Determination of HbA$_{1c}$ concentrations in patients with acute myocardial infarction: comparison of the DCA 2000 device with the HPLC method

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**Summary**

**Background:** Recent studies suggest that HbA$_{1c}$ is an important predictor of the glycometabolic state of patients admitted for acute myocardial infarction (AMI).

**Objective:** We aimed at comparing the results of HbA$_{1c}$ concentrations obtained by 2 different methods in patients with AMI.

**Research design and methods:** In a first study, HbA$_{1c}$ was measured in all patients consecutively hospitalized for AMI, during a 6-month period using the HPLC method and the DCA 2000 device in the biochemistry laboratory. In a second study, HbA$_{1c}$ measured by the DCA 2000 device in the intensive care unit was compared with HbA$_{1c}$ determined by HPLC in the biochemistry laboratory in a similar sample of patients. In patients without personal history of diabetes, those patients with HbA$_{1c}$ > 6.5% (HPLC method), were classified as possible diabetes.

**Results:** A total of 146 patients were included (119 males, 27 females; mean age: 63 ± 15 years). Twenty-seven of the patients had a personal history of diabetes. HbA$_{1c}$ determined by 2 techniques were highly correlated ($r = 0.939$, $P < 0.0001$). The mean of the differences (Bland and Altman analysis) was 0.4 ± 0.3%. Compared with the HPLC method, the sensitivity of DCA 2000 device for the detection of possible diabetes was 81.8 ± 11.6 and the specificity was 99.1 ± 0.9%. The diagnostic accuracy of DCA method was 97.5 ± 1.4%.

In the second study, the HbA$_{1c}$ concentrations of 21 additional subjects, determined in an intensive care unit, were not different from the first 21 patients of the first study.

**Conclusions:** HbA$_{1c}$ can be effectively determined using the DCA2000 device. This method is reliable and easy to be implemented in an intensive care unit.

**Key-words:** Acute myocardial infarction · Diabetes · Screening · HbA$_{1c}$.

**Résumé**

**Détermination de la concentration d’HbA$_{1c}$ chez des patients présentant un infarctus myocardique aigu : comparaison du dispositif DCA 2000 et de la méthode HPLC**

**État de la question :** Des études récentes suggèrent que l’HbA$_{1c}$ est un important prédicteur de l’état glycométabolique des patients hospitalisés pour infarctus myocardique aigu (IMA).

**Objectifs :** Nous avions pour objectif de comparer les résultats de concentrations d’HbA$_{1c}$ obtenues par 2 méthodes différentes chez des patients avec IMA.

**Design de l’étude et méthodes :** Dans une première étude, l’HbA$_{1c}$ a été mesurée chez tous les patients consécutivement hospitalisés pour AMI, pendant une période de 6 mois, en utilisant la méthode HPLC et le dispositif DCA 2000 dans le laboratoire de biochimie. Dans une seconde étude, l’HbA$_{1c}$ mesurée par DCA 2000 dans l’unité de soins intensifs a été comparée à celle déterminée par HPLC dans le laboratoire de biochimie dans un échantillon similaire de patients.

**Résultats :** Un total de 146 patients a été inclus (119 hommes, 27 femmes ; âge moyen: 63 ± 15 ans). Un antécédent personnel de diabète était connu chez 27 patients. Les HbA$_{1c}$ déterminées par les 2 techniques étaient en corrélation étroite ($r = 0.939$, $P < 0.0001$). La moyenne des différences (analyse de Bland et Altman) était de 0.4 ± 0.3%.

**Mots-clés :** Infarctus myocardique aigu · Diabète · HbA$_{1c}$ · Dépistage.
Introduction

Prevalence of undiagnosed diabetes at the time of acute myocardial infarction is quite high, ranging from 4.3 to 30% according to different studies. The determination of HbA1c has been proposed as a diagnostic tool to establish diabetes at the time of AMI [4]. As intensive glucose control has been shown to reduce coronary heart disease morbidity-mortality in diabetic patients [5], it is therefore important to identify undiagnosed diabetes patients as early as possible. Moreover, improved glycemic control by insulin therapy may be associated with worsening retinopathy in patients with type 2 diabetes [6]. The prevalence of retinopathy in newly diagnosed patients with type 2 diabetes may be quite high, at 37% in the UKPDS study [7].

