Postprint of a Study Evaluating the Effect of Outpatient Education on Glycemic Profiles in Patients with Type 2 Diabetes Based on Continuous Glucose Monitoring Results

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Date: 2024-03-11T00:00:00+00:00

Abstract

Background Continuous Glucose Monitoring (CGM) is less commonly used in outpatient treatment, and the impact of diabetes education based on CGM, which aims to change unhealthy lifestyle and dietary habits, on the glycemic profile remains unclear. Objective Based on retrospective CGM results, to conduct outpatient education on diet, exercise, etc., for outpatients with type 2 diabetes mellitus (T2DM) using oral hypoglycemic agents, and to evaluate its impact on patients' glycemic profiles. Methods A total of 88 outpatients with T2DM using oral hypoglycemic agents who visited the Endocrinology Department of Nanjing First Hospital from 2021 to 2021 were selected, including 60 males and 28 females, and were provided with CGM. The enrolled patients received outpatient education, i.e., maintaining the original hypoglycemic treatment regimen and lifestyle habits on days 1-3; downloading and analyzing CGM data on day 4, combined with outpatient education on diet, exercise, etc.; removing the CGM sensor and recorder on day 6 and downloading data. The continuous glucose monitoring data on day 2 and day 5 were compared [24-hour mean blood glucose (MBG), mean amplitude of glycemic excursions (MAGE), time in range (TIR)]. Results Based on CGM results, after receiving outpatient education (on day 5), MBG in T2DM patients decreased from (8.34$±1.97)*mmol/Lto*(7.85±1.65)*mmol/L, TIRincreasedfrom*(78.21±24.64)±21.87)±2.25)*mmol/Lto*(3.80± mmol/L (P<0.05). Stratified analysis by diabetes duration and age: both the <10 years duration group and the $ $10 years duration group showed decreased MBG after intervention, and the <10 years duration group showed reduced MAGE and standard deviation (SD) compared with the $ $10 years duration group (P<0.05); when divided into <65 years and $ $65 years groups by age, MBG in both groups decreased after intervention, and the <65 years group showed reduced MAGE and SD compared with the $ $10 years duration group (P<0.05). Conclusion Based on CGM results, conducting outpatient education on diet, exercise, etc., for outpatients with T2DM using oral hypoglycemic agents can effectively improve patients' MBG, increase TIR levels, and ameliorate glycemic variability; patients aged <65 years with diabetes duration <10 years benefit more.

Full Text

Introduction

The prevalence of diabetes among Chinese adults continues to rise, reaching 12.8% by 2021 [1]. Multiple studies, including UKPDS and DCCT, have demonstrated that poor glycemic control is closely associated with diabetic complications [2-3]. However, the rate of achieving glycemic targets among patients receiving treatment remains only 50.1% [4], underscoring the urgent need for improved diabetes prevention and management. Several guidelines for type 2 diabetes mellitus (T2DM) management recommend using hemoglobin A1c (HbA1c) as the "gold standard" for long-term glycemic control [5,7], yet HbA1c has notable limitations: it cannot reflect intraday or interday glycemic variability and is susceptible to interference from hematologic disorders, hemolytic anemia, and renal failure.

Continuous glucose monitoring (CGM) systems measure glucose concentrations in interstitial fluid, offering valuable insights into relationships between meals, physical activity, medication, and glycemic fluctuations while helping detect occult hypoglycemia [6]. CGM provides a more comprehensive and accurate reflection of glycemic profiles and variability, serving as an effective complement to traditional glucose monitoring methods [7]. Metrics such as time-in-range (TIR) and mean amplitude of glycemic excursion (MAGE) enable more thorough evaluation of diabetes treatment status. This study employs TIR and MAGE as dynamic glycemic indicators to assess changes in glycemic variability and improvement.

The development and progression of diabetes are strongly linked to unhealthy lifestyle and dietary habits. Poor lifestyle behaviors such as physical inactivity and high-calorie diets likely contribute to the low HbA1c target achievement rates among T2DM patients. Diabetes education based on CGM data can provide more intuitive and effective counseling. While CGM is widely used in hospitalized patients, its application in outpatient settings remains limited. This study aims to evaluate the impact of outpatient diabetes education, guided by glycemic profiles from retrospective CGM, on glycemic patterns in outpatients with T2DM using oral hypoglycemic agents.

