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Clinical diagnosis for dusk phenomenon of diabetes

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Abstract

The diabetes dusk phenomenon (spontaneous and transient pre-dinner hyperglycemia) anecdotally exists but has not been investigated.

A total of 80 diabetic patients that received continuous subcutaneous insulin infusions were retrospectively studied. They were grouped into a routine group (R) (consecutive δDG [dusk blood glucose difference] <0 mmol/L) and a classic dusk phenomenon group (CDP, consecutive δDG≥0 mmol/L). δDG represents differences in blood glucose measurements between pre-dinner and post-lunch (δDG: dusk blood glucose difference). Other patients were placed in a suspicious group (S). The suspicious group was further divided into 3 groups based on the frequency at which the δDG occurred: suspicious 1 group (S1), δDG≥0 mmol/L occurred once only; suspicious 3 group (S3), δDG < 0 mmol/L occurred once only, and the remaining patients were grouped in the suspicious 2 group (S2).

We identified the CDP and S3 groups as the "clinical dusk phenomenon" group (CLDP). We confirmed that the S1 and R groups to be in the "clinical routine" group. The S2 group was significantly different from the CDP group. In addition, the S2 group had significant differences in δDG measurements and post-lunch blood glucose values compared with the R group, but no differences in other parameters were seen. Multiple comparisons with the other suspicious groups also showed no statistical difference in many parameters. Thus, we placed these patients into the "suspicious clinical dusk phenomenon" group (SDP). The δDG cut-off for the CLDP group was 1.0167 mmol/L. The pre-dinner-pre-lunch blood glucose cut-off for this group was 2.72 mmol/L. The δDG cut-off for the SDP group was −0.95 mmol/L. The pre-dinner-pre-lunch blood glucose cut-off for this group was 0.87 mmol/L. The cut-off points for the post-dinner-post-lunch blood glucose measurements in the CLDP and SDP groups were both 1.2667 mmol/L.

A consecutive δDG≥0 or a once only δDG < 0 could be diagnosed as falling into the CLDP group. The CLDP could be excluded when a consecutive δDG < 0 or a once only δDG≥0 was found. Patients falling into other categories were placed into the SDP group.

Abbreviations: δDG = (dusk blood glucose difference): represents differences in blood glucose measurements between pre-dinner and post-lunch, CDP = classic dusk phenomenon group, CLDP = clinical dusk phenomenon group, R = routine group, S1 = suspicious 1 group, S2 = suspicious 2 group, S3 = suspicious 3 group, SDP = suspicious clinical dusk phenomenon group.

Keywords: diabetes, diagnosis, dusk phenomenon, pre-dinner hyperglycemia

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1. Introduction

The dusk phenomenon in diabetic patients (a clinical spontaneous and transient pre-dinner hyperglycemia) is common but often ignored by doctors. Pre/post-dinner and bedtime blood glucose in diabetic patients with this phenomenon is difficult to control.[1] Thus, these patients need more attention in clinical medicine. There are many scientific articles about this phenomenon in diabetic patients, but only a few scientific descriptions. Only 1 study regarding continuous subcutaneous insulin infusions inducing basal insulin secretions during dawn and dusk period has been reported.[2] And, our group identified 8 patients with severe, spontaneous, and transient pre-dinner hyperglycemia that received continuous subcutaneous insulin infusions (4 patients had type 1 and other 4 patients had type 2 diabetes). Pre-dinner blood glucose values in the 8 patients were stable and persistently higher than the post-lunch blood glucose values,[1] which proved that the dusk phenomenon exists. Meanwhile, some of the nondusk phenomenon patients had symptoms suspicious as being compatible with those of the dusk phenomenon. The incidence of the dusk phenomenon may be underestimated. Thus, a study regarding the mechanism behind this phenomenon is needed with establishment of diagnostic criteria to assist with clinical interventions. Unfortunately, no reports on the criteria exist. The dawn phenomenon is another spontaneous and transient hyperglycemia,[3] with similarities to the dusk phenomenon, but occurring earlier in the day. Also, there are over 180 research papers about the dawn phenomenon.[4] Since there are similarities, the diagnosis criteria for patients suffering from the

dawn phenomenon can be used as a reference for those patients suffering from the dusk phenomenon. The criteria for the dawn phenomenon are as follows: after GH (growth hormone) concentrations increase by $\geq 5 \mu g/L$, $\delta DG > 0.56$ mmol/L (absolute difference between minimum blood glucose values at night and before breakfast). Recently, continuous glucose monitoring (CGM) has become widely used with other diagnostic methods including $\delta G > 1.11$ mmol/L;[5,6] and $\delta G\% > 6.9\%$.[6] However, these methods are difficult to use because factors that influence the dusk phenomenon are different than those that influence the dawn phenomenon. Meanwhile, it is difficult to complete large clinical trials in a short period of time. Thus, cut-off points for the diagnosis of the dusk phenomenon should be generated to establish a diagnosis. We also supplemented cases and used clinical judgment as the basis for this study, which is the first to provide clinical diagnostic criteria for this clinical phenomenon.

