

# Spontaneous and transient predinner hyperglycemia in some patients with diabetes

## Dusk phenomenon

Wei Li, BA, Si-na Du, BA, Min-jia Shi, BA, Zhan-zhan Sun, BA

### Abstract

Blood glucose fluctuations have higher risk than absolute blood glucose level in diabetic chronic complications. At present, “dawn phenomenon” is well known by clinicians, but “dusk phenomenon” has not been recognized. This study explored the objective existence of “dusk phenomenon” (spontaneous and transient predinner hyperglycemia) and its clinical significance.

The data of 54 patients with diabetes, who received routine insulin pump therapy between December 2010 and October 2012 in our hospital, were retrospectively analyzed. These patients included 4 patients with type 1 diabetes mellitus (DM) (T1DM) and 50 patients with type 2 DM (T2DM). According to the difference between predinner and postlunch blood glucose levels, the 50 patients with T2DM were divided into dusk phenomenon group (4 patients, all the differences  $\geq 0$  mmol/L during insulin pump therapy), nondusk phenomenon group (12 patients, all the differences  $< 0$  mmol/L during insulin pump therapy), and suspicious group (34 patients, the differences were uncertain during insulin pump therapy). In the 4 patients with T1DM of this study, the differences all were more than 0 mmol/L during insulin pump therapy. The changes in blood glucose levels were observed, and the correlations of blood glucose level with other factors were analyzed in T1DM and T2DM patients, respectively.

In T1DM patients, blood glucose level was significantly higher in predinner than in prebreakfast and prelunch (all  $P < 0.01$ ), and in postdinner 2 hour than in postlunch 2 hour ( $P = 0.021$ ). The predinner blood level had no significant correlations with the blood glucose level at other time points and insulin dosages (all  $P > 0.05$ ). In T2DM patients, the predinner blood glucose level was significantly higher in dusk phenomenon group than in suspicious group and nondusk phenomenon group (all  $P < 0.05$ ). In dusk phenomenon group, the blood glucose level remained rising from predinner to prebed, and the predinner blood glucose level was only significantly correlated with postdinner 2-hour blood glucose level ( $P < 0.05$ ).

The “dusk phenomenon” (spontaneous and transient predinner hyperglycemia) is an objective existence in some patients with diabetes. The predinner hyperglycemia can affect blood glucose control between postdinner and prebed. Awareness of the “dusk phenomenon” has important clinical significance.

**Abbreviations:** BMI = body mass index, DM = diabetes mellitus, FBG = fasting blood glucose, T1DM = type 1 diabetes mellitus, T2DM = type 2 diabetes mellitus.

**Keywords:** diabetes mellitus, dusk phenomenon, predinner hyperglycemia

## 1. Introduction

The incidence of type 2 diabetes mellitus (DM) (T2DM) is higher and higher. In 2014, there were approximately 387 million people with diabetes worldwide, and it is estimated that its

prevalence was 8.3%, and probably will increase by 10% before 2030.<sup>[1]</sup> In 2014, about 4.9 million died of diabetes, costing 612 billion dollars for health care.<sup>[1]</sup> More than 80% of patients who died of diabetes are from low- and middle-income countries. Of the 2 kinds of diabetes, T2DM is widespread globally, accounting for over 90% of all patients with diabetes.<sup>[2]</sup> A systematic review carried out in 2012 showed a rapid increase in prevalence over the last 2 decades in the Asian region.<sup>[3]</sup>

With the increase in the incidence of DM, prevention and control for diabetes have been improving. The famous studies, diabetes control and complications trial and UK prospective diabetes study, have confirmed the advantages and risks from strict blood glucose control.<sup>[4–6]</sup> It is very important for the treatment of diabetes to control blood glucose within normal limits. However, for some specific patients with diabetes, it is difficult to control blood glucose within normal limits due to abnormal fluctuation in blood glucose such as “dawn phenomenon.” Since the conception of “dawn phenomenon” was reported by Schmidt et al<sup>[7]</sup> for the first time in 1981, it attracted a great deal of attention, so the features and mechanism about “dawn phenomenon” have been gradually elaborated and improved. Oppositely, another abnormal fluctuation in blood glucose described in this study is greatly ignored. In clinical practice, we have found that there is a remarkable rise in blood glucose before dinner in some patients with diabetes, and the increased blood glucose also affects the blood glucose level from

Editor: Marco G. Alves.

Funding/support: The present study was supported by Science and Technology project of people's livelihood from Ningbo City (no. 2013C51016).

The authors have no conflicts of interest to disclose.

Department of Endocrinology, Cixi People's Hospital (Affiliated Cixi Hospital, Wenzhou Medical University), Cixi, China.