The use of HbA1c determination to identify patients with diabetes at the time of AMI was based on HPLC method. We aimed to assess the value of the BAYER-DCA 2000 device for the emergency determination of HbA1c concentrations. Results obtained with this device were compared to those obtained by the routine, non urgent, high-performance-liquid-chromatography (HPLC) method in patients with AMI.

Research design and methods

First study

All patients consecutively admitted to the Poitiers University Hospital for suspected AMI in a 6-month period were eligible for the study. Myocardial infarction was defined according to ESC/ACC criteria [8]. All patients with AMI, defined as myocardial infarction that had lasted for less than 48 hours upon admission, were eligible for the study. Exclusion criteria included chronic renal failure (defined as creatinine clearance lower than 30 ml/min, according to the Cockcroft formula [9]) and post-AMI coronary artery by-pass graft surgery. Patients with recurrent AMI already included in the study were only analyzed once.

Patients and their general practitioners were carefully interviewed to assess diabetes status. Patients with a personal history of diabetes mellitus were considered to have "previously diagnosed diabetes" (PDD), regardless of whether hypoglycemic agents were prescribed or not. In patients without PDD, those patients with high HbA1c (> 6.5% using HPLC method) were classified as "Possible Diabetes" (PD), those with HbA1c < 6.5% were classified as Non Diabetes (ND).

Blood glucose was regularly monitored for AMI patients. Patients with blood glucose concentrations > 11.1 mmol/l were routinely given insulin, regardless of whether diabetes had previously been diagnosed or not. This corresponds to normal practice in our center.

In this first study, HbA1c was measured by the two methods in the biochemistry laboratory.

The protocol was reviewed by the institutional clinical research board of the Poitiers University Hospital. All patients gave informed consent. This study was in conformity with the Helsinki declaration.

Second study

HbA1c determined by the DCA 2000 device in the intensive care unit was compared with HbA1c determined by HPLC in the biochemistry laboratory in a similar sample of patient. The results of the 21 additional patients were compared with those from the first 21 patients in the first study.

Analytical methods

Blood sample was taken upon admission for routine emergency measurement of cardiac enzymes, clotting factors, plasma creatinine and glucose concentrations. Commercial kits were used to measure CK and CK MB (Roche Diagnostics — Meylan, France). Troponin I was measured by a chemoluminescent immunometric method (DPC-Gagny, France). Creatinine concentrations were determined using the modified Jaffé’s method and plasma glucose was measured using the glucose oxidase method (Roche Diagnostics — Meylan, France).

HbA1c was assessed in blood samples collected on EDTA using the Bayer DCA 2000 device (Bayer Diagnostics — Puteaux, France). This uses an immunological method to measure HbA1c. Normal values range from 4 to 6%. We also used the HPLC method (Biorad — DIAMAT, Ivry-sur-Seine, France) to determine HbA1c concentrations. Normal values range from 4.5 to 6.5%.

Statistical analysis

Data are given as means ± one SD or as median (ranges). Categorical variables were analyzed using the chi-square tests. The HbA1c values determined by HPLC and the DCA 2000 device were analyzed using correlation coefficient. The mean of the differences between both methods was plotted as described by Bland and Altman [10]. Ability of both methods to detect PD was compared using HPLC as the reference method. The sensitivity, specificity and diagnostic accuracy of the DCA 2000 method were determined. A two-sided P value of < 0.05 was considered to be statistically significant.

Results

First study

There were 174 patients who were presumed to be eligible for the study during the 6-month period of study: 8 were excluded for non acute myocardial infarction (> 48 hours), 6 because of no increase in troponin Ic and/or
CK, 9 for renal failure and 5 for lack of HbA1c determination. Study population has been already described elsewhere [11]. Briefly, 119 patients were males and 27 females. Mean age was 63 ± 15 years and mean body mass index (BMI) was 26.6 ± 5.0 kg/m². Plasma glucose concentration on admission was 8.35 ± 3.71 mmol/l.

The results generated by the two techniques of HbA1c determination were highly correlated (r = 0.939, P < 0.0001). The mean of the differences (Bland and Altman analysis) between both techniques was 0.4 ± 0.3% both in the whole cohort (Fig 1) and in patients without PDD (Fig 2). Thus, the threshold at 6.5% according to the HPLC method corresponded to 6.1% according to the DCA 2000 device.