2. Materials and methods

2.1. Materials

Data on diabetic patients that received continuous subcutaneous insulin infusion over a short period at the Cixi People's Hospital of Zhejiang Province from October 2009 and October 2012 were retrospectively analyzed. Fasting blood glucose values of incipient diabetic patients were higher than 15 mmol/L, or previous fasting blood glucose values were higher than 10 mmol/L. The current diagnostic criteria for diabetes are based on the Guidelines for prevention and control of type 2 diabetes in China (2007 Edition).[7] The classification of diabetes is based on disease history and clinical information. Research factors include blood glucose values (pre-breakfast, 2 hours after breakfast, pre-lunch, 2 hours after lunch, pre-dinner, 2 hours after dinner, and before sleep), and blood glucose differences (pre-dinner – post-lunch, pre-dinner – pre-lunch, post-dinner – post-lunch).

Inclusion criteria: Valid blood glucose monitoring days for ≥ 3 days.

Exclusion criteria (by one or more of these): Hypoglycemia after lunch, additional insulin, and extra-dining; a post-lunch blood glucose <4.4 mmol/L. Lack of pre-lunch or post-dinner blood glucose test data. In line with one or more nonvalid data assessments, the same day monitoring data are not included in the statistics.

2.2. Methods

The study is a retrospective study with no invasive procedures, only data collection and statistical analysis. There is no risk of privacy leaks. The ethical approval was not necessary. All patients receiving continuous subcutaneous insulin infusion were given a short-acting insulin analog (insulin aspart or insulin lispro) that was added to the insulin pump (IIS, Dana, South Korea). No technical problems, such as tube plugging, occurred. The initial insulin dose given to patients already using insulin was the same insulin dose as was already being used by the patient, or 0.5 U/kg of insulin was given to patients receiving insulin for the first time. The sum of 3 pre-prandials doses and basal insulin accounted for 50% each. The pre-prandial dose (pre-breakfast: 1/3 pre-prandial dose + 1 U; pre-lunch: 1/3 pre-prandial dose −1 U; pre-dinner: 1/3 pre-prandial dose). Basal insulin (dawn phenomenon and low insulin resistance status at midnight were used as the default): 0:00–4:00, the average basal dose −0.1 U/h; 4:00–8:00, the average basal dose + 0.1 U/h; 8:00–24:00, the average basal dose. The pre-prandial dose was adjusted (large dose, basal dose, temporary additional dose) according to changes in blood glucose levels. During 8:00–24:00 hours, single basal doses was always given. When the post-lunch blood glucose ≤ 13.9 mmol/L, the blood glucose data during insulin pump applications were summarized. A total of 80 patients qualified for the study.

2.2.1. Grouping. During continuous subcutaneous insulin infusion therapy, the patients were grouped based on δDG (dusk blood glucose difference). The patients with consecutive $\delta DG < 0$ mmol/L were grouped into the routine (R) group, and those with consecutive $\delta DG \geq 0$ mmol/L were grouped into the classic dusk phenomenon (CDP) group. Other patients were grouped into the suspicious (S) group, which was further divided into 3 groups based on the frequency of δDG occurrences. The suspicious 1 (S1) group: $\delta DG \geq 0$ mmol/L, only one occurrence; the suspicious 3 (S3) group: $\delta DG < 0$ mmol/L, only one occurrence. The rest of the patients were grouped into the suspicious 2 (S2) group (Table 1).

2.2.2. Statistical analysis. SPSS 22.0 software was used to analyze the data, and a $P < .05$ indicated statistical significance. Data were expressed as the mean $\pm$ SD, and comparison among groups was analyzed by the analysis of variance. Enumeration data were expressed as a percentage, and comparison among groups was analyzed by the chi-square test. The data of multiple time points were analyzed by repeated measures ANOVA.