Methods

Study Subjects

We enrolled 88 outpatients with T2DM who were treated with oral hypoglycemic agents at the Endocrinology Department of Nanjing First Hospital in 2021, including 60 males and 28 females aged 32–84 years with a mean age of 61.00 (51.25, 67.75) years and a median diabetes duration of 5 (2, 10) years. Inclusion criteria were: (1) diagnosis of T2DM according to 1999 WHO criteria [8]; (2) voluntary participation with signed informed consent; (3) stable oral hypoglycemic medication doses for 2 months prior to enrollment; and (4) willingness to use CGM. Exclusion criteria included: (1) severe cardiopulmonary insufficiency or acute infection; (2) acute diabetic complications (diabetic ketoacidosis, hyperosmolar hyperglycemic state, lactic acidosis); (3) current treatment with glucocorticoids or immunosuppressants; (4) psychiatric disorders unsuitable for CGM use; and (5) other conditions deemed unsuitable by investigators (e.g., alcohol abuse, drug misuse). This study was approved by the hospital ethics committee (approval number: KY20191108-03), and all participants provided informed consent meeting inclusion and exclusion criteria.

Data Collection and Metabolic Indicators

Dedicated personnel collected patient information including age, disease duration, oral hypoglycemic medication types and doses, height, weight, waist circumference, and hip circumference. Hemoglobin (Hb) was measured using an automated hematology analyzer. Blood urea nitrogen (BUN), serum creatinine (Scr), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (Alb), total protein (TP), uric acid (UA), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were detected using a Beckman automated biochemical analyzer. HbA1c was measured by ion-exchange high-performance liquid chromatography using a Bio-Rad D100 HbA1c analyzer.

CGM Monitoring

Retrospective CGM was performed using the iPro2 system (Medtronic MiniMed, USA; recorder model MMT-7745WW, sensor model MMT-7708), with all procedures and training conducted by the same nurse. The CGM sensor and recorder were installed on day 1, data were downloaded during an outpatient visit on day 4, and the devices were removed with data downloaded on day 6. During CGM wear, patients were required to self-monitor capillary blood glucose at least 4 times daily (before three meals and at bedtime) and record any local or systemic allergic reactions or alarms. Patients also documented meal times and content, snack times and amounts, exercise duration and type, and hypoglycemic events (with instructions to consume carbohydrates when glucose <3.9 mmol/L and record details).

Outpatient Diabetes Education Based on CGM Profiles

During the CGM period, days 1-3 maintained the original hypoglycemic regimen and lifestyle. On day 4, patients returned to the specialty outpatient clinic for data download. Endocrinologists and diabetes specialist nurses jointly reviewed and analyzed glycemic trend graphs (including CGM mean glucose, peaks, nadirs, TIR) with patients, providing diabetes education tailored to dietary structure and exercise patterns. This included analyzing causes of glycemic variability and delivering targeted health education on meal composition rationality and potential improvements, as well as the impact of exercise type and timing on glucose levels.

CGM Parameter Definitions and Comparison

Day 2 and day 5 CGM data were compared using the following parameters: (1) 24-hour mean blood glucose (MBG): average glucose level reflecting overall glycemic control; (2) MAGE: average glucose excursion amplitude calculated after excluding fluctuations <1 SD, based on the direction of the first effective fluctuation; (3) Standard deviation (SD): square root of the arithmetic mean of squared deviations from the mean glucose, reflecting overall glucose dispersion; (4) TIR: percentage of time glucose values were within target range (3.9–10 mmol/L); (5) Time above range (TAR): percentage of time glucose >10 mmol/L; and (6) Time below range (TBR): percentage of time glucose <3.9 mmol/L.

Statistical Analysis

CGM variability parameters were analyzed using CGM Report Management System V2.0. Statistical analysis was performed using IBM SPSS Statistics 26. Normally distributed continuous variables were expressed as mean ± standard deviation (x-±s) and compared using paired t-tests. Non-normally distributed variables were expressed as median (P25, P75) and compared using paired rank-sum tests. $P<0.05$ was considered statistically significant.

Results

Baseline Characteristics

The mean HbA1c of the 88 patients was (6.85\$±\$0.97)%, with a target achievement rate (HbA1c<7%) of 65.91%. Other baseline clinical data are detailed in Table 1 .

Glycemic Profile Changes

Following outpatient education and lifestyle intervention based on CGM (day 5), MBG improved compared with pre-intervention (day 2) at hours 1, 7, 8, 10, 11, 12, 13, 14, 15, 19, and 20, with statistically significant differences ($P<0.05$), as shown in Table 2 .