Correspondence: Wei Li, Department of Endocrinology, Cixi People's Hospital (Affiliated Cixi Hospital, Wenzhou Medical University), No. 999, South Second Cycle, Hushan Street, Cixi 315300, Zhejiang Province, China (e-mail: liweixbin@163.com)

Copyright © 2016 the Author(s). Published by Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

Medicine (2016) 95:47(e5440)

Received: 30 July 2016 / Received in final form: 27 September 2016 / Accepted: 27 October 2016

<http://dx.doi.org/10.1097/MD.0000000000005440>

postdinner to before prebed. We called it “dusk phenomenon.” So far, “dusk phenomenon” has not been reported. In this study, we retrospectively analyzed the clinical data of patients with diabetes who received insulin pump-intensive treatment and explored the objective existence of “dusk phenomenon” and its clinical significance, providing a basis for the diagnosis and treatment of “dusk phenomenon.”

## 2. Subjects and methods

All study methods were approved by the Ethics Committee of Cixi People’s Hospital Affiliated to Wenzhou Medical University. All patients gave written informed consent to participate in this study.

### 2.1. Subjects

Between December 2010 and October 2012, 54 diabetic patients, who received insulin pump-intensive treatment in our hospital due to poor blood glucose control, were enrolled in this study. These patients received routine insulin pump therapy for 4 to 14 days due to many economic reasons. The 54 patients included the cases that were diagnosed with DM for the first time and had fasting blood glucose (FBG)  $>15$  mmol/L, and the cases who were followed up and had the FBG  $>10$  mmol/L. The clinical data, including sex, age, height, weight, body mass index (BMI), type of diabetes, blood glucose levels (prebreakfast, postbreakfast 2 hour, prelunch, postlunch 2 hour, predinner, postdinner 2 hour and prebed), insulin dosages (basal insulin and preprandial insulin), and glycosylated hemoglobin level, were retrospectively analyzed in the 54 patients (310 individuals day). And then the analysis of dusk phenomenon-related factors was performed in type 1 DM (T1DM) and T2DM, respectively. The diagnosis of DM was made according to the criteria suggested in “Guidelines for prevention and treatment of type 2 diabetes in China”<sup>[8]</sup> in 2007. The patients, who had acute cardiac-cerebral vascular events, infection, ketosis, stress state, liver and/or kidney dysfunction, anemia, or other endocrine disorders, were excluded from this study. The patients, who had hypoglycemia, or required supplemental insulin or extra meals after lunch, also were excluded from this study.

### 2.2. Treatment

All patients received rapid-acting insulin analogs (insulin aspart or insulin lispro) which were pumped by DANA insulin pump (II s type, Shenzhen Danner Science and Technology Co., Ltd, Shenzhen, China). No technical problems, such as tube plugging, occurred in all patients. The initial total amount of insulin was determined according to the previous total amount of insulin or 0.5 U/kg. Basal insulin and preprandial insulin accounted for 50% of the total amount, respectively. The distribution of preprandial insulin dosage was 1/3 + 1 U before breakfast, 1/3 to 1 U before lunch, and 1/3 before dinner. The distribution of basal insulin dosage was average dosage  $-0.1$  U/h from 0:00 to 4:00, average dosage  $+0.1$  U/h from 4:00 to 8:00 and average dosage from 8:00 to 24:00. Blood glucose disorder was severe in the patients of this study, so the data of these patients began to be collected when the postlunch blood glucose level was close to 10 mmol/L after insulin pump therapy.

### 2.3. Grouping

In T2DM patients, during insulin pump therapy, the patients whose differences between predinner and postlunch blood

glucose levels were all 0 mmol/L or more, were enrolled in dusk phenomenon group. The patients, whose differences between predinner and postlunch blood glucose levels were all less than 0 mmol/L, were enrolled in nondusk phenomenon group. The rest patients, whose differences between predinner and postlunch blood glucose levels were uncertain (sometimes 0 mmol/L or more, and sometimes less than 0 mmol/L), were enrolled in suspicious group. In the 4 patients with T1DM of this study, the differences between predinner and postlunch blood glucose levels all were more than 0 mmol/L during insulin pump therapy. After grouping, the relationship of blood level at different time points between patients with various differences could be observed, and the correlation of predinner blood glucose level with other factors in each kind of patients could be analyzed. These may provide a basis for further researches on “dusk phenomenon.”

### 2.4. Statistical analysis

Statistical treatment was performed using SPSS 16.0 software (IBM, Chicago, Illinois, USA). Measurement data were expressed as mean  $\pm$  standard deviation and were analyzed using variance analysis or *t* test. Enumeration data were expressed as frequency and analyzed using the  $\chi^2$  test. The analysis of variance of repeated measurement data were used for multiple time-point measurement data. The correlations between variables were performed using Pearson analysis. Statistical significance was established at  $P < 0.05$ .