Using the HPLC method, 11 of the 119 patients without PDD were classified as PD and 108 as ND. According to the DCA 2000 technique, using the 6.1% threshold, 10 patients were PD and 109 were ND. Plasma glucose concentration on admission in PD patients was 8.4 ± 2.1 mmol/l (6.2-13.7 mmol/l). In ND patients, it was 7.7 ± 2.9 mmol/l (4.7-23.4 mmol/l). Compared with the HPLC method, sensitivity of the DCA 2000 method for the detection of PD was 81.8 ± 11.6 and specificity was 99.1 ± 0.9%. Diagnostic accuracy of the DCA method was 97.5 ± 1.4%.

Second study

A total of 21 patients was considered for the secondary study, after the first study was completed. In the first 21 patients, there were 5 PDD and 4 PD. In the second study, there were 4 PDD and 1 PD. Age did not differ between patients from the secondary and the first 21 patients from the first study: 66 ± 12 vs 68 ± 11 years; P = 0.49. There was no difference in plasma glucose concentrations on admission between the two groups (8.5 ± 5.1 vs 9.3 ± 3.4 mmol/l; P = 0.53). Values of HbA1c were similar between patients from the second and the first 21 patients from the first study using HPLC: 6.2 ± 1.3 vs 6.3 ± 1.1%; P = 0.85, respectively and using DCA 2000: 5.9 ± 1.4 vs 6.10 ± 1.2%; P = 0.81, respectively. Mean of the differences (Bland and Altman analysis) between both techniques was 0.28% (-0.40 to +0.90) in the second study group and 0.25% (-0.60 to +0.90) in the first study group (P = 0.80). Correlation between both techniques of determination of HbA1c was not different in the first and the second studies (Fig 3).

Discussion

In this paper, we showed that the DCA 2000 device was suitable for the determination of HbA1c levels in patients with acute myocardial infarction. It has an excellent diagnostic accuracy for the identification of patients with “possible diabetes”. It was feasible and reliable to implement the DCA 2000 in the intensive care unit.

Question of the use of an emergency method to determine HbA1c concentration is of interest. In a recent study, Norhammar et al. have shown that type 2 diabetes prevalence was very high in patients with no personal history of diabetes after acute myocardial infarction [12]. In this study, HbA1c was the only predictive independent factor of diabetes or glucose intolerance.
In the DIGAMI study, a strict metabolic control was associated with a reduction of cardiovascular morbidity after acute myocardial infarction in diabetic patients. It is thus of interest to identify those patients who might dramatically benefit by intensive metabolic control [13].

Prevalence of retinopathy in newly diagnosed patients with type 2 diabetes may be high, reaching 37% in patients included in the UKPDS study [7]. Furthermore, HbA1c determination has been recently shown to predict diabetic retinopathy in a population of Japanese subjects without known diabetes [14]. Improved glycemic control by insulin therapy may be associated with worsening retinopathy in patients with type 2 diabetes [6]. Thus, the emergency determination of HbA1c could help to identify patients with “possible diabetes” and also to identify those patients who should be referred for ophthalmological examination.
The classification of diabetes we used tried to identify patients who would benefit from strict metabolic control. “Possible diabetes” does not refer to a validated classification, but rather indicates those patients with a very high risk of type 2 diabetes, as mentioned previously [11].

In our study, we showed that the DCA 2000 device generated similar results as compared with the HPLC method with a mean minimization by 0.4% in diabetic and non diabetic AMI patients. A large scale multicenter evaluation of the DCA 2000 was performed in 1016 diabetic patients. It also confirmed the precision of the determination of HbA1c concentration [15]. We also found that it was feasible and reliable to implement the DCA 2000 device in a cardiology intensive care unit. This confirms the results of a previous study comparing DCA 2000 device determination in a pediatric, gynecologic and general practice clinic with the HPLC method determined in a biochemistry laboratory [16].

To our knowledge, the present study is the largest one studying the DCA 2000 device in a population of non diabetic patients, at high risk of glycometabolic abnormalities. Some limit is that the second study did not truly compare the results of the DCA 2000 determination of HbA1c concentration in an intensive care unit and in the biochemistry laboratory. We namely compared 21 additional patients with the first 21 patients in the first study. However, our results strongly suggest that the determination of HbA1c by the DCA 2000 device generated equivalent results in an intensive care unit or in a biochemistry laboratory.

In conclusion, DCA 2000 device is a reliable method for determining HbA1c levels in patients with acute myocardial infarction and to identify patients with possible diabetes. Whether the determination of patients with possible diabetes, that may lead to an intensive glycemic control, leads to an improved survival after acute myocardial infarction remains to be determined.

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References