3. Results

3.1. Basic information

Around 53 males, and 27 females; age: 55.24 ± 15 years old; height: 167 ± 7.32 cm; body weight: 65.94 ± 12.35 kg; BMI: 23.49 ± 5.24 kg/m^2; HbA1c: $11.1 \pm 1.52\%$; disease course: 24.5 ± 5.3 months. The data of each group had no statistical

Table 1					
Dividing groups.					
			Suspicious (S)		
Grouping	Routine (R)	S1	S2	S3	Classic dusk phenomenon (CDP)
Basis	Consecutive $\delta DG < 0$	$\delta DG \geq 0$ only one occurrence	The rest	$\delta DG < 0$, only one occurrence	Consecutive $\delta DG \geq 0$
Conclusion	The CLDP could be excluded		Suspicious clinical dusk phenomenon (SDP)	Clinical dusk phenomenon (CLDP)	

δDG = (dusk blood glucose difference): represents differences in blood glucose measurements between pre-dinner and post-lunch, CDP = classic dusk phenomenon group, CLDP = clinical dusk phenomenon group, R = routine group, S1 = suspicious 1 group, S2 = suspicious 2 group, S3 = suspicious 3 group, SDP = suspicious clinical dusk phenomenon group.
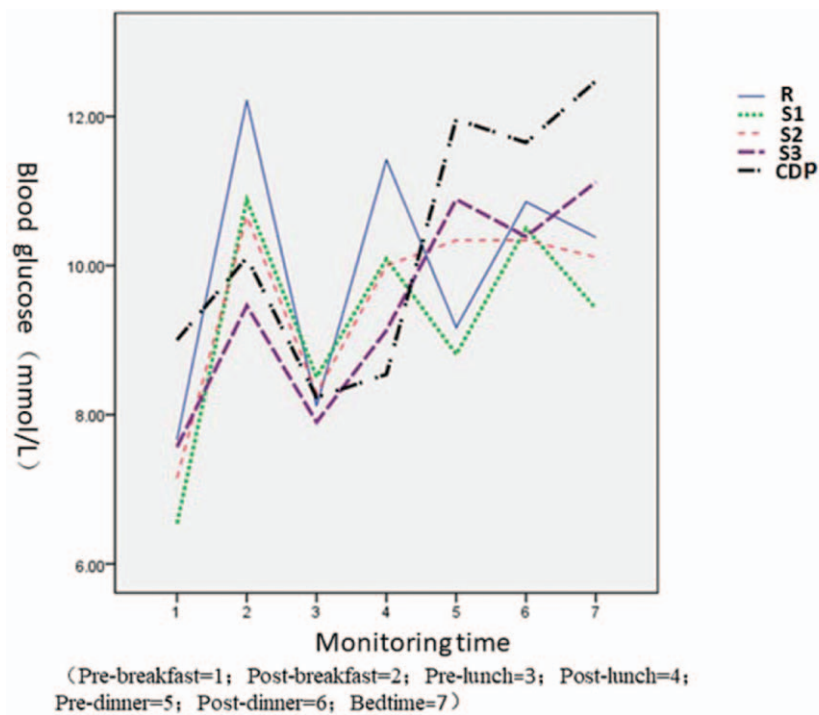
Figure 1. Line chart showing the average blood glucose value in each group.

difference among groups. There was no statistical difference in insulin dose among groups.

3.2. Number of patients and rate

A total of 80 patients were enrolled in the study. Nine patients were placed in the R group (9.8%), 13 in the S1 group (14.1%), 35 in the S2 group (38%), 12 in the S3 group (13%), and 11 in CDP group (12%). Seven patients had type 1 diabetes, and of those, 4 were in CDP group, one was in the S3 group, and 2 were in the S2 group. All other patients had type 2 diabetes.

3.3. Line charts showing the average blood glucose levels in each group (Fig. 1)

3.4. Bar chart showing the average blood glucose difference (Figs. 2–4)

3.5. Multiple comparisons of statistically significant parameters among the groups (Table 2)

The results were as follows:

There was a statistical difference in the CDP group compared with the R, S1, and S2 groups. Except for the bedtime blood glucose values, S3 was not statistically different from the CDP group. Except for the post-dinner blood glucose values, the S3 group had statistical differences with the R group. This concurred with our clinical observations. The patients in the S3 and CDP groups should have DP (dusk phenomenon) attributes. Those patients with a $\delta DG < 0$ occurring only once could have fluctuations due to blood glucose variability.

The S1 group patients were not different from the R group patients but were different from the CDP group. Thus, the S1 group belongs to the clinical R group, as does the R group. The patients with $\delta DG \geq 0$ occurring only once could have fluctuations due to blood glucose variability.

### 3.6. Best cut-off value of dusk phenomenon

The S3 and CDP groups were confirmed as belonging to the clinical dusk phenomenon (CLDP) group, and the receiver operating characteristic (ROC) curves were drawn (Fig. 5, Table 3).