CGM Parameters Before and After Intervention

After health education and lifestyle intervention based on CGM (day 5), MBG, SD, MAGE, and TAR decreased while TIR increased, all with statistically significant differences ($P<0.05$), as presented in Table 3 . Postprandial 2-hour glucose levels after breakfast, lunch, and dinner also improved compared with pre-intervention, with statistically significant differences ($P<0.05$), as shown in Table 4 .

Stratified Analysis

When stratified by diabetes duration into <10 years and \$ \$10 years groups, both groups showed reduced MBG after intervention. The <10 years group exhibited significantly greater reductions in MAGE and SD compared with the \$ \$10 years group ($P<0.05$), as detailed in Table 5 . When stratified by age into <65 years and \$ \$65 years groups, both groups demonstrated decreased MBG after intervention, with the <65 years group showing more pronounced reductions in MAGE and SD compared with the \$ \$65 years group ($P<0.05$), as shown in Table 6 .

Discussion

Poor glycemic control is closely associated with diabetic complications and target organ damage. Current glycemic target achievement rates in China remain low. Wang et al. [4] reported that the prevalence of diabetes among Chinese adults increased from 10.9% in 2013 to 12.4% in 2018, with awareness (36.7%), treatment (32.9%), and overall glycemic target achievement (16.5%) rates remaining low in 2018. Even among treated patients, the achievement rate was only 50.1%, indicating a concerning situation.

Blood glucose monitoring is essential for effective glycemic control. Traditional methods primarily include point-of-care glucose testing and HbA1c measurement. Point-of-care testing cannot reflect diurnal glucose patterns or determine the rate and direction of glucose changes, limiting its clinical utility [9]. HbA1c reflects average glucose levels over the preceding 2–3 months but fails to capture glycemic variability and can be affected by hemoglobin disorders, pregnancy, or chronic kidney disease [10-11].

CGM has gained widespread clinical use, providing continuous monitoring that reveals full-day glycemic profiles and variability, helping identify relationships between meals, exercise, medication, and glucose fluctuations while detecting occult hypoglycemia [6]. CGM serves as an effective complement to traditional monitoring methods [12]. Retrospective CGM avoids excessive interference by clinicians and patients during monitoring, objectively reflecting glycemic patterns under daily living conditions and facilitating analysis of glucose trends. Diamond et al. [13] proposed retrospective CGM as a cost-effective tool for individualized T2DM management in primary care, with multiple randomized controlled trials demonstrating significant HbA1c reductions compared with capillary glucose monitoring [14-15].

Glycemic control is influenced by multiple factors including diet, exercise, medication, psychological status, and sleep. Lack of physical activity and high-calorie diets likely contribute to low overall target achievement rates in T2DM. This study utilized retrospective CGM to monitor outpatients using oral hypoglycemic agents, providing dietary and exercise education guided by glycemic profiles to correct unhealthy lifestyle habits. Results showed MBG decreased from (8.34$±1.97)*mmol/Lto*(7.85±$1.65) mmol/L, with improved 2-hour postprandial glucose levels. Diabetes requires lifelong management, and correcting unhealthy dietary and lifestyle habits is crucial for glycemic control. CGM-based education allows patients to visually observe lifestyle impacts on glucose, transforming passive recipients into active participants and improving compliance [16]. CGM provides greater benefits for individuals seeking to understand how food types, exercise patterns, treatment regimens, and psychological factors affect glucose variability [17] and represents an important supplement to HbA1c [18-19]. The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) guidelines confirm that CGM improves glycemic control and that expanded CGM use enhances patient health outcomes [20].

International consensus identifies TIR, TAR, and TBR as key metrics for short-term glycemic assessment [21], with guidelines recommending TIR as a therapeutic target complementary to HbA1c [7]. Beck et al. [22] demonstrated correlations between TIR and microvascular complications in T2DM. In this study, TIR increased from (78.21$±24.64)±$21.87)%, indicating that CGM-based dietary and exercise education improves TIR.

MAGE is the gold standard for assessing glycemic variability. Studies by Okada et al. [23] and Gerbaud et al. [24] have linked glycemic variability to acute myocardial infarction, retinopathy, and nephropathy. Randomized trials show CGM significantly reduces glycemic variability compared with capillary testing [14-15]. In our study, MAGE decreased from (4.53$±2.25)*mmol/Lto*(3.80±1.80)*mmol/L, andSDdecreasedfrom*(1.80±0.8)*mmol/Lto*(1.62±$0.74) mmol/L, suggesting that unhealthy lifestyle habits are closely associated with glycemic variability and that retrospective CGM-guided lifestyle modification helps reduce glucose variability.

