Can J Diabetes 39 (2015) 428–433

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

Original Research

High Incidence of Hypoglycemia in Stable Insulin-Treated Type 2 Diabetes Mellitus: Continuous Glucose Monitoring vs. Self-Monitored Blood Glucose. Observational Prospective Study

Marcos Pazos-Couselo RN, PhD [a,*], Jose Manuel García-López MD, PhD [a], Maria González-Rodríguez RD [a], Francisco Gude MD, PhD [b], Jose Manuel Mayán-Santos MD, PhD [c], Santiago Rodríguez-Segade [d], Javier Rodríguez-García MD, PhD [d], Felipe Casanueva MD, PhD [a,e]

[a] *Hospital Complex Santiago de Compostela, Endocrinology and Nutrition Service, Santiago de Compostela, Spain*
[b] *Hospital Complex Santiago de Compostela, Clinical Epidemiology Unit, Santiago de Compostela, Spain*
[c] *University of Santiago de Compostela, Gerontology Department, Santiago de Compostela, Spain*
[d] *University of Santiago de Compostela, Biochemistry and Molecular Biology, Santiago de Compostela, Spain*
[e] *Physiopathology of Obesity and Nutrition Biomedical Research Network Consortium, Santiago de Compostela, Spain*

ARTICLE INFO

Article history:
Received 24 February 2015
Received in revised form
24 April 2015
Accepted 6 May 2015

Keywords:
continuous glucose monitoring
hypoglycemia
self-monitored blood glucose
type 2 diabetes

ABSTRACT

Objectives: Hypoglycemia is a limiting factor in the achievement of strict glycemic control. The primary objective of this 9-week study was to determine the frequency of hypoglycemia in patients with stable insulin-treated type 2 diabetes mellitus by comparing self-monitored blood glucose (SMBG) measurement with continuous glucose monitoring (CGM).
Methods: This was an observational prospective study. Included in the study were 63 stable, insulin-treated patients with type 2 diabetes. They were instructed to record 2 daily capillary blood glucose readings, pre- and/or postprandial, in a sequential way during 8 consecutive weeks. A CGM system was worn during an additional week. We evaluated the frequency of hypoglycemia using the 8-week SMBG profile and the 1 CGM week.
Results: SMBG revealed that 50% of the patients had experienced hypoglycemia. CGM found hypoglycemia in 59% of patients. Significantly higher percentages of hyperglycemic and hypoglycemic episodes were detected by CGM than by capillary blood glucose measurements (61.1% vs. 50.8%; p=0.047) and (3.8% vs. 1.7%; p=0.016); 33% of patients experienced nocturnal hypoglycemia, and 19% of patients who had no data concerning hypoglycemia recorded in the capillary blood glucose diary had experienced hypoglycemia as measured by CGM, and the hypoglycemia occurred mainly during the nocturnal period.
Conclusions: In stable well-controlled, insulin-treated patients with type 2 diabetes, CGM showed higher numbers of hypoglycemic events than did SMBG, especially at night. CGM is a useful tool that provides clinically valuable information about glucose control in these patients.

Mots Clés :
surveillance du glucose en continue
hypoglycémie
autosurveillance glycémique du diabète de type 2

RÉSUMÉ

Objectifs : L'hypoglycémie est un facteur limitant dans l'exécution d'un contrôle strict de la glycémie. L'objectif principal de cette étude de 9 semaines était de déterminer la fréquence de l'hypoglycémie chez les patients atteints d'un diabète de type 2 stable, traité à l'insuline, en comparant les mesures d'autosurveillance glycémique (ASG) avec celles d'une surveillance du glucose en continu (SGC).
Méthodes : Il s'agit d'une étude prospective observationnelle. Soixante trois patients stables avec un diabète de type 2 traité à l'insuline ont été inclus. Ils ont été invités à enregistrer 2 lectures quotidiennes de glycémie capillaire, avant et / ou après le repas, d'une manière séquentielle pendant 8 semaines consécutives. Un dispositif de SGC a été porté pendant une semaine supplémentaire. Nous avons évalué la fréquence de l'hypoglycémie en utilisant le profil de l'ASG de 8semaines et celui de la semaine sous SGC.
Résultats : L'ASG a révélé que 50% des patients avaient présenté une hypoglycémie. La SGC a montré une hypoglycémie chez 59% des patients. Des pourcentages significativement plus élevés d'épisodes hyperglycémiques et hypoglycémiques ont été détectés par SGC plutôt que par des mesures de glycémie

* Address for correspondence: Marcos Pazos-Couselo, RN, PhD, Endocrinology and Nutrition Service, Hospital de Conxo, Santiago de Compostela, 15702, Spain.
E-mail address: marcospazos@gmail.com

1499-2671/$ – see front matter © 2015 Canadian Diabetes Association
http://dx.doi.org/10.1016/j.jcjd.2015.05.007

capillaire (61,1% contre 50,8%, p = 0,047) et (3,8% contre 1,7%; p = 0,016); 33% des patients ont eu une hypoglycémie nocturne, et 19% des patients qui n'ont pas eu de données d'hypoglycémie enregistrées dans le registre de glycémie capillaire ont expérimenté une hypoglycémie mesurée par SGC, et cette hypoglycémie avait lieu surtout pendant la nuit.

Conclusions : Chez les patients avec un diabète de type 2 stable, bien contrôlé et traité à l'insuline, la SCG a rapporté un plus grand nombre d'événements hypoglycémiques que l'a fait l'ASG, surtout la nuit. La SCG est un outil utile qui fournit des informations cliniquement précieuses sur le contrôle du glucose chez ces patients.

