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Study on the changes of blood glucose in hemodialysis patients with diabetes

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SUMMARY

OBJECTIVE: The aims of this study were to observe the regularity of blood glucose changes in hemodialysis patients with diabetes, time of onset of hypoglycemia and blood glucose level during dialysis, and to explore the sensitive early warning indicators of hypoglycemia in dialysis patients.

BACKGROUND: Diabetes patients have a high incidence of hypoglycemia during hemodialysis.

METHODS: A total of 124 maintenance hemodialysis patients with diabetes were selected for this study. Before dialysis, one, two, and three h after dialysis, and when hypoglycemia symptoms occurred, the blood glucose changes were monitored, the blood glucose drop range was observed when hypoglycemia symptoms occurred, and the correlation between the two was analyzed.

RESULTS: After the start of the dialysis, the patient's blood glucose showed a downward trend. The symptoms of hypoglycemia were most obvious within one–two hours, with an incidence rate of 57.9%. When the blood glucose drop percentage reached 37.7%, the specificity and sensitivity of early warning hypoglycemia symptoms were 84.6 and 73%, respectively.

CONCLUSIONS: For hemodialysis patients with diabetes, attention should be paid to the symptoms of hypoglycemia during dialysis, and blood glucose should be monitored before dialysis and after 1–2 h of dialysis. If the blood glucose drop percentage is greater than 37.7%, the timely measures should be taken.

KEYWORDS: Diabetes mellitus. Hemodialysis. Blood glucose.

INTRODUCTION

In maintenance hemodialysis patients with diabetes, the incidence of hypoglycemia during dialysis is as high as 16.9–47.6%, which may cause heart and cerebrovascular accidents in severe cases[1,2]. Hypoglycemia can be diagnosed in diabetic patients with a blood glucose value of ≤3.9 mmol/L. However, since the blood glucose of patients in dialysis is in a state of non-physiological decline, some patients will have symptoms of hypoglycemia earlier before the blood glucose value reaches 3.9 mmol/L, and some patients have unperceived hypoglycemia. More experienced nursing staff should not only pay attention to low blood glucose levels but also combine the observation of the symptoms of hypoglycemia and the blood glucose drop range to achieve early detection and early prevention.

The focus of this study was to find the impact of the blood glucose drop range during hemodialysis on the clinical symptoms of hypoglycemia in patients with diabetic nephropathy and to use the blood glucose drop percentage as a reminder to carry out nursing interventions for patients in advance, so as to reduce the occurrence of hypoglycemia in patients with

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diabetic nephropathy during hemodialysis and ensure the safety and comfort of patients during dialysis.

METHODS

Clinical data

A total of 124 maintenance hemodialysis patients with diabetes who were treated in Renji Hospital Affiliated to Medical College of Shanghai Jiaotong University, Shanghai Sixth People's Hospital, and Punan Hospital in Pudong New Area, Shanghai from October 2018–July 2019 were selected as research groups.

The inclusion criteria were as follows:

a) patients who were clinically diagnosed as end-stage diabetic nephropathy or end-stage nephropathy with diabetes, wherein diabetes meets the WHO diagnostic criteria, and nephropathy meets the diagnostic criteria of the Nephrology Branch of Chinese Medical Association;
b) patients with informed consent to participate in the investigation and research;
c) patients with regular hemodialysis duration longer than 3 months–i.e., hemodialysis was performed three times a week four hours each time;
d) patients with complete cognitive ability and who cooperated with the research and investigation;
e) patients who were above 18 years old.

The exclusion criteria were as follows:

a) patients with severe consumptive diseases such as malignant tumor;
b) patients with severe complications such as hypertension and heart failure;
c) patients who did not cooperate with the investigation and research;
d) patients who took drugs that affect blood glucose during dialysis, such as glucocorticoids (prednisone, dexamethasone, etc.), contraceptives, anti-asthmatic drugs, antituberculosis drugs, diuretics, adrenaline, antipsychotics, and immunosuppressive drugs;
e) patients who suffered from mental and neurological diseases; and
f) patients who did not follow the physician's advice for dialysis.

Research methods

This study is an investigative study, focusing on the observation of blood glucose changes, hypoglycemia symptoms, and time of onset of hypoglycemia in hemodialysis patients with diabetes.

