Frequency and Severity of the Dawn Phenomenon in Type 2 Diabetes

Relationship to age

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OBJECTIVE—To know whether age has an independent effect on the dawn phenomenon in noninsulin-using type 2 diabetes.

RESEARCH DESIGN AND METHODS—Eighty-one individuals with type 2 diabetes were matched for HbA_{1c} and divided by age into three subgroups of 27 individuals (1: ≥70 years; 2: 60–69 years; and 3: ≤59 years). All underwent ambulatory continuous glucose monitoring for quantifying the dawn phenomenon (i.e., the absolute [∂G, mg/dL] or relative [∂G%] increments from nocturnal nadirs to prebreakfast time points).

RESULTS—HbA_{1c} levels and 24-h glycemic profiles were similar across the three groups. Glucose increments (mean ± SEM) were identical in the three groups: ∂G (mg/dL), 22.0 ± 4.7 (1), 21.3 ± 3.6 (2), and 18.0 ± 3.6 (3) and δG (%), 19.9 ± 4.9 (1), 21.6 ± 4.4 (2), and 17.6 ± 4.2 (3). Using the most common definition (∂G >10 mg/dL), the prevalence of the dawn phenomenon was 52, 70, and 59% in groups 1, 2, and 3, respectively.

CONCLUSIONS—The dawn phenomenon is present in the elderly.

Diabetes Care 35:2597–2599, 2012

The dawn phenomenon is a feature of dysglycemia likely to be common in most subjects with type 1 or type 2 diabetes (1–3). However, the definition of this condition remains somewhat unclear, and controversy still exists about its magnitude and frequency, especially in elderly individuals with type 2 diabetes (4,5). For that reason, we set out to explore whether the magnitude and frequency of the dawn phenomenon in type 2 diabetes varied across different age categories.

RESEARCH DESIGN AND METHODS

This study was conducted in 81 individuals with type 2 diabetes who were divided into three groups of 27 patients according to whether the ages were ≥70 years (group 1), between 60 and 69 years (group 2), or ≤59 years (group 3). The three groups were matched for HbA_{1c}.

Modalities of treatment were classified into three categories and similarly distributed within the three groups: *1*) insulin sensitizers alone (metformin and/or thiazolidinediones), *2*) insulin secretagogues alone (sulfonylureas or glinides), and *3*) combinations of insulin secretagogues and insulin sensitizers.

The study was observational in design. All participants were investigated at the outpatient clinic of the University Hospital in Montpellier from 2005–2010 and gave informed consent in accordance with French law in article L-1121-1 of the Code for Public Health concerning the conductance of Biomedical Research (6).

HbA_{1c} levels were determined using a high-performance liquid chromatography assay (Menarini Diagnostic, Florence, Italy) (7). All patients underwent ambulatory continuous interstitial glucose monitoring for 3 consecutive days by second-generation Minimed systems (Medtronic, Northridge, CA). All calculations were derived from data averaged over a 48-h period on 2 consecutive days.

The dawn phenomenon was quantified by detecting the exact time point and value of the glucose nadir during the nocturnal period (starting at midnight) and subtracting this value from that observed just before the beginning of breakfast. The breakfast time was recorded by each individual in a logbook. When all nocturnal glucose values were above the prebreakfast glucose value, the blood glucose rise in the early morning was considered to be absent, and its magnitude and duration were recorded as being equal to 0. The duration was assessed by measuring the time interval between the nadir and prebreakfast time points. On the basis of published studies (2,8,9), three definitions were used: an absolute dawn increase in glucose level above either 10 or 20 mg/dL and a relative increase >6.9% (10). The features of the dawn phenomenon as defined by these three criteria were compared among the three groups of subjects investigated.

Results are given as means ± SEM. Comparisons of magnitude of the dawn phenomenon in the different groups were made using ANOVA. Prevalence of the dawn phenomenon was compared among the three groups by using the χ^2 Fisher exact test for comparison of frequency. Statistical comparisons were considered significant when P values were ≤0.05. Analyses were performed with the Statview statistical package, version 5 for Macintosh (SAS Institute, Cary, NC).

RESULTS

The demographic characteristics of the patients were as follows in groups 1, 2, and 3, respectively: mean HbA_{1c} levels ± SEM, 7.96 ± 0.28, 7.97 ± 0.29, and 7.97 ± 0.27%; mean age ± SEM, 73.4 ± 0.5, 64.0 ± 0.5, and 53.2 ± 1.1 years; and mean BMI ± SEM, 30.3 ± 1.2, 30.1 ± 1.0, and 29.9 ± 1.1 kg/m^2. Mean glucose profiles are illustrated in Fig. 1*A*. No

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Received 27 February 2012 and accepted 18 June 2012.
DOI: 10.2337/dc12-0385