## 3. Results

### 3.1. T1DM

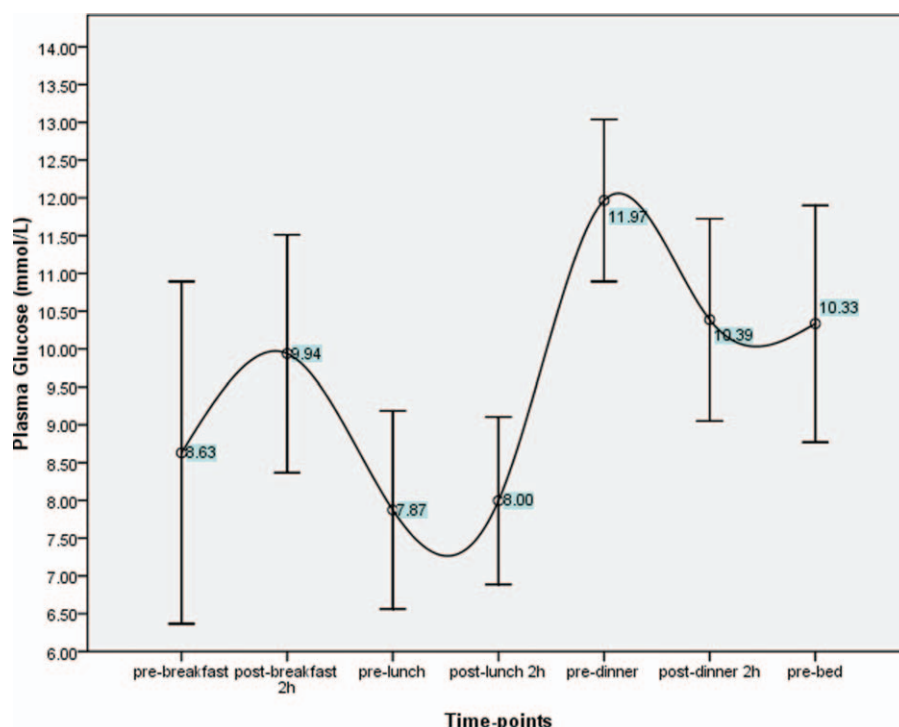
General data: This study included 4 T1DM patients. The 4 patients all had “dusk phenomenon”. Of the 4 patients, 3 were men and 1 woman, with a mean age of  $(34.25 \pm 24.55)$  years, a mean body height of  $(162.25 \pm 5.91)$  cm, a mean body weight  $(47.63 \pm 4.82)$  kg, a mean BMI of  $(18.08 \pm 1.44)$  kg/m, a mean disease course of  $(13.50 \pm 10.25)$  months and a mean glycosylated hemoglobin level of  $(7.26 \pm 16)$  mmol/L.

*Changes in blood glucose:* The changes in blood glucose at each-time point were in line with a quadratic curve in the 4 T1DM patients. There was statistical significance in blood glucose levels among each time points in T1DM patients ( $F = 5.883$ ,  $P = 0.001$ ). Predinner blood glucose level was significantly higher than prebreakfast and prelunch blood glucose levels (all  $P < 0.01$ ), and postdinner 2-hour blood glucose level was also significantly higher than postlunch 2-hour blood glucose level ( $P = 0.021$ ) (Fig. 1).

*Correlation analyses of predinner blood glucose level with the blood glucose levels at other time points and insulin dose:* Results indicated that the predinner blood level had no significant correlation with the blood glucose levels at other time points (all  $P > 0.05$ , Table 1), basal insulin dosage at each time period, and preprandial insulin dosage for each meal (all  $P > 0.05$ , Table 2).

### 3.2. T2DM

General data: This study included 50 T2DM patients. According to the difference between predinner and postlunch blood glucose levels, the 50 patients were divided into dusk phenomenon group (4 patients), suspicious group (34 patients), and nondusk phenomenon group (12 patients). There were no significant differences in sex, age, height, weight, BMI, disease course, and glycosylated hemoglobin level among the 3 groups (all  $P > 0.05$ , Table 3).



**Figure 1.** Changes in blood glucose levels at different time points in the patients with type 1 diabetes mellitus. Predinner blood glucose level is significantly higher than prebreakfast and prelunch blood glucose levels (all  $P < 0.01$ ), and postdinner 2-hour blood glucose level is also significantly higher than postlunch 2-hour blood glucose level ( $P = 0.021$ ).