Blood glucose monitoring tools

Johnson & Johnson blood glucose meter and the supporting test papers were used. The blood glucose meter was calibrated once a day by the professional staff of Johnson & Johnson using a special simulated blood glucose solution (quality control solution), and the error value was within ±10%. During the entire research process, the brands of blood glucose meters and test papers were not changed. The blood glucose meter and blood glucose test paper were checked for the validity period of the quality inspection, and there was no damp and mildew.

Observation indicators

Blood glucose level: The blood glucose level was noted before dialysis, one, two, and three h after dialysis, and when hypoglycemia symptoms occurred. When the blood glucose value is <3.9 mmol/L, the patient is diagnosed as hypoglycemia.

Hypoglycemia symptoms: according to the "Expert Consensus on the Management of Hypoglycemia in Diabetic Patients in China," hypoglycemia symptoms are divided into autonomic symptoms and neurological hypoglycemia symptoms. Symptoms of the autonomic nervous system include hunger, sweating, anxiety, paresthesia, palpitations, tremors, pale complexion, tachycardia, and pulse pressure. And symptoms of the neurological hypoglycemia include weakness, dizziness and headache, confusion, abnormal behavior, cognitive impairment, blurred vision, diplopia, central blindness, hypothermia, epilepsy, and coma. During the research and observation process, the patients were given health education about the symptoms of hypoglycemia in advance, and they were instructed to inform the nurses of their feelings when any of the above symptoms of hypoglycemia occurred. At the same time, researchers should also pay close attention to the patient's physical signs.

Time of onset of hypoglycemia: when the patient complains of any of the above symptoms of hypoglycemia or the researcher observes that the patient has symptoms of hypoglycemia, the accurate time of the appearance of the hypoglycemia symptoms is recorded immediately, with the unit of time accurate to the minute. During the entire dialysis process, if the patient has neither the symptoms of hypoglycemia nor the measured blood glucose value per hour that is ≥3.9 mmol/L, it means that the patient has not had a hypoglycemia event during the four hours dialysis process.

Research implementation process

The experiment was introduced to the patient, the patient's consent was received, and the informed consent form was signed.

The general information of the patient were recorded.

Interpretation and education: patients were guided to understand hypoglycemia symptoms correctly and to timely inform researchers when any hypoglycemic symptoms appear.

If the patient has no complaints of hypoglycemic symptoms during the entire hemodialysis process, he/she should be monitored at 1-h intervals (before dialysis, and one, two, and three h during dialysis), and if the blood glucose value of the four measurements is not <3.9 mmol/L, it means that the patient does not have hypoglycemia during hemodialysis.

If the patient does not complain of hypoglycemia symptoms during hemodialysis, but the blood glucose value measured during hourly monitoring is ≤3.9 mmol/L, it means that the patient has hypoglycemia during hemodialysis and the time should be recorded.

If the patient complains of any symptoms of hypoglycemia during hemodialysis, immediately measure the blood glucose value at that time and the time should be recorded.

Taking into account the safety of the patient: After the patient has symptoms of hypoglycemia and/or blood glucose value <3.9 mmol/L, it is recommended that the patient is allowed to eat or be given glucose treatment. Then, the patient's symptoms should be closely observed, and the blood glucose level should be monitored 15 min later to ensure the safety of patients during hemodialysis.

Statistical methods

Double entry of patient data was checked and eliminated, and the data were analyzed by SPSS23.0 statistical software. The χ^2 test was used for the comparison of count data, and $p<0.05$ indicates that the difference was statistically significant. The χ^2 test was used to compare the incidence of hypoglycemia in different time periods, and $p<0.05$ was considered statistically significant. The receiver operating characteristic (ROC) curve was used to evaluate the specificity and sensitivity of blood glucose level, blood glucose drop range, and blood glucose drop percentage to the occurrence of hypoglycemia symptoms, with $\alpha=0.05$ as the test level.

RESULTS

General information

As shown in Table 1, there is no significant difference between the basic data and the clinical information of patients in the hypoglycemia group and the nonoccurring group.

Comparison of the occurrence of hypoglycemia symptoms in each time period

There are differences in the incidence of hypoglycemia in the four time periods, and the differences are statistically significant. The incidence of hypoglycemia in 60–120 min is the highest, with an incidence of 69.4%. The test level is α:0.05/6=0.0083. After pairwise comparison, it can be found that the incidence of hypoglycemia at 60–120 min is the highest, and the difference is statistically significant.

