 26–42%) had
a high risk of developing diabetes and 91 (66%; 95% CI: 58–74%) were prediabetic. All (12/12) of the newly diagnosed diabetic patients and 81% of the non-diabetic patients (86/106 with available data) had cortical or posterior subcapsular cataract, the subtypes classically associated with diabetic cataract [1].

The main characteristics of the 125 non-diabetic patients are shown in Table 1. In these patients, HbA1c levels were higher in those without ocular cataract risk factors \( (n = 73; 58\%) \) compared with those with cataract risk factors \( (n = 52; 42\%) \): 5.92 ± 0.30% and 5.57 ± 0.29%, respectively \( (P < 0.001) \).

### 3.3. Prevalences of newly diagnosed diabetes and a high risk of diabetes

Fig. 1 shows the prevalence data from our study population together with the corresponding estimates found in the general populations (serving as control populations) that clearly indicate an increased risk (between four- and 11-fold) of both undiagnosed diabetes and a high risk of diabetes in our middle-aged cataract patients compared with the general populations.

Morphological parameters according to HbA1c subcategories were available for the Dutch study [10], comprising 2753 subjects aged 40 to 65 years and 47% male, both characteristics matching our present patient population. Dutch subjects with normal glucose metabolism and those with intermediate

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients with HbA1c &lt; 6.5% ( (n = 125) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, ( n ) (%)</td>
<td>59 (47)</td>
</tr>
<tr>
<td>Age, mean ± SD (years)</td>
<td>57.3 ± 6.1</td>
</tr>
<tr>
<td>Cataract type (available for 106 patients), ( n ) (%)</td>
<td>20 (19)</td>
</tr>
<tr>
<td>Nuclear</td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>40 (38)</td>
</tr>
<tr>
<td>Posterior subcapsular</td>
<td>46 (43)</td>
</tr>
<tr>
<td>Previous contralateral cataract surgery, ( n ) (%)</td>
<td>40 (32)</td>
</tr>
<tr>
<td>Ocular cataract risk factors(^a), ( n ) (%)</td>
<td>52 (42)</td>
</tr>
<tr>
<td>Family history of type 2 diabetes, ( n ) (%)</td>
<td>39 (31)</td>
</tr>
<tr>
<td>Patients taking antihypertensive drugs, ( n ) (%)</td>
<td>30 (24)</td>
</tr>
<tr>
<td>Patients taking hypolipidaemic drugs, ( n ) (%)</td>
<td>21 (17)</td>
</tr>
<tr>
<td>Smoking history (past or present), ( n ) (%)</td>
<td>33 (26)</td>
</tr>
<tr>
<td>Body mass index, mean ± SD (kg/m(^2))</td>
<td>25.5 ± 4.2</td>
</tr>
<tr>
<td>Body mass index ≥ 30 kg/m(^2), ( n ) (%)</td>
<td>21 (17)</td>
</tr>
<tr>
<td>Waist circumference, mean ± SD (cm)</td>
<td>92.8 ± 13.0</td>
</tr>
<tr>
<td>Abdominal obesity(^b), ( n ) (%)</td>
<td>53 (42)</td>
</tr>
<tr>
<td>Fasting blood glucose, mean ± SD (mg/dL)</td>
<td>98 ± 10</td>
</tr>
<tr>
<td>HbA1c, mean ± SD (%)</td>
<td>5.81 ± 0.30</td>
</tr>
<tr>
<td>HbA1c ≥ 5.7% but &lt; 6.5% (prediabetes), ( n ) (%)</td>
<td>91 (73)</td>
</tr>
<tr>
<td>HbA1c 5.7–5.9%, ( n ) (%)</td>
<td>44 (35)</td>
</tr>
<tr>
<td>HbA1c ≥ 6.0% but &lt; 6.5% (high risk for diabetes), ( n ) (%)</td>
<td>47 (38)</td>
</tr>
</tbody>
</table>

\(^a\) Previous ocular trauma or inflammation of the affected eye and high myopia (≥ –6.0 diopters and/or axial length ≥ 26 mm)

\(^b\) Defined as greater or equal to 102 cm in men and greater or equal to 88 cm in women.

To convert fasting blood glucose to mmol/L, multiply by 0.0555. SD: standard deviation.