*Changes in blood glucose:* There was statistical significance in blood glucose levels among each time points in each group ( $F = 65.878, P < 0.001$ ). There were statistical differences in pre-breakfast, postbreakfast 2 hour, prelunch, postlunch 2 hour, predinner, postdinner 2 hour, and prebed blood glucose levels among the 3 groups (all  $P < 0.05$ ); especially, predinner blood glucose level was significantly higher in dusk phenomenon group than in suspicious group and nondusk phenomenon group (all  $P < 0.05$ ). There was a cross-action between dusk phenomenon grouping and blood glucose level ( $F = 9.262, P < 0.001$ ), and the changes in the cross-action was consistent with quartic curve ( $F = 0.605, P = 0.547$ ) (Fig. 2).

*Correlation analyses of predinner blood glucose level with the blood glucose levels at other time points and insulin dose:* In overall T2DM patients, predinner blood glucose level was significantly correlated with prebreakfast, prelunch, postbreakfast 2 hour, postlunch 2 hour, postdinner 2 hour, and prebed blood glucose levels (all  $P < 0.05$ ) (Table 1) but was not significantly correlated with basal insulin dosage at each time period and preprandial insulin dosage for each meal (all  $P > 0.05$ , Table 2). After all the T2DM patients were divided into

nondusk phenomenon group, suspicious group and dusk phenomenon group; in each group, the correlation analyses are shown in Tables 4 and 5. In nondusk phenomenon group and suspicious group, the predinner blood glucose level was also significantly correlated with prebreakfast, prelunch, postbreakfast 2 hour, postlunch 2 hour, postdinner 2 hour, and prebed blood glucose levels (all  $P < 0.05$ ) (Table 4) and was not significantly correlated with basal insulin dosage at each time period and preprandial insulin dosage for each meal (all  $P > 0.05$ ) (Table 5). However, in dusk phenomenon group, the predinner blood glucose level was only significantly correlated with postdinner 2-hour blood glucose level ( $P < 0.05$ ) (Table 4) and was also not significantly correlated with basal insulin dosage at each time period and preprandial insulin dosage for each meal (all  $P > 0.05$ ) (Table 5).

#### 4. Discussion

This study was inspired by a special patient. The patient received oral metformin combined with subcutaneous NovoMix 30 Penfill (Novo Nordisk [Chinese] Pharmaceutical Co. Ltd, Tianjin, China)

**Table 1**  
Correlation analyses of predinner glucose levels with the blood glucose levels at other time points in T1DM and T2DM patients.

	Prebreakfast glucose	Prelunch glucose	Postbreakfast 2-h glucose	Postlunch 2-h glucose	Postdinner 2-h glucose	Prebed glucose
Predinner glucose	0.144 0.314*	0.198 0.355*	0.014 0.216*	0.386 0.563*	0.162 0.560*	-0.100 0.522*

Notes: The Pearson correlation coefficients of T1DM patients are shown in the first row and T2DM in the second row. T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.  
\*  $P < 0.01$ .

**Table 2****Correlation analyses of blood glucose levels at different time points with insulin dosages in T1DM and T2DM patients.**

	Basal insulin 00–04	Basal insulin 04–08	Basal insulin 08–24	Prebreakfast insulin	Prelunch insulin	Predinner insulin
Prebreakfast glucose	−0.452*	−0.339	−0.485*	0.146	−0.111	−0.460*
	−0.031	0.067	0.028	0.065	0.043	0.004
Prelunch glucose	−0.148	−0.289	−0.160	0.474*	0.271	−0.162
	0.019	−0.012	0.098	0.047	0.085	0.013
Predinner glucose	−0.223	−0.168	−0.281	−0.132	0.006	−0.210
	−0.005	−0.009	0.070	−0.090	−0.068	−0.108
Postbreakfast 2-h glucose	0.184	−0.012	0.108	0.682†	0.365	0.109
	−0.023	−0.084	0.092	0.171†	0.124*	0.044
Postlunch 2-h glucose	−0.088	−0.422*	−0.189	0.257	0.443*	−0.243
	0.068	0.044	0.117*	0.001	0.065	−0.016
Postdinner 2-h glucose	−0.140	−0.357	−0.197	0.216	0.290	−0.225
	0.104	0.131*	0.151*	0.047	0.103	0.042
Prebed glucose	−0.317	−0.269	−0.379	0.122	−0.074	−0.404
	0.053	0.126*	0.064	−0.055	−0.060	−0.107

Notes: The Pearson correlation coefficients of T1DM patients are shown in the first row and T2DM in the second row. T1DM = type 1 diabetes mellitus, T2DM = type 2 diabetes mellitus.