Table 1. Comparison of patient's basic information.

Basic information		Hypoglycemia group	Non-hypoglycemic group (n)	t/χ^2	p-value
Gender	Male	62	6	0.440	0.506
	Female	49	7		
Age		58.40±2.41	60.17±0.60	-0.911	0.364
Years of hemodialysis		5.45±0.67	5.15±0.19	0.511	0.611
Primary disease	Diabetic nephropathy	75	5	0.980	0.323
	End-stage nephropathy with diabetes	43	1		
Years of diabetes		6.92±0.49	7.89±0.16	-1.784	0.077
Medication or not	No	63	8	0.110	0.742
	Yes	48	5		
Type of hypoglycemic drugs before current dialysis	Oral	17	3	0.550	0.458
	Insulin injection	23	2		

The ROC analysis of blood glucose level, blood glucose drop range, blood glucose drop percentage, and the occurrence of hypoglycemia

As shown in Figure 1 and Table 2, it can be found that the area under the ROC curve (AUC) of blood glucose when symptoms occur is 0.183, p=0.000.

The AUC of the blood glucose drop range is 0.686, p=0.028, the critical value is 4.05, the sensitivity is 67.6%, and the specificity is 69.2%.

The AUC of the blood glucose drop percentage is 0.834. When the AUC is between 0.7–0.9, the experimental accuracy is high, p=0.000. The critical value of the blood glucose drop percentage is 37.7%, the sensitivity is 73%, and the specificity is 84.6%. When the blood glucose drop percentage is 37.7%, it is prone to symptoms of hypoglycemia, which is worthy of clinical vigilance.

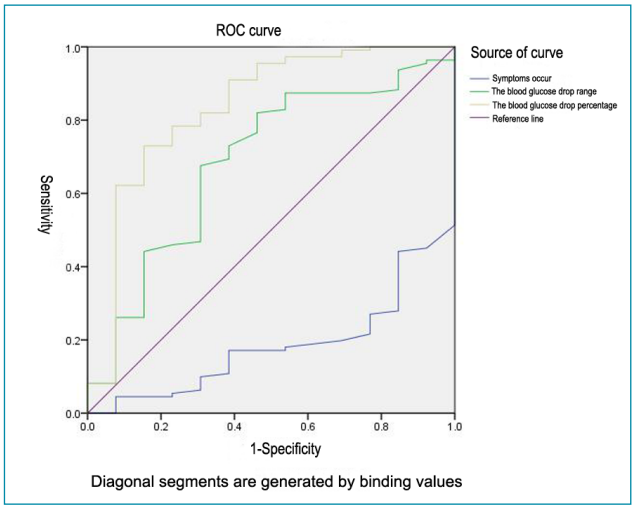

Figure 1. Area under the receiver operating characteristic curve.

Comparing the areas under the three curves, it can be seen that the AUC of the blood glucose drop percentage is 0.834, indicating that the blood glucose drop percentage is more accurate in diagnosing the occurrence of hypoglycemia symptoms than the blood glucose level and the blood glucose drop range.

DISCUSSION

Hemodialysis patients with diabetes have many reasons for frequent hypoglycemia during dialysis. First, the patient's own kidney failure, the kidney's inactivation and excretion of insulin, or hypoglycemic drugs are reduced, resulting in the accumulation of insulin in the body[3-4]. Second, during hemodialysis, insulin is a macromolecular substance and cannot be easily removed by dialysis treatment, while glucose, as a small molecular substance, can freely pass through the filter membrane of the dialyzer. Third, due to the difficulty in storage of glucose-containing dialysate and the occurrence of nosocomial events, sugar-free dialysate is widely used in hospitals in China. Guo Jianzhong et al.[5] found that with the sugar-free dialysate, about 5.5–6.0 g glucose can be lost per hour. Once serious hypoglycemia occurs and the treatment is not timely, it will not only affect the quality and comfort of the dialysis patients but also cause cardiovascular and cerebrovascular accidents[6,7]. The ratio of complication and mortality of hemodialysis patients with diabetic nephropathy to that of patients with nondiabetic nephropathy is 2:1[1]. Nursing staff should pay close attention to the changes in blood glucose in patients with diabetic nephropathy during dialysis.