When stratified by disease duration, both <10 years and $ $10 years groups showed improved MBG after intervention. However, the <10 years group demonstrated significant reductions in SD and MAGE, while the $ $10 years group showed no improvement in glycemic variability. In the natural history of T2DM, pancreatic β-cell function progressively declines with increasing duration, leading to greater reliance on exogenous glucose-lowering measures [7]. Thus, patients with shorter disease duration derive greater benefit from lifestyle interventions.

As population aging intensifies, elderly diabetic patients have become the mainstream diabetes demographic. Recent data indicate that China has the world' s largest elderly diabetic population (one-quarter of the global total), and this is trending upward [25-26]. Few studies have used CGM to explore lifestyle impacts on glycemic profiles in elderly diabetic patients. In our study, 33 patients (37.5%) were aged $ $65 years. Both age groups showed improved MBG and TIR after intervention, but glycemic variability improved more markedly in the <65 years group.

In summary, this study employed retrospective CGM to monitor outpatients with T2DM using oral hypoglycemic agents, providing outpatient education and lifestyle modifications based on CGM results. This approach effectively improved MBG, increased TIR, and reduced glycemic variability. Stratified analysis indicated that patients younger than 65 years and with diabetes duration less than 10 years derived greater benefits.

References

[1] LI Y Z, TENG D, SHI X G, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study[J]. BMJ, 2020, 369: m997. DOI: 10.1136/bmj.m997.

[2] STRATTON I M, ADLER A I, NEIL H A, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study[J]. BMJ, 2000, 321(7258): 405-412. DOI: 10.1136/bmj.321.7258.405.

[3] Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group[J]. Lancet, 1998, 352(9131): 854-865.

[4] WANG L M, PENG W, ZHAO Z P, et al. Prevalence and treatment of diabetes in China, 2013-2018[J]. JAMA, 2021, 326(24): 2498-2506. DOI: 10.1001/jama.2021.22208.

[5] Chinese Society of Endocrinology, Chinese Medical Association. Expert Consensus on Comprehensive Management of Type 2 Diabetes Mellitus with Obesity in China[J]. Chinese Journal of Diabetes Mellitus, 2016, 8(11): 662-666. DOI: 10.3760/cma.j.issn.1674-5809.2016.11.006.

[6] POOLSUP N, SUKSOMBOON N, KYAW A M. Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes[J]. Diabetol Metab Syndr, 2013, 5: 39. DOI: 10.1186/1758-5996-5-39.

[7] Chinese Diabetes Society, Chinese Medical Association. Guidelines for the Prevention and Treatment of Type 2 Diabetes Mellitus in China (2020 Edi-

tion)[J]. Chinese Journal of Endocrinology and Metabolism, 2021, 37(4): 311-398. DOI: 10.3760/cma.j.cn311282-20210304-00142.

[8] PUAVILAI G, CHANPRASERTYOTIN S, SRIPHRAPRADAENG A. Diagnostic criteria for diabetes mellitus and other categories of glucose intolerance: 1997 criteria by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (ADA), 1998 WHO consultation criteria, and 1985 WHO criteria. World Health Organization[J]. Diabetes Res Clin Pract, 1999, 44(1): 21-26. DOI: 10.1016/s0168-8227(99)00008-x.

[9] Tan Xingrong, Wang Yi, Yang Gangyi. Research Progress in Blood Glucose Monitoring Technology[J]. Journal of Chongqing Medical University, 2022, 47(6): 688-692. DOI: 10.13406/j.cnki.cyxb.003040.

[10] SHERWANI S I, KHAN H A, EKHZAIMY A, et al. Significance of HbA1c test in diagnosis and prognosis of diabetic patients[J]. Biomark Insights, 2016, 11: 95-104. DOI: 10.4137/BMI.S38440.

[11] WRIGHT J J, HU J R, SHAJANI-YI Z, et al. Use of continuous glucose monitoring leads to diagnosis of hemoglobin c trait in a patient with discrepant hemoglobin a1c and self-monitored blood glucose[J]. AACE Clin Case Rep, 2019, 5(1): e31-e34. DOI: 10.4158/ACCR-2018-0149.

[12] Chinese Diabetes Society, Chinese Medical Association. Continuation of the Guidelines for Clinical Application of Blood Glucose Monitoring in China (2011 Edition)[J]. Chinese Medical Information Herald, 2011, 26(9): 19-20.

[13] DIAMOND K. Improving glucose control in patients with type 2 diabetes using retrospective continuous glucose monitoring[J]. J Am Assoc Nurse Pract, 2023, 35(7): 425-433. DOI: 10.1097/JXX.0000000000000831.