\*  $P < 0.05$ .

†  $P < 0.01$ .

twice a day. In the patient, postdinner hyperglycemia was very intractable, although the blood glucose levels at other time points (4-point blood glucose monitoring: fasting + 2 hour after 3 meals a day) were well controlled. In the patient, the intractable postdinner hyperglycemia was difficultly controlled by premixed insulin because increased predinner insulin dosage was likely to lead to fasting hypoglycemia at midnight. In the patient, the response of postdinner blood glucose level to insulin dosage was not consistent with routine response. Therefore, insulin pump therapy was used for controlling blood glucose in this patient. After application of insulin pump therapy in this patient, we found that except pre- and postdinner hyperglycemia, blood glucose levels at the rest time points were controlled well (7-point blood glucose monitoring: before 3 meals a day + 2 hour after 3 meals a day + before bed). This condition of a spontaneous and transient rise in blood glucose occurred in dusk period; so we called it “dusk phenomenon.” After literature review, there have not been reports on the transient rise in blood glucose during dusk period (before and after dinner). Subsequently, we systematically and retrospectively analyze data from the patients who received insulin pump therapy in our hospital. Predinner hyperglycemia cannot be observed in the patients who received subcutaneous injection of insulin, because 4-point blood glucose monitoring (fasting + 2 hour after 3 meals a day) was adopted in these patients. However, in the patients who received insulin pump therapy, we found many suspicious cases of “dusk phenomenon” because these patients underwent 7-point blood glucose monitoring (before 3 meals a day + 2 hour after 3

meals a day + before bed). Therefore, we retrospectively analyzed the clinical data of patients with diabetes who received insulin pump-intensive treatment and explored the objective existence of “dusk phenomenon” and its clinical significance.

“Dusk phenomenon” in this study refers to spontaneous and transient hyperglycemia during dusk period (before and after dinner) under the condition of stable and satisfactory blood glucose control and no hypoglycemia in the afternoon.

So far, the concept of “dusk phenomenon” has not been reported, and even no clinical diagnostic criteria. In this study, grouping was based on differences between predinner and postlunch blood glucose levels. During insulin pump therapy, the differences between predinner and postlunch blood glucose levels all  $\geq 0$  mmol/L were regarded as “dusk phenomenon”. Statistical analyses of this study have confirmed that “dusk phenomenon” is a kind of special hyperglycemic status.

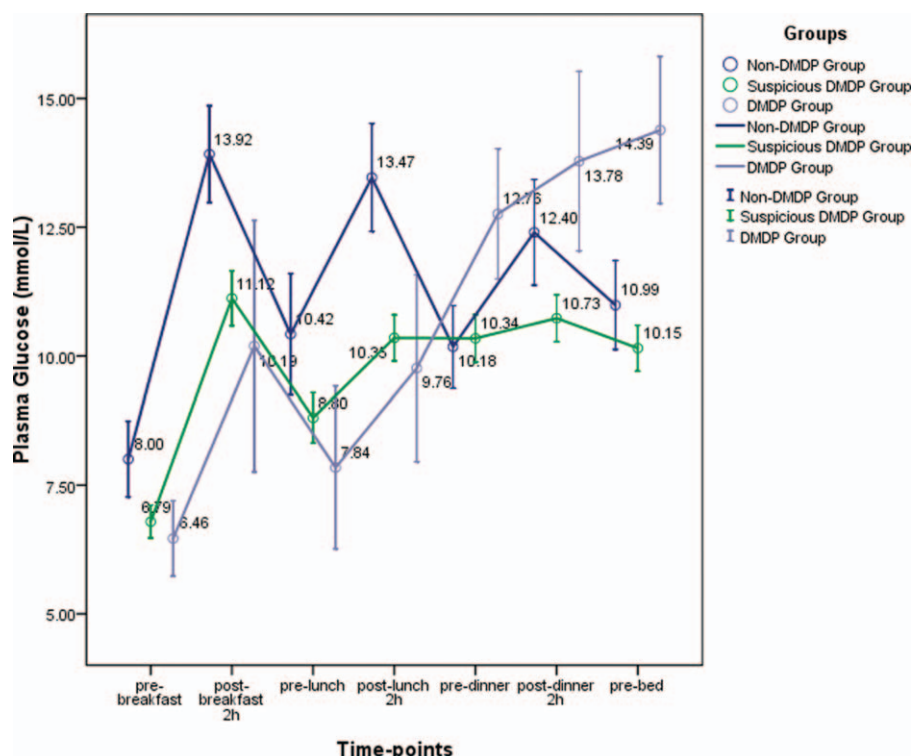
In this study, although there were only 4 T1DM patients, they all had “dusk phenomenon”, suggesting that “dusk phenomenon” may be strongly associated with poor islet function in T1DM. In the 4 T1DM patients, predinner blood glucose level was significantly higher than prebreakfast and prelunch blood glucose levels, and predinner hyperglycemia led to a rise in postdinner 2-hour blood glucose, allowing the blood glucose level during dusk period to be difficultly controlled within ideal level.