In previous studies, many scholars have proposed the importance of monitoring blood glucose and observing the symptoms of hypoglycemia during dialysis. Domestic researcher Zhang Ronghua[8] proposed that during dialysis for diabetic nephropathy, blood glucose should be monitored before dialysis and one, two, and three h after dialysis, and timely measures should be taken to control the occurrence of hypoglycemia. Although diabetic

Table 2. Receiver operating characteristic analysis of blood glucose level, blood glucose drop range, blood glucose drop percentage, and the occurrence of hypoglycemia.

Area under the curve					
Test result variable	Area	Standard error[a]	p-value	Asymptotically 95%(CI)	
				Lower limit	Upper limit
Blood glucose at symptom onset	0.183	0.047	0.000	0.090	0.276
Blood glucose drop range	0.686	0.080	0.028	0.530	0.843
Blood glucose drop percentage	0.834	0.070	0.000	0.696	0.972

[a]Under the nonparametric assumption.

patients are diagnosed with hypoglycemia only when their blood glucose value is <3.9 mmol/L, domestic scholar Wang Jianhua[9-13] proposed that hypoglycemia can also occur if blood glucose is not low. In most cases, the severity of hypoglycemia symptoms such as hunger, palpitation, and sweating is basically consistent with the blood glucose level of patients, but there are also exceptions. Clinically, when some diabetic patients have symptoms of hypoglycemia such as palpitation and hunger, the results of immediate blood glucose test are not low. This phenomenon is called "hypoglycemia reaction." Although the blood glucose in "hypoglycemic response" is not low, it should not be overlooked or ignored. In principle, it should be treated the same as hypoglycemia, and appropriate amount of carbohydrates must be supplemented in time before the blood glucose level drops to 3.9 mmol/L to quickly relieve the symptoms of hypoglycemia and prevent cardiovascular and cerebrovascular accidents.

During this study, the blood glucose level showed a downward trend in the process of hemodialysis, and the main symptom of hypoglycemia was hunger. During this experiment, there was no case of severe hypoglycemia (endangering the patient's heart and cerebral vessels and even life, and blood glucose value <2.8 mmol/L). After the patient developed symptoms of hypoglycemia, he/she was treated immediately, instead of using the blood glucose value of 3.9 mmol/L as the judgment standard, so as to effectively reduce the occurrence of severe hypoglycemia. It can be seen that although the incidence of hypoglycemia in patients with diabetic nephropathy is high in hemodialysis, as long as the nursing staff pay close attention to the changes of blood glucose and the symptoms and signs of hypoglycemia and intervene in advance before the blood glucose value reaches 3.9 mmol/L, it can effectively reduce the occurrence of malignant hypoglycemia.

As shown in Figure 1 and Table 2, the ROC curve analysis shows that the critical value of the blood glucose drop percentage is 37.7% with AUC=0.834 (p=0.00). A curve is drawn with sensitivity as the ordinate and 1-specificity as the abscissa. The larger the AUC, that is, the closer the curve is to the upper left, the higher the sensitivity and specificity that this method can achieve at the same time, and the greater the diagnostic value. When the AUC>0.7, it indicates that the blood glucose drop percentage has certain specificity and sensitivity for the prediction of hypoglycemia symptoms. This study changed the previous medical staff's cognition of hypoglycemia in patients with diabetic nephropathy during hemodialysis that 3.9 mmol/L is not the only and accurate standard for the diagnosis of hypoglycemia. Since the symptoms of hypoglycemia in patients with diabetic nephropathy during hemodialysis are earlier than the blood glucose value of 3.9 mmol/L, the blood glucose drop percentage can be used to indicate the occurrence of hypoglycemia more in advance and more accurately. In future clinical practice, blood glucose management process in dialysis can be formulated according to the blood glucose drop percentage.

CONCLUSION

Through this study, during hemodialysis, it is proved that the percentage of blood glucose drop reaching 37.7% is more accurate for predicting the symptoms of hypoglycemia in patients with diabetic nephropathy.

AUTHORS' CONTRIBUTIONS

LSHL: Conceptualization. **YY:** Data Curation, Formal Analysis. **PC:** Writing – original draft, Writing – review & editing. **SYZ:** Writing – original draft, Writing – review & editing. **HFQ:** Data Curation, Formal Analysis. **CYY:** Writing – review & editing. **HFZ:** Writing – review & editing.

ETHICS APPROVAL

This study was conducted in accordance with the Declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Renji Hospital, School of Medicine, Shanghai Jiao Tong University. Written informed consent was obtained from all participants.

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