[14] LIND M, POLONSKY W, HIRSCH I B, et al. Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial[J]. JAMA, 2017, 317(4): 379-387. DOI: 10.1001/jama.2016.19976.

[15] AJJAN R A, JACKSON N, THOMSON S A. Reduction in HbA1c using professional flash glucose monitoring in insulin-treated type 2 diabetes patients managed in primary and secondary care settings: a pilot, multicentre, randomised controlled trial[J]. Diabetes Vasc Dis Res, 2019, 16(3): 285-291. DOI: 10.1177/1479164119827456.

[16] KLONOFF D C, AHN D, DRINCIC A. Continuous glucose monitoring: a review of the technology and clinical use[J]. Diabetes Res Clin Pract, 2017, 133: 178-192. DOI: 10.1016/j.diabres.2017.08.005.

[17] Zhao Xiaolong, Wu Chenwei. Guidance on Clinical Application of Flash Glucose Monitoring in Primary Care Settings[J]. Chinese Journal of Diabetes Mellitus, 2023, 15(4): 377-382. DOI: 10.3760/cma.j.cn115791-20221019-00614.

[18] Cai Yuli, Yi Bo, Chen Xiaolin, et al. Advances in Continuous Glucose

Monitoring Technology and Clinical Research[J]. Chinese Journal of Diabetes, 2021, 29(12): 933-940. DOI: 10.3969/j.issn.1006-6187.2021.12.010.

[19] Jin Baihan, Song Jingyun, Xie Junhao, et al. Clinical Value and Influencing Factors of Continuous Glucose Monitoring in Outpatients with Type 2 Diabetes Mellitus[J]. Chinese Journal of Diabetes, 2019, 27(1): 11-15. DOI: 10.3969/j.issn.1006-6187.2019.01.004.

[20] FONSECA V A, GRUNBERGER G, ANHALT H, et al. Continuous glucose monitoring: a consensus conference of the American association of clinical endocrinologists and American college of endocrinology[J]. Endocr Pract, 2016, 22(8): 1008-1021. DOI: 10.4158/EP161392.CS.

[21] VIGERSKY R A, MCMAHON C. The relationship of hemoglobin A1C to time-in-range in patients with diabetes[J]. Diabetes Technol Ther, 2019, 21(2): 81-85. DOI: 10.1089/dia.2018.0310.

[22] BECK R W, BERGENSTAL R M, RIDDLESWORTH T D, et al. Validation of time in range as an outcome measure for diabetes clinical trials[J]. Diabetes Care, 2019, 42(3): 400-405. DOI: 10.2337/dc18-1444.

[23] OKADA K, HIBI K, GOHBARA M, et al. Association between blood glucose variability and coronary plaque instability in patients with acute coronary syndromes[J]. Cardiovasc Diabetol, 2015, 14: 111. DOI: 10.1186/s12933-015-0275-3.

[24] YANG Y, HU Y Z. Comment on gerbaud et al. glycemic variability is a powerful independent predictive factor of midterm major adverse cardiac events in patients with diabetes with acute coronary syndrome. diabetes care, 2019, 42: 674-681[J]. Diabetes Care, 2019, 42(10): e168-169. DOI: 10.2337/dc19-1159.

[25] National Center for Gerontology, Chinese Geriatrics Society (Chinese Medical Association), Diabetes Professional Committee of China Association of Geriatric Care. Guidelines for the Diagnosis and Treatment of Diabetes in the Elderly in China (2021 Edition)[J]. Chinese Journal of Diabetes Mellitus, 2021, 13(1): 14-46. DOI: 10.3760/cma.j.cn115791-20201209-00707.

[26] SINCLAIR A, SAEDI P, KAUNDAL A, et al. Diabetes and global ageing among 65-99-year-old adults: findings from the International Diabetes Federation Diabetes Atlas, 9th edition[J]. Diabetes Res Clin Pract, 2020, 162: 108078. DOI: 10.1016/j.diabres.2020.108078.

Author Contributions

ZHOU Xiao conceptualized the study, designed the research protocol, performed statistical analysis, and drafted the manuscript. ZHOU Yunting, KONG Xiaocen, LIU Xiaomei, and YUAN Lu conducted the research and collected data. JING Ting and WANG Weiping were responsible for CGM installation. LI Huiqin supervised the research conduct and provided quality control and revision of the manuscript.

Conflict of Interest

This article has no conflict of interest.

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