Introduction

The benefits of strict glycemic control in patients with diabetes mellitus have been demonstrated clearly (1,2), but hypoglycemia remains a limiting factor in reaching this objective.

Data concerning the rates of hypoglycemia in patients with type 2 diabetes are scarce, even though there is a general opinion that it occurs with low frequency (3). There are some limitations in reporting hypoglycemia because many hypoglycemic events are asymptomatic (4), and many patients fail to register these episodes. Also, the frequency of occurrence of hypoglycemia is usually underestimated.

Nocturnal hypoglycemia is common, and more than half of the occurrences are asymptomatic. Usually, they are not detected by the normal patterns of self-monitored blood glucose (SMBG) levels performed prior to meals, occasionally postprandially and less commonly at night (5). SMBG is a reliable tool for the assessment of glucose control, but it provides an incomplete image of glucose oscillations and does not provide data about nocturnal periods.

Continuous glucose monitoring (CGM) allows us to obtain a 24-hour measurement of blood glucose and gives us information about nocturnal periods that is commonly missed when patients are using SMBG. Our aim was to determine which of the current glucose-monitoring methods (SMBG or CGM) gives us more useful information about glucose control in stable, insulin-treated patients with type 2 diabetes, especially in detecting hypoglycemia.

Methods

This was an observational prospective study, 9 weeks in duration, of stable, insulin-treated patients with type 2 diabetes conducted in a single centre, the Hospital Clínico Universitario de Santiago de Compostela in northwestern Spain.

Patients

We enrolled 63 patients in this 9-week study. The characteristics of the study group are presented in Table 1. The inclusion criteria were 1) being older than 40 years of age; 2) having a body mass index <40 kg/m^2; 3) having type 2 diabetes for at least 1 year; 4) being on insulin therapy for at least 3 months before recruitment; 5) having the ability to perform self-monitoring; 6) being able to wear a CGM system during 1 week and 7) having a stable metabolic situation, defined as having no need to add new treatments or make any changes in insulin dosage of more than 10% in the preceding 2 months (6).

The exclusion criteria included 1) advanced micro- or macrovascular diabetic complications; 2) clinically significant systemic disease; 3) psychiatric disease that impairs compliance; 4) pregnancy or breast feeding; 5) corticosteroid use or any medication that could produce a major interference with glucose control; 6) alcohol or drug abuse and 7) inability to fulfill the protocol.

Of the 63 patients recruited, 4 did not complete the study, and 7 were excluded for failure to meet the inclusion criteria.

Of the 52 patients who completed the 9-week protocol period, 42 fulfilled the complete protocol, including the continuous glucose monitoring. The reasons for exclusion in this analysis were as follows: 2 patients left the study on the basis of their own decisions; 3 patients did not provide enough data for device calibration; 3 patients were excluded for loss of CGM data due to bad adherence of the glucose sensor to the skin and 2 were excluded because of insufficient glucose data due to loss of signal.

Study procedure

The patients were recruited from our diabetes clinic when they came for their routine checks. The recruitment period extended from June 2012 to June 2013. We required 4 visits to our clinic. The initial consultations occurred after obtaining informed consent and included complete clinical evaluations of the patients, who were instructed in SMBG using BG Star (Sanofi-Aventis, Paris, France). Blood samples were obtained for plasma glycated hemoglobin (A1C) measurements. The patients were instructed to record daily blood glucose measurements and to document in their diaries any hypoglycemic episodes. During the study time, they had free access to blood-test strips and were asked to maintain their usual diets and pharmacologic treatments.

During a period of 8 weeks, the patients underwent structured pre- and postprandial blood glucose monitoring at the 3 main meals, alternating throughout the week following this pattern: day 1, prebreakfast and 2 hours postbreakfast; day 2, prelunch and 2 hours postlunch; day 3, predinner and 2 hours postdinner; and day 4, pre- and postprandial 6-point profile. This pattern was repeated during the 8 weeks.

At week 9, a blind continuous glucose-monitoring system sensor (iPro2; Medtronic MiniMed, Inc. Northridge, California, USA) was inserted subcutaneously in the abdominal periumbilical area. The sensor used was Enlite Medtronic. This allowed subcutaneous interstitial glucose levels to be monitored on an ambulatory basis over a period of 7 consecutive days. Technical details have been described previously (7). At the last visit, the CGM devices were

Table 1
Clinical characteristics of patients

Number	52
Men	31 (60%)
Women	21 (40%)
Age (years)	62±7
Duration of diabetes (years)	11±7
BMI (kg/m^2)	31.7±4.0
Insulin*	
Basal insulin	17 (33%)
Mixtures of standard insulin	15 (29%)
Basal insulin +3 rapid insulin	20 (38%)
Treatment	
Insulin alone	18 (35%)
Insulin + OAD monotherapy	21 (40%)
Insulin + OAD combination	13 (25%)

BMI, Body mass index; *OAD,* oral antidiabetic drugs.

* Basal insulin: insulin detemir (Novo Nordisk); insulin glargine (Sanofi-Aventis); mixtures of standard insulin: Human insulin 30/70 (Novo Nordisk); human insulin 50/50 (Novo Nordisk); basal insulin +3 rapid insulin (Insulin Novorapid; Novo Nordisk), insulin Apidra (Sanofi Aventis); insulin Humalog Kwikpen (Eli Lilly).