3.7. The S2 group was confirmed to be in the suspicious clinical dusk phenomenon (SDP) group, and the ROC curves were drawn (Fig. 6, Table 4)

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4. Discussion

The dusk phenomenon is a transient and spontaneous hyperglycemia at dusk (before and after dinner) diabetic patients that are otherwise under adequate control with a post-lunch blood glucose with no hypoglycemic episodes.[1] After we identified the first patient that was having unusual pre-dinner hyperglycemia, we tried to understand the mechanism into why it was occurring and to identify a clinical diagnosis. This often ignored and abnormal increase in blood glucose could cause one to adjust the hyperglycemia in error, as the blood glucose during this period is spontaneous and transient. Nonintervention can lead to fluctuations in blood sugar, and over-intervention could cause hypoglycemia. Insulin intervention must be specific, or it can lead to haphazard blood glucose fluctuations.[1] Because the dusk phenomenon is often ignored during clinical evaluation, no comprehensive fundamental research has been performed. The transient and spontaneous hyperglycemia has many similar
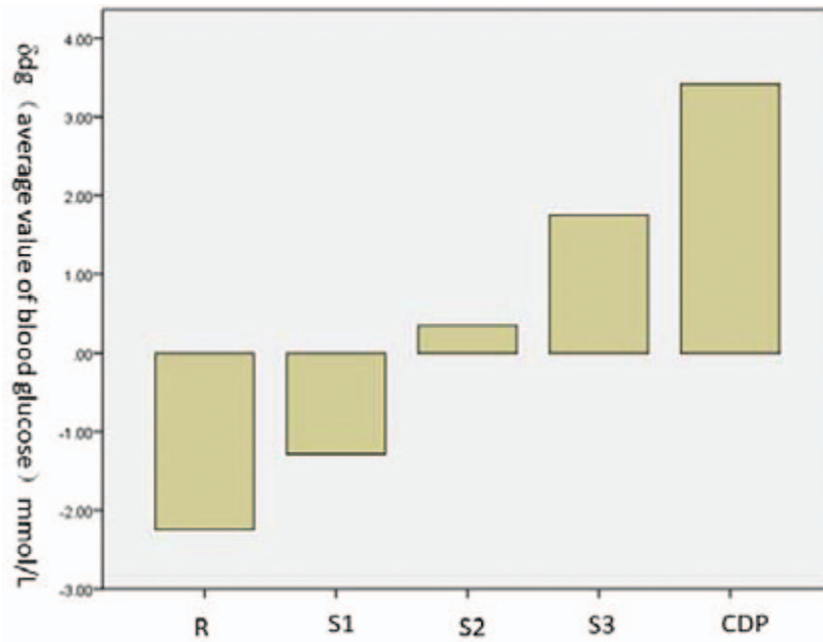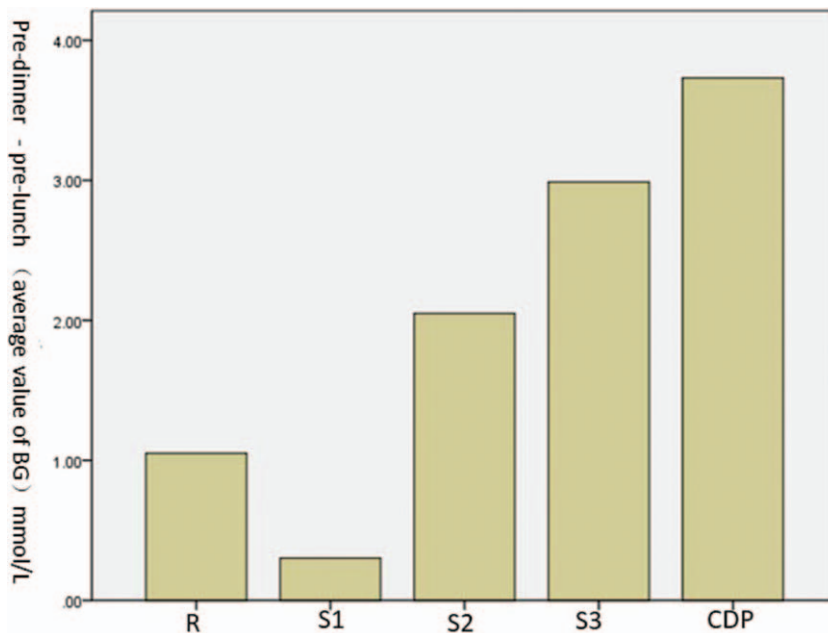
Figure 2. Bar chart showing the average blood glucose difference (bar Chart of the δDG ratios) δDG (pre-dinner-post-lunch blood glucose). δDG = (dusk blood glucose difference).

symptoms to the dawn phenomenon. Their differences are only the time of occurrence. We compared the dusk phenomenon with the dawn phenomenon, which provided a reference for our research. Previous studies reported that the dawn phenomenon result from increased production of endogenous glucose and persistent insulin resistance based on the hypofunction of pancreatic β-cells. Studies suggest that during the morning hours, increases in antagonistic insulin hormones (mainly growth hormone) lead to a damage of insulin signaling systems[8,9] and improvement in lipolysis,[10–13] which further aggravates insulin

resistance increasing the endogenous glucose production (including glycogenolysis and gluconeogenesis) and weakening the effect of insulin in peripheral tissue. Meanwhile, due to effects from the circadian rhythm of insulin,[14,15] this cascade of events ultimately causes the dawn phenomenon.

