ORIGINAL ARTICLE

Carbohydrate Supplement before Hemodialysis to Prevent Hypoglycemia and Low Blood Glucose in Diabetic and ESKD Patients

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Objective: The benefits of carbohydrate supplementation before hemodialysis (HD) in diabetic patients are unclear. The present study assessed the impact of a pre-dialysis carbohydrate snack.

Materials and Methods: A quasi-experimental study was conducted in type 2 diabetes patients undergoing HD with baseline blood glucose levels between 80 and 200 mg/dL across six centers in Nakhon Ratchasima Province, Thailand. Blood glucose was measured at baseline and at 1, 2, 3, and 4 hours during HD. A 15 g carbohydrate snack was given 15 to 30 minutes before the start of HD. The incidence of hypoglycemia and blood glucose levels below 90 mg/dL during HD were compared between sessions with and without the snack. Secondary outcomes included intradialytic hypotension and patient satisfaction.

Results: One hundred thirteen participants, with a mean age of 56 years and a BMI of 24 kg/m^2, were included. Participants had a mean diabetes duration of 13 years, HbA1c of 6.5%, and had been on dialysis for 33 months. Forty-four percent were not on anti-diabetic medication. Hypoglycemia during HD occurred in 0.4% of sessions. Low blood glucose during HD decreased from 29.2% without the snack to 20.4% with the snack (risk reduction 0.08, 95% CI –0.02 to 0.2, p=0.12). Intradialytic hypotension was comparable between groups, and most participants reported high satisfaction with the snack.

Conclusion: From the quasi-experimental study, carbohydrate snacks before dialysis show a trend to reduce low blood glucose during HD without increasing intradialytic hypotension.

Keywords: Carbohydrate supplement; Diabetes; Hemodialysis; Hypoglycemia

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Diabetes is the most common cause of end-stage kidney disease (ESKD) requiring dialysis worldwide[1]. Blood glucose dysregulation is common in patients with diabetes who are undergoing hemodialysis (HD), and maintaining the blood glucose level in the optimal range without hypoglycemia is a challenging issue. ESKD-related factors such as decreased gluconeogenesis and poor intake, and dialysis-related factors such as decreased insulin clearance and antidiabetic drugs, glucose loss into the dialysate