### 4. Discussion

In the present study, the prevalence of HbA1c-based undiagnosed diabetes and a high risk of developing diabetes was four to 11 times higher than in the corresponding population-based estimates from France [9] in a slightly older age group (55–74 years) and from the Netherlands [10] in exactly the same age group; both European populations had been examined in 2006/2007. In a US population during 1988 to 2006 [11], undiagnosed diabetes and a high risk of diabetes were four and nine times less frequent, respectively, in the group aged 40 to 59 years compared with our study population. Thus, in contrast to the distribution of blood glucose values in the general populations, the present study highlights a dramatic shift in our middle-aged cataract population towards an increased frequency of abnormal glucose metabolism. Overall, of the 200 cataract patients considered for our study, 66 (33%; 95% CI: 27–40%) had known or newly discovered diabetes, 46% were prediabetic and 21% were normoglycaemic. This is in striking contrast to the Dutch study where 7% of subjects were diabetic, 16% were prediabetic and 77% were normoglycaemic, despite having similar morphological parameters according to HbA1c subcategories [10]. These results suggest a continuum of cataract risk according to glucose levels, starting at high normal values and increasing further with diabetic values of blood glucose.

In diabetic patients, a causal relationship between hyperglycaemia and cataract is supported by the observed enhanced
cataract risk according to increased HbA1c levels [2,3] and its reduction with effective hypoglycaemia treatment [5,6]. The main proposed mechanisms linking increased blood glucose and accelerated cataract formation include the contribution of osmotic and oxidative stress, due to polyol accumulation in the lens, in which glucose is converted to sorbitol by the action of aldose reductase [12,13], and an increased non-enzymatic formation of advanced glycation end-products (AGEs), leading to irreversible crosslink formation between protein fibrils or oxidative products and a subsequently altered lens structure [14,15].

However, although these mechanisms may well be present at non-diabetic levels of blood glucose elevation, the link between hyperglycaemia and cataract formation has been poorly assessed in prediabetic patients. The metabolic syndrome, which is based on the association of factors including hyperglycaemia, hypertension, abdominal obesity and dyslipidaemia [16], has been found more frequently in cataract patients [4,17,18], but these studies included diabetic as well as prediabetic patients. In the longitudinal Beaver Dam Eye Study, increased HbA1c was associated with an increased risk of cataract only in non-diabetic women, who were 43 to 84 years of age [19]. The Australian Blue Mountains Eye Study showed a two-fold (95% CI: 1.20–3.36) greater 10-year incidence of cataract in participants with impaired fasting glucose (6.0–7.0 mmol/L) after controlling for age, gender, obesity, hypertension and lipids [4]. Our present study provides new data in favour of a role for subdiabetic hyperglycaemia in cataractogenesis. However, to reach any firm conclusions in this regard, further studies are needed to assess whether effective preventative strategies for diabetes can lower cataract incidence in prediabetic patients.

Our main study outcome is the identification of middle-aged patients undergoing cataract surgery as an important target population for diabetes screening. Indeed, 43% of the study patients had HbA1c values greater or equal to 6.0%, levels at which effective interventions are clearly recommended. French non-diabetic subjects aged 30 to 65 years with HbA1c greater than 5.9% showed a 50% risk of developing diabetes within 6 years [20]. A Japanese study found that the 3-year risk of developing overt diabetes in subjects with HbA1c greater or equal to 6.0% was 20.2% compared with 1.2% for HbA1c values of 5.5 to 5.9% [21]. In a US study, baseline HbA1c values of 6.0 to 6.4% were associated with a 44% 15-year incidence of diabetes, and a doubling of the risk of cardiovascular disease and death [22].

Cataract surgery is the most commonly performed operation in the developed countries with 600,000 people per year in France and 1.5 million people per year in the US undergoing the procedure, one-third of whom are aged less than 65 years. HbA1c testing has no practical issues in terms of daycare surgery, which is the rule in such cases, and is also unaffected by the acute perturbations in glucose levels that are generally expected during such procedures.

In conclusion, whereas no routine medical testing has been shown to improve the safety of cataract surgery [23], HbA1c measurement may be recommended at that time in middle-aged patients to screen for diabetes and its prevention, as such patients show a much higher prevalence of abnormal blood glucose levels than does the corresponding general population.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Financial support: none

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