However, as the dusk phenomenon becomes increasingly known, spontaneous and transient hyperglycemia in diabetic patients seen at different time periods is increasingly reported. A diabetic patient with glaucoma blindness that had an abnormal hyperglycemic period from 21:00 to 1:00 the following day was

Figure 3. Bar chart showing the average blood glucose difference (bar chart of the pre-dinner-pre-lunch blood glucose).
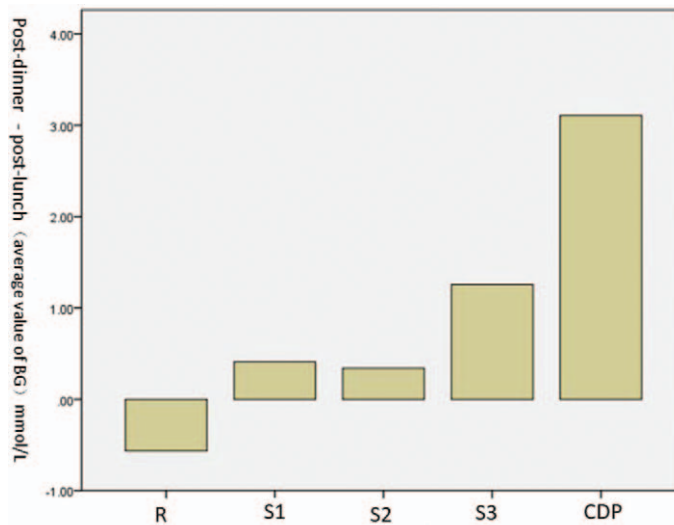
Figure 4. Bar chart showing the average blood glucose difference (bar chart of the post-dinner-post-lunch blood glucose).

difficult to diagnose using traditional methods. Previous studies mainly focused on hormone changes at midnight on an empty stomach, but ignored changes occurring throughout the day. Two issues that influence episodes of hyperglycemia with no hypoglycemia are insufficient insulin doses and an increase in hyperglycemic hormones. For diabetic patients, insufficient insulin is inevitable. However, at times of the low blood glucose, during the midnight and post-lunch hours, the possibility of having decreased insulin secretion is low, which signifies that an increase in hyperglycemic hormone concentrations is the main cause. Under non-stress states, the influence of the biological clock makes hyperglycemic hormone secretion fluctuate periodically.

In 1800s, the biological clock was proposed when scientists found a regular 24-hours-autonomous oscillation phenomenon in plants that occurred with the earth's rotation. Then, mammal studies found that almost all physiological activities and extrinsic behaviors had rhythm,[16,17] which was controlled with the brain influenced with circadian rhythm. Coordination of the rhythms in different tissues depended on signals from light. In mammals, the periodic circadian system is integrated using a time-controlled mechanism in the suprachiasmatic nucleus (SCN) of anterior

Table 2

Blood glucose values in each group and multiple comparisons of statistically significant parameters among the groups.

	Blood glucose (mmol/L) among groups					
	R	S1	S2	S3	CDP	P value
Pre-breakfast	7.66±1.89	6.54±0.96	7.15±1.79	7.57±2.04	9.00±3.34	
Post-breakfast	12.22±2.85	10.88±3.21	10.66±2.27	9.46±2.42	10.10±1.74	
Pre-lunch	8.12±2.77	8.51±2.29	8.29±2.04	7.90±1.53	8.23±1.98	
Post-lunch	11.42±1.21	10.09±1.36	10.00±1.90	9.13±1.98	8.54±1.59	Total R vs S2*, S3#, CDP vs R#, S1#, S2#
Pre-dinner	9.17±1.61	8.81±1.21	10.34±2.12	10.89±1.73	11.96±1.44	Total R vs S3*, CDP#, S2 vs CDP S1vsS2#, S3#, CDP#
Post-dinner	10.85±1.87	10.50±2.28	10.34±2.08	10.39±1.76	11.65±2.56	
Bedtime	10.38±2.22	9.43±1.61	10.11±2.03	11.12±2.60	12.48±2.55	Total CDP vs R*, S1#, S2#
δDG	−2.25±1.44	−1.28±0.49	0.34±1.42	1.76±1.18	3.42±2.18	Total R vs S2#, S3#, CDP#, S1 vs S2#, S3#, CDP S2 vs S3*, CDP#
Pre-dinner — pre-lunch	1.05±2.31	0.30±1.86	2.05±2.14	2.99±1.61	3.73±2.45	Total R vs S3*, CDP#, S1 vs S2*, S3#, CDP S2 vs CDP*
Post-dinner — post-lunch	−0.57±1.85	0.41±1.49	0.34±1.75	1.26±1.37	3.11±2.03	Total R vs S3*, CDP#, S1 vs CDP#, S2 vs CDP#