In the 4 T2DM patients, the predinner blood glucose level was not significantly correlated with both blood glucose levels at other time points and insulin dosages, suggesting that predinner

**Table 3****General data in T2DM patients.**

	Nondusk phenomenon group	Suspicious group	Dusk phenomenon group	Statistic	P
Sex (men/women)	8/4	23/11	3/1	0.102	0.950
Age	59.67 ± 17.84	59.06 ± 14.54	53.75 ± 8.54	0.249	0.781
Height	166.00 ± 8.46	167.09 ± 6.89	168.25 ± 8.88	0.165	0.848
Weight	73.25 ± 11.48	66.47 ± 13.19	66.25 ± 8.22	1.342	0.271
BMI	26.50 ± 2.91	23.74 ± 3.90	23.39 ± 2.06	2.780	0.072
Disease course, mo	6.79 ± 6.15	43.09 ± 63.63	9.75 ± 2.87	2.417	0.100
HbA1c	9.77 ± 1.49	11.03 ± 2.32	9.46 ± 2.98	2.011	0.145

Notes: BMI = body mass index, HbA1c = glycosylated hemoglobin, T2DM = type 2 diabetes mellitus.



**Figure 2.** Changes in blood glucose levels at different time points in the patients with type 2 diabetes mellitus. Predinner blood glucose level is significantly higher in dusk phenomenon group than in suspicious group and nondusk phenomenon group (all  $P < 0.05$ ). DMDP = diabetes mellitus dusk phenomenon.

hyperglycemia (dusk phenomenon) may be a spontaneous and transient symptom.

Our results are not completely same as that reported by Schmidt et al<sup>[7]</sup> who raised dawn phenomenon. In the T1DM patients observed by Schmidt et al,<sup>[7]</sup> hyperglycemia during dawn period was found, but hyperglycemia during dusk period failed to be observed. This may be that blood glucose disorder was more severe in the T1DM patients of this study, because they had diabetes for many years and poor blood glucose control; predinner hyperglycemia was easily found in the patients of this study, because postlunch blood glucose was able to be controlled well due to insulin pump treatment; and in this study, prebreakfast insulin dosage was 1/3 + 1 U and basal insulin dosage from 4:00 to 8:00 was average dose + 0.1 U/h, so predinner blood glucose level higher than prebreakfast blood glucose level is unable to imply that the blood glucose level during dusk period is really higher than that during dawn period.

Meanwhile, “dusk phenomenon” also was found in some T2DM patients of this study. In the T2DM patients of this study, there were no significant differences in sex, age, height, weight, BMI among dusk phenomenon group, suspicious group, and nondusk phenomenon group, further confirming independence of the “dusk phenomenon”.

In the T2DM patients of this study, pre- and postdinner blood glucose levels were significantly higher in dusk phenomenon group than in suspicious group and nondusk phenomenon group, and then postdinner 2 hour and prebed blood glucose level remained rising in dusk phenomenon group. This severely affects blood glucose control in the patients with dusk phenomenon during dusk period.

In suspicious group and nondusk phenomenon group, predinner blood glucose level was significantly correlated with the blood glucose levels at other time points, suggesting that the blood glucose control at other time points affects predinner blood

**Table 4**

**Correlation analyses of predinner glucose levels with the blood glucose levels at other time points in dusk phenomenon group, suspicious group, and nondusk phenomenon group.**

	Prebreakfast glucose	Prelunch glucose	Postbreakfast 2-h glucose	Postlunch 2-h glucose	Postdinner 2-h glucose	Prebed glucose
Predinner glucose	0.337*	0.582*	0.392*	0.762*	0.539*	0.580*
	0.363*	0.335*	0.228*	0.613*	0.568*	0.497*
	-0.189	0.252	0.156	0.414	0.638*	0.297

Notes: The Pearson correlation coefficients of nondusk phenomenon group are shown in the first row, suspicious group in the second row and dusk phenomenon group in the third row. \*  $P < 0.01$ .

