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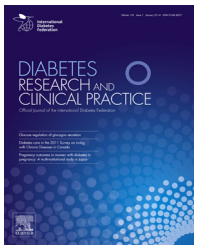

Evaluation of blood glucose fluctuation in Japanese patients with type 1 diabetes mellitus by self-monitoring of blood glucose and continuous glucose monitoring

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ABSTRACT

Aims: Accurate assessment of blood glucose fluctuation is essential for managing blood glucose control while avoiding hypoglycemia in patients with diabetes mellitus. In this study, blood glucose was measured by continuous glucose monitoring (CGM) in patients with type 1 diabetes mellitus (T1DM) whom self-monitoring of blood glucose (SMBG) was carried out three or more times per day, and evaluation was performed using blood glucose fluctuation parameters obtained by CGM and SMBG.

Methods: Twenty-nine insulin-depleted patients with T1DM were enrolled. Their blood glucose fluctuations were measured at the same time by SMBG and CGM, and the correlations were evaluated.

Results: Correlations were found between the following values obtained by SMBG and CGM: mean and standard deviation of blood glucose levels, average daily risk range, Morbus value and high-blood-glucose index. The hypoglycemia duration and the nocturnal hypoglycemia duration showed no correlation with any of the blood glucose fluctuation parameters obtained by SMBG.

Conclusions: The findings suggest that routine SMBG and glycated hemoglobin (HbA1c) measurement are sufficient for evaluation of hyperglycemia in T1DM. On the other hand, blood glucose fluctuation parameters obtained by SMBG and HbA1c have been shown to have no correlations with either hypoglycemia duration or nocturnal hypoglycemia duration.

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1. Introduction

In the Diabetes Control and Complications Trial (DCCT) with type 1 diabetes mellitus (T1DM), the development and progression of microvascular complications was found to be lower in the intensive therapy group than in the conventional therapy group, and similar results were found in the UK Prospective Diabetes Study (UKPDS), carried out with type 2 diabetes mellitus (T2DM) [1,2]. Therefore, strict blood glucose control has been recommended for preventing the development and progression of diabetic complications. On the contrary, the frequency of hypoglycemia has been found to increase in the intensive therapy group [1,2]. The successively reported results of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial and the Veterans Affairs Diabetes Trial (VADT), all of them showed no decrease in the risk of developing cardiovascular diseases with strict blood glucose control, but in fact suggested the possibility of an excessively strict blood glucose control leading to severe hypoglycemia and weight gain [3–6]. In the ACCORD trial in particular, the total mortality risk in the intensive therapy group exceeded that in the conventional therapy group after a mean period of 3.5 years, and the intervention trial was therefore terminated at that time [3]. It has been reported that there are associations between severe hypoglycemia and increased cardiovascular disease risk, lethal arrhythmias and dementia [7–9]. Furthermore, it has been suggested that nocturnal hypoglycemia can result in dead-in-bed syndrome even in T1DM [10,11]. Therefore, it is essential to define and establish therapeutic targets for individual patients, taking into consideration factors such as age, and risk of hypoglycemia with currently available diabetes treatment methods [12].

In clinical use, continuous blood glucose monitoring (CGM) and self-monitoring of blood glucose (SMBG) are used for evaluation of blood glucose fluctuation. Furthermore, in addition to mean blood glucose concentration, parameters that can be calculated on the basis of SMBG and CGM include standard deviation (SD), Morbus value (M-value), average daily risk range (ADRR), and mean amplitude of glycemic excursions (MAGE), and these have been reported to be useful as indices of blood glucose fluctuation [13–16].

Accurate assessment of blood glucose fluctuation is essential for managing blood glucose control while avoiding hypoglycemia in patients with diabetes mellitus. The objectives of the present study were to clarify whether there are correlations between (i) blood glucose fluctuation parameters obtained by CGM and by SMBG; and (ii) hypoglycemia duration, nocturnal hypoglycemia duration and hyperglycemia duration obtained by CGM and blood glucose fluctuation parameters obtained by SMBG, in insulin-depleted patients with T1DM. In the present study, blood glucose fluctuation was measured by SMBG carried out at least three times per day, and blood glucose fluctuation was measured by CGM at the same time. Furthermore, the relationships between glycated hemoglobin (HbA1c) and blood glucose fluctuation parameters obtained by CGM and SMBG were evaluated.

2. Materials and methods

2.1. Subjects

The subjects of this study were patients with type 1 diabetes mellitus who had been treated with intensive insulin therapy for over 12 months at the Division of Diabetes Endocrinology and Metabolism, Department of Internal Medicine, Hyogo College of Medicine (Hyogo, Japan). Patients had *ad libitum* serum C-peptide immunoreactivity (CPR) <0.3 ng/mL, and exhibited severe impairment of endogenous insulin secretion. This study was performed in accordance with the Helsinki Declaration. This study was approved by the Ethics Committee of Hyogo College of Medicine. All subjects were given sufficient explanations using appropriate documents, and the informed consent of each was obtained.

The exclusion criteria were as follows:

(a) Severe hepatic and/or renal impairment.
(b) Severe infection, perioperative status, or severe trauma.
(c) The insulin formulation had been changed within the previous 1 month.
(d) The insulin dose was changed by 10% or more during the study period.
(e) The HbA1c changed by 10% or more during 3 months before and/or after the study.
(f) Ischemic heart disease, either currently being treated or as previous history.
(g) Cancer.
(h) Other reasons leading the physician in charge to judge the patient to be unsuitable.

2.2. SMBG

SMBG was carried out using MediSafe Fit (Terumo Co., Ltd., Tokyo, Japan), OneTouch Ultra (Johnson and Johnson, New Brunswick, New Jersey, USA), or Glutest Neo α (Sanwa Kagaku Kenkyusho Co., Ltd., Nagoya, Japan). It was primarily on an out-patient basis, and blood glucose measurement by SMBG was carried out at least three times per day for 14 days or more but less than 31 days.

2.3. CGM

CGM was carried out using CGMS Gold® or iPro™ 2 Monitor (Medtronic Minimed, Northridge, California, USA). Blood glucose fluctuation was measured by CGM for at least 3 days and the data for 3 consecutive days were used.

2.4. Blood glucose fluctuation parameters

The mean and median blood glucose levels were calculated from SMBG and CGM data. In addition, as blood glucose fluctuation parameters, SD, interquartile range (IQR), M-value, ADRR, low blood glucose index (LBGI), and high blood glucose index (HBGI) were calculated [13,17–19]. Furthermore, MAGE and mean of daily difference (MODD) were calculated from CGM data [20].