Correlations among blood glucose values from each group analyzed by one-way analysis of variance. Comparisons among groups were performed on data with statistical significance. After the homogeneity of variance test, the Tamhane method was used to perform multiple comparisons among the different δDG groups. The LSD (least-significant difference) method was used for the other groups.

δDG = (dusk blood glucose difference): represents differences in blood glucose measurements between pre-dinner and post-lunch, CDP = classic dusk phenomenon group, R = routine group, S1 = suspicious 1 group, S2 = suspicious 2 group, S3 = suspicious 3 group.

* $P < .05$.
# $P < .01$.
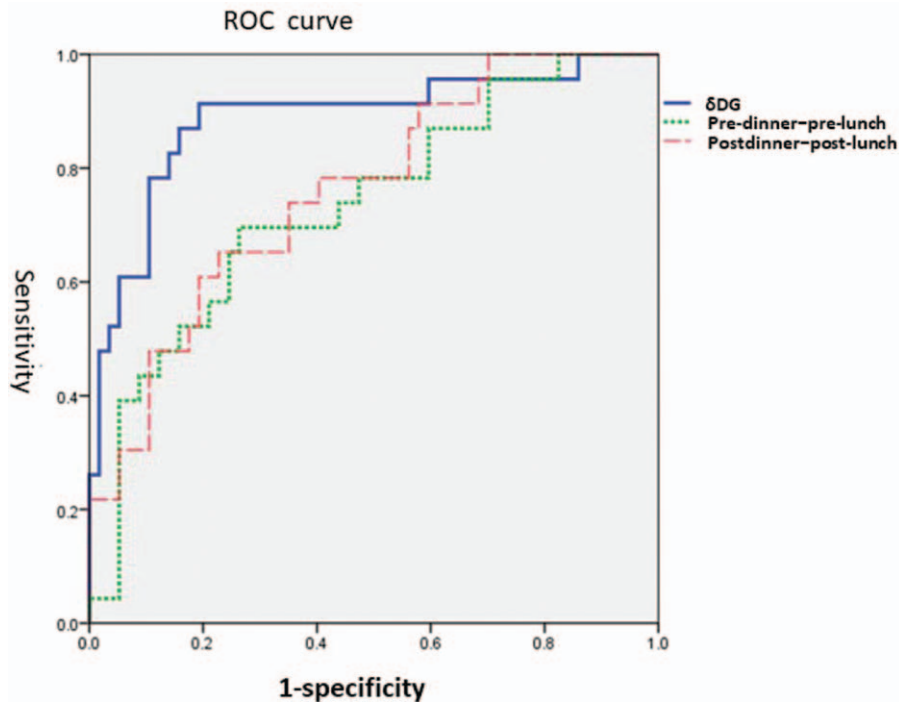
Figure 5. Best cut-off value of dusk phenomenon. The ROC curve of the diabetic clinical dusk phenomenon (CLDP). CLDP = clinical dusk phenomenon, ROC = receiver operating characteristic.

hypothalamus.[18,19] Intracellular gene expression in the SCN biological clock were expressed in a circadian way in other areas of the brain, peripheral organs and cultured cells, in vitro.[20–22] The pancreas secretes insulin and glucagon into plasma, which provides stable control of blood glucose. Moreover, these hormones have 24 h-fluctuations during fasting.[23] The biological clock genes PERl, PER2, BMALl, CLOCK, and REV-ERBα are expressed in the pancreas and found to fluctuate during a 24 hours period.[24] And, highly expressed transcription factors and biological clock genes that control the d-binding protein and the thyrotrophembryonic factor exist in human pancreatic islet cells, and levels change in insulin-secreting cells at night and in the day.[25] These findings prove the existence of biological clock genes in pancreatic islet cells. Moreover, the external environment can regulate biological rhythm and the insulin biological clock. It has been reported that sleep deficiency is associated with an increase in the incidence of diabetes.[26] Even if the amount of sleep is sufficient, circadian oscillation disorders can increase the diabetic risk by changing the sleep schedule.[27] All the studies concerning the biological clock suggest that its complexity, universality, objectivity, and variability are based on blood glucose levels. Many instances have shown that various hormones periodically oscillate during the dawn phenomenon.