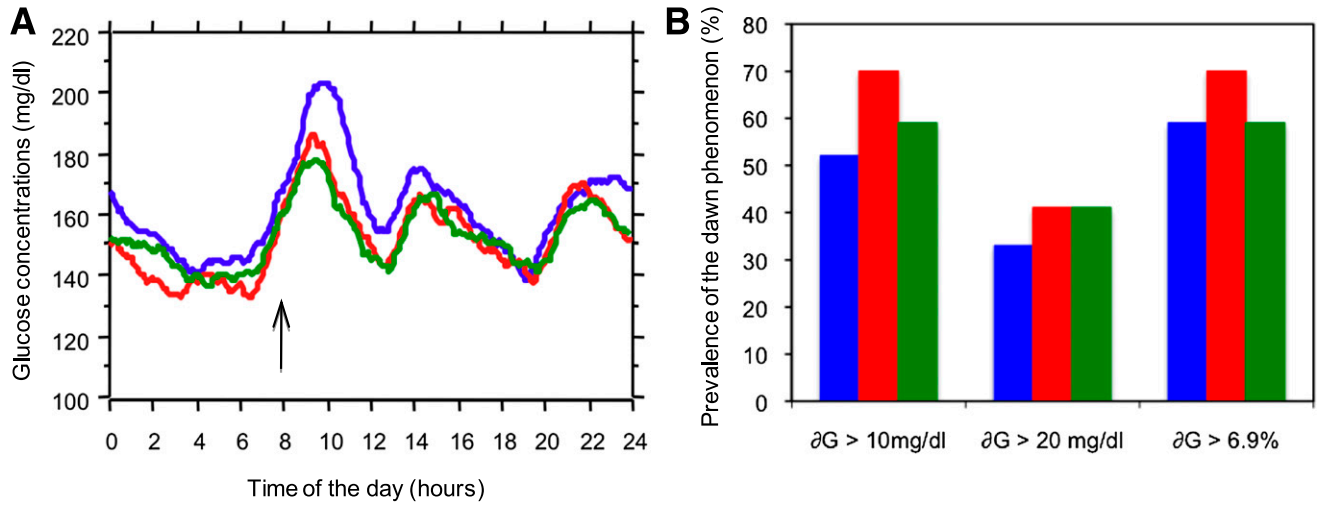

Figure 1—*Twenty-four–hour continuous glycemic profiles* (A) *and prevalence of the dawn phenomenon expressed as percentage* (B) *in the three groups of patients divided according to whether ages were: ≥70 years (group 1, blue curve or columns), 60–69 years (group 2, red curve or columns), and ≤59 years (group 3, green curve or columns). The prevalence of the dawn phenomenon was calculated for the three definitions that were used: ∂G > 10 mg/dL, ∂G > 20 mg/dL, and ∂G > 6.9%. The mean breakfast time in the population considered as a whole is indicated by the vertical arrow (7:45 A.M.) with an SD of 55 min.*

statistical differences were observed among the three groups.

In the three groups of patients, the absolute glucose increments (∂ glucose, mg/dL) from nocturnal glucose nadir to prebreakfast value were similar: 22.0 ± 4.7 mg/dL (group 1), 21.3 ± 3.6 mg/dL (group 2), and 18.0 ± 3.6 mg/dL (group 3). In addition, no differences were found when the results were expressed as relative glucose increments from value at nadir to those observed at prebreakfast time point (∂ glucose, %): 19.9 ± 4.9 (group 1), 21.6 ± 4.4 (group 2), and 17.6 ± 4.2 (group 3). Mean durations of the dawn phenomenon were not statistically different between the three groups: 171 ± 28 min (group 1), 204 ± 23 min (group 2), and 166 ± 27 min (group 3).

Frequencies were similar between the different age-groups irrespective of the criteria used for the definition of the dawn phenomenon (Fig. 1*B*).

CONCLUSIONS—The frequency of the dawn phenomenon did not differ when the subjects with type 2 diabetes were compared by age. In addition, the mean magnitude of blood glucose rise in the early morning from nocturnal nadirs to prebreakfast values did not show any difference among the groups and was equal to ~20 mg/dL. One of the main strength of the current study is that the quantification of the dawn phenomenon was assessed with continuous glucose monitoring systems that permit calculation of the absolute differences between nocturnal nadirs and prebreakfast glucose values with an accuracy not previously available (11–13).

Reverting to the frequency of the dawn phenomenon across categories of age, it must be noted that the percentages are similar for the different definitions that were used. As a consequence, this dysglycemic state should be taken into consideration in the treatment of individuals with type 2 diabetes, even of those who are >70 years of age. This position is reinforced by the fact that the dawn phenomenon is usually followed by an abnormally high postbreakfast glucose excursion, which corresponds to what is commonly referred to as the extended dawn phenomenon (11), a glycemic disorder that can be simply explained by the remnant effect of the hepatic glucose overproduction during the morning period (14) in combination with the dietary intake of carbohydrates at breakfast time. The dawn and extended dawn phenomena are both weak links in the management of many individuals with type 2 diabetes (11).

The glycemic patterns as observed in the current study demonstrate that both phenomena are evident in elderly type 2 diabetic subjects >70 years old to the same extent as those who are <70 years old.

In conclusion, failing to address the dawn and extended dawn phenomena can contribute to inadequate overall glycemic control and increase the risk for development or progression of diabetes complications even in the elderly. Due to the small size of the investigated population, the present results warrant further investigation.

Acknowledgments—This study was supported by academic funds provided by the University of Montpellier I.

No potential conflicts of interest relevant to this article were reported.

L.M. contributed to the design of the study, analyzed data of the study, and wrote, reviewed, and edited the manuscript. C.C. contributed to the analysis of data and reviewed and edited the manuscript. M.S. and G.B. participated in the clinical care and follow-up of the patients. A.R.-Z. and D.O. contributed to the design and reviewed the manuscript. L.M. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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