**Table 5****Correlation analyses of blood glucose levels at different time points with insulin dosages in dusk phenomenon group, suspicious group, and nondusk phenomenon group.**

	Basal insulin 00–04	Basal insulin 04–08	Basal insulin 08–24	Prebreakfast insulin	Prelunch insulin	Predinner insulin
Prebreakfast glucose	−0.171	−0.201	−0.305*	−0.189	−0.277*	−0.286*
	0.001	0.120	0.120	0.105	0.092	0.079
	0.815†	0.419	0.789†	−0.015	−0.212	−0.368
Prelunch glucose	−0.130	−0.160	−0.182	−0.269*	−0.314*	−0.261*
	0.066	0.012	0.198†	0.109	0.167*	0.088
	−0.234	0.023	−0.306	−0.314	−0.366	−0.444
Predinner glucose	0.023	−0.004	−0.109	−0.182	−0.237	−0.160
	0.000	0.000	0.130	−0.059	0.001	−0.070
	−0.119	0.548*	−0.086	0.206	−0.095	−0.212
Postbreakfast 2-h glucose	−0.002	−0.073	−0.038	−0.181	−0.153	−0.139
	−0.026	−0.094	0.136*	0.214†	0.138*	0.081
	0.092	0.294	0.054	0.171	−0.018	−0.165
Postlunch 2-h glucose	−0.015	−0.073	−0.109	−0.167	−0.194	−0.092
	0.111	0.082	0.212†	0.003	0.082	0.004
	0.012	0.236	0.073	−0.158	−0.311	−0.361
Postdinner 2-h glucose	0.338†	0.322*	0.222	0.203	0.211	0.307*
	0.076	0.143*	0.175*	0.010	0.090	0.011
	0.067	0.640†	0.138	0.671†	0.357	0.138
Prebed glucose	0.280*	0.301*	0.088	−0.032	−0.039	0.015
	0.025	0.146*	0.094	−0.045	−0.029	−0.090
	0.423	0.617†	0.354	0.451	0.131	−0.088

Notes: The Pearson correlation coefficients of nondusk phenomenon group are shown in the first row, suspicious group in the second row and dusk phenomenon group in the third row.

\*  $P < 0.05$ .

†  $P < 0.01$ .

glucose level. In dusk phenomenon group, predinner blood glucose level was only significantly correlated with postdinner 2-hour blood glucose level, suggesting that it is very important for obtaining a satisfactory blood glucose level of dusk period to control predinner blood glucose level.

This study has proved the existence of predinner spontaneous and transient hyperglycemia in some T1DM and T2DM patients, and the hyperglycemia also affects postdinner and prebed blood glucose control. We call this phenomenon “dusk phenomenon”.

The conception of “dawn phenomenon” was reported by Schmidt et al<sup>[7]</sup> in 1981 in T1DM patients. Subsequently, Bolli and Gerich<sup>[9]</sup> found the “dawn phenomenon” in T2DM patients in 1984. Since then, “dawn phenomenon” has attracted a great deal of attention, so the features and mechanism about “dawn phenomenon” have been further elaborated and improved. So far over 180 articles about “dawn phenomenon” have been published.<sup>[10]</sup> The mechanism of “dawn phenomenon” includes Growth hormone is regarded as the primary factor in T1DM patients and as the second factor in T2DM patients, and the effect of growth hormone on glucose metabolism is time-dependent<sup>[11]</sup>; Endogenous glucose production and insulin sensitivity exhibit circadian rhythm<sup>[12,13]</sup>; Fibroblast growth factor-21 also shows circadian rhythm<sup>[14]</sup>; and Carroll et al<sup>[11]</sup> found that the effects of glucagon and cortisol on hyperglycemia during dawn period is more affirmative, but the contribution of catecholamine to hyperglycemia during dawn period is limited.<sup>[12]</sup> These studies above all suggest that rhythmic changes in hormone secretion

lead to “dawn phenomenon”. However, there may be other potential mechanisms for “dusk phenomenon”. The exact mechanism of “dusk phenomenon” remains to be further confirmed by clinical and basic researches.

Different from the widely concerned “dawn phenomenon,” “dusk phenomenon” has been greatly ignored. This may be that it is difficult for 4-point blood glucose monitoring (in China: fasting + after 3 meals a day, in Europe and America: before bed + after 3 meals a day) to discover “dusk phenomenon”; and not as simple as the “dawn phenomenon”, the blood glucose level during dusk period is associated with many factors such as meal, prandial insulin dosage, and exercise.

#### 4.1. Judgment for “dusk phenomenon”

This study has confirmed the objective existence of “dusk phenomenon” and pointed out the clinical characteristics of “dusk phenomenon.” However, the number of patients in dusk phenomenon group of this study was too small to determine the diagnostic cutoff value of “dusk phenomenon.” The number of patients with “dusk phenomenon” in this study is small because insulin pump therapy is not within medical insurance; and after cognizance of “dusk phenomenon” (after October 2012), we regulated up insulin dosage before dinner by insulin pump to control hyperglycemia once we found the patients with “dusk phenomenon.” Therefore, the diagnostic criteria for “dusk phenomenon” remain to be further improved by collecting more data.

#### 4.2. Significance of “dusk phenomenon”

Diabetes damages body’s tissues and organs mainly through 2 ways: chronic persistent rise and wide fluctuations in blood glucose levels. Diabetic chronic complications are associated with both blood glucose level and blood glucose stability. Blood glucose stability may be completely different in various individuals with the similar blood glucose level. Blood glucose fluctuations have higher risk than absolute blood glucose level in diabetic chronic complications. Satisfactory blood glucose control includes quantity control (blood glucose level and glycosylated hemoglobin) and quality control (blood glucose level stability).<sup>[15]</sup> No target interventions to these phenomena will produce more problems. At present, “dawn phenomenon” is well known by clinicians, but “dusk phenomenon” has not been recognized. This study will greatly promote the management and research for the transient and spontaneous rise in predinner blood glucose level.

#### 4.3. Cautions for diagnosis of “dusk phenomenon”

In a patient who has no basal insulin deficiency, and no hypoglycemia, no extra meal and abnormal exercise after lunch, and no Somogyi in the afternoon, if he has a remarked rise in postdinner blood glucose level, it is necessary to monitor predinner blood level.

In summary, for the “dusk phenomenon,” many problems such as its mechanism, intervention targets, diagnostic cutoff values, and its relationship with glycosylation, the “dawn phenomenon” and islet function remain to be resolved. At last, we hope this study can provide a basis for the research on “dusk phenomenon” and attract people’s attention to the “dusk phenomenon.”

#### References

- [1] International Diabetes Federation Diabetes Atlas Sixth Edition Poster Update 2014. Brussels, Belgium: International Diabetes Federation; 2014.

- [2] World Health Organization Diabetes Fact Sheet. 2015; Available from: <http://www.who.int/mediacentre/factsheets/fs312/en/>. [cited June 15, 2015].
- [3] Jayawardena R, Ranasinghe P, Byrne N, et al. Prevalence and trends of the diabetes epidemic in South Asia: a systematic review and meta-analysis. *BMC Public Health* 2012;12:380.
- [4] Donaghue KC, Chiarelli F, Trotta D, et al. Microvascular and macrovascular complications associated with diabetes in children and adolescents. *Pediatr Diabetes* 2009;(suppl 12):195–203.
- [5] Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS35): prospective observational study. *Brit Med J* 2000;321:405–12.
- [6] UK Prospective Diabetes Study (UKPDS) Group Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS33). *Lancet* 1998;352:837–53.
- [7] Schmidt MI, Hadji-Georgopoulos A, Rendell M, et al. The dawn phenomenon, an early morning glucose rise: implications for diabetic intraday blood glucose variation. *Diabetes Care* 1981;4:579–85.
- [8] Diabetes Branch of Chinese Medical Association Guidelines for prevention and treatment of type 2 diabetes branch (2007 edition). *Zhonghua Yi Xue Za Zhi* 2008;88:1227–45.
- [9] Bolli GB, Gerich JE. The “dawn phenomenon”—a common occurrence in both non insulin-dependent and insulin dependent diabetes mellitus. *N Engl J Med* 1984;310:746–50.
- [10] Porcellati F, Lucidi P, Bolli GB, et al. Thirty years of research on the dawn phenomenon: lessons to optimize blood glucose control in diabetes. *Diabetes Care* 2013;36:3860–2.
- [11] Carroll MF, Hardy KJ, Burge MR, et al. Frequency of the dawn phenomenon in type 2 diabetes: implications for diabetes therapy. *Diabetes Technol Ther* 2002;4:595–605.
- [12] Rybicka M, Krysiak R, Okopień B. The dawn phenomenon and the Somogyi effect—two phenomena of morning hyperglycaemia. *Endokrynol Pol* 2011;62:276–84.
- [13] Monnier L, Colette C, Rabasa-Lhoret R, et al. Morning hyperglycemic excursions: a constant failure in the metabolic control of non-insulin-using patients with type 2 diabetes. *Diabetes Care* 2002;25:737–41.
- [14] Yu H, Xia F, Lam KS, et al. Circadian rhythm of circulating fibroblast growth factor 21 is related to diurnal changes in fatty acids in humans. *Clin Chem* 2011;57:691–700.
- [15] Del Prato S. In search of normoglycemia in diabetes: controlling postprandial glucose. *Int J Obes Relat Metab Disord* 2002;26(suppl 3):9–17.