Meanwhile, specific transient hyperglycemia at different time periods can be explained. It is possible that the pancreatic hormones, living conditions, blood glucose-related biological clock adjustment system disorders, and biological clock redistributions increase oscillations and induce the dawn or dusk phenomena. The degree of hyperglycemia can vary and hyperglycemia can also be caused by other specific and transient causes.

The hypothesis behind the dusk phenomenon needs proof to be provided through fundamental, clinical research. In nature, the dusk phenomenon is not the comparison between pre-dinner and post-lunch blood glucose, but it measures pre-dinner basal hyperglycemia, eliminating the effect of lunch. It is challenging to observe in clinical settings. Continuous subcutaneous insulin infusions, in our study, provided an ideal platform for the observation of the dusk phenomenon. The preprandial basal insulin can be compared to the preprandial blood glucose. Giving the preprandial insulin via a continuous pump can eliminate the influence of increased blood glucose and simulate a single spike of glucose similar to the dawn phenomenon. The abnormally increased blood glucose in the patients with the dusk phenomenon will then be exposed to show higher blood glucose levels pre-dinner compared with post-lunch.[1] The dusk phenomenon is not a disease, but a poorly understood disorder in the initial stages of research. In this study, our primary goal was to confirm cases according to clinical observations. Then, we applied statistics to objectively and specifically prove the validity of this disorder. The interval cut-offs established clinical standards mathematically.

In the clinic, the frequency with which δDG≥0 mmol/L occurred was closely related to the severity of the dusk phenomenon and the difficulty in controlling post-dinner blood glucose levels. The line chart (Fig. 1) indicated that no statistical differences were seen in blood glucose levels before and after

Table 3

The ROC curve of the diabetic clinical dusk phenomenon (CLDP).

	Cut-off point	Sensitivity	Specificity	AUC
δDG	1.0167	0.913	0.807	0.887
Pre-dinner − pre-lunch	2.72	0.696	0.737	0.735
Post-dinner − post-lunch	1.2667	0.652	0.772	0.760

δDG = (dusk blood glucose difference): represents differences in blood glucose measurements between pre-dinner and post-lunch, AUC = area under curve, CLDP = clinical dusk phenomenon group, ROC = receiver operating characteristic.

Figure 6. ROC curves of the diabetic suspicious clinical dusk phenomenon (SDP). ROC = receiver operating characteristic, SDP = suspicious clinical dusk phenomenon.

breakfast and before lunch. The pre-lunch blood glucose levels almost found a common starting point; however, after lunch, blood glucose values began to change. However, the trends changes in the R and the S1 groups were consistent. This consistency was also seen between the S3 and the CDP groups, but the chart for the CDP group was more extreme. The S2 group was in an intermediate state. Multiple statistical analyses performed on each group also proved the hypothesis (Figs. 2–4, Table 2) that since no gold standard for the dusk phenomenon exists; we confirmed that S3 and CDP groups fell within the CLDP group. ROC curves were drawn to reveal the δDG of the clinical dusk phenomenon to have a cut-off point of 1.0167 mmol/L (19.2 mg/dL). This point had good sensitivity and specificity. The area under curve (AUC) was 0.887, which suggested good diagnostic accuracy (Fig. 5, Table 3).

We found that the best starting point to measure blood glucose in each group was pre-lunch. After this time, blood glucose values moved in different directions. The patients in the CLDP group had significantly lower post-lunch blood glucose. Before dinner, the blood glucose levels jumped (Fig. 1). When the dose of insulin is not significantly changed, the patients in the CLDP group had excellent post-lunch blood glucose values, indicating good therapeutic sensitivity. However, the pre-dinner blood glucose levels rapidly increased, which suggested that a specific hyperglycemic hormone increased sharply. The periodic oscillation of the hyperglycemic hormone in patients from the CLDP group was the most drastic. Patients in the CDP group had severe oscillations, but those in the S3 group were milder. We measured

blood glucose 7 times daily during continuous subcutaneous insulin infusion therapy. Thus, it was easy to measure δDG and to recognize the dusk phenomenon. However, conventional blood glucose monitoring methods measure, fasting blood glucose + blood glucose after 3 meals and blood glucose before 3 meals + bedtime blood glucose. The diagnosis of the dusk phenomenon is easily missed. In clinics, we find that pre-lunch blood glucose levels were normal, the pre-dinner levels increased, making the dusk phenomenon highly possible. Meanwhile, post-dinner blood glucose in the CLDP group significantly increased and was hard to control. The post-dinner blood glucose was not different among the groups; however, blood glucose levels significantly increased compared with post-lunch blood glucose levels (Fig. 4, Table 2). Moreover, the bedtime blood glucose in the CLDP group significantly increased, suggesting a lag in the dusk phenomenon influence. In addition, the pre-dinner-pre-lunch blood glucose differences (Fig. 3) indicated significant differences between the CLDP and the R groups.

We analyzed the blood glucose differences (pre-dinner – pre-lunch, post-dinner – post-lunch) during conventional therapy after discontinuing the insulin pump, and confirmed the diagnostic cut-off point and the decision to combine the groups. However, because this is a retrospective research study, therapy became complicated after the pump was discontinued, which made an effective observation of the data difficult. Finally, data obtained during continuous subcutaneous insulin infusion were used for analysis. Furthermore, as with the other clinical cut-off points, those involving the CLDP were calculated. Other cut-off points of the CLDP were pre-dinner – pre-lunch blood glucose (blood glucose before 3 meals + bedtime blood glucose) of 2.72 mmol/L with an AUC of 0.735, which suggests diagnostic accuracy. The post-dinner – post-lunch blood glucose (fasting blood glucose + blood glucose after 3 meals) was 1.2667 mmol/L (22.8 mg/dL) with good sensitivity and specificity of the cut-off values. The AUC was 0.76, which suggests diagnostic accuracy (Fig. 6, Table 4).

The S2 group was significantly different from the CDP group and was different from the R group in the δDG and the post-lunch blood glucose. Multiple statistical comparisons with the S1 and S 3 groups indicated that the S2 group was not different in many

Table 4

ROC curves of the diabetic suspicious clinical dusk phenomenon (SDP).

	Cut-off point	Sensitivity	Specificity	AUC
δDG	−0.95	0.845	0.909	0.901
Pre-dinner − pre-lunch	0.8708	0.793	0.636	0.748
Post-dinner − post-lunch	1.2667	0.652	0.772	0.654

δDG = (dusk blood glucose difference): represents differences in blood glucose measurements between pre-dinner and post-lunch, AUC = area under curve, ROC = receiver operating characteristic.

parameters observed. Thus, we decided that this group belonged in the suspicious clinical dusk phenomenon group, and because many patients were in this group (35/80), large variabilities among patients existed, and the observation time was too short; therefore, no further groupings were done. The patients in this group were between the R group and CLDP group. We decided to increase emphasis on the dusk phenomenon in the clinical setting by placing this group in the SDP group and confirmed the cut-off point to be δDG: -0.95 mmol/L. The pre-dinner-pre-lunch cut-off point was 0.87 mmol/L; the post-dinner-post-lunch cut-off point was 1.2667 mmol/L. However, the cut-off points of the post-dinner-pre-lunch blood glucose in the CLDP and the SDP groups were the same. This similarity suggests that in these 2 indices, the overlap between the SDP group and CLDP group exists. When it reaches the suspicious standard, pre-dinner blood glucose monitoring is needed to guarantee diagnostic accuracy.

This study took a clinical disorder as the main observation. The patients had high blood glucose levels and had been given continuous subcutaneous insulin infusion therapy, but this did not represent all diabetic patients. Due to medical insurance restrictions, the total number of patients using insulin pumps is small. At the same time, when we find the diabetes dusk phenomenon, we must intervene based on clinical and ethical requirements. The way to deal with the phenomenon of dusk is to increase the basal insulin, which can control the blood sugar steadily. So we can't see abnormally high pre-dinner blood glucose, so these cases cannot be added to this study. In fact, there are many similar clinical cases that were later discovered, and this is not a rare phenomenon. As long as blood glucose monitoring is performed 7 times daily during continuous subcutaneous insulin infusion therapy, it is very easy to find similar cases. At the same time we have begun to summarize the intervention studies of the phenomenon of dusk. Such as the method of giving patients metformin tablets in advance, or the method of using subcutaneous insulin in advance, or changing the basic distribution of insulin pump. Through the above 3 methods, we have achieved good results. In this study, a large number of clinical cases provide more significance to confirm the incidence of the dusk phenomenon and to detail the clinical characteristics of the patients, which can provide a basis for dusk phenomenon research.

5. Conclusions

A persistent δDG ≥ 0 or a once only δDG < 0 can be diagnosed with the CLDP. The CLDP can be excluded when the consecutive δDG < 0 or the once only δDG ≥ 0. Other patients are evaluated as having the SDP. The δDG cut-off for the CLDP group was 1.0167 mmol/L. The pre-dinner-pre-lunch blood glucose cut-off for this group was 2.72 mmol/L. The δDG cut-off for the SDP group was -0.95 mmol/L. The pre-dinner-pre-lunch blood glucose cut-off for this group was 0.87 mmol/L. The cut-off points for the post-dinner-post-lunch blood glucose measurements in the CLDP and SDP groups were both 1.2667 mmol /L.

Acknowledgments

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Methodology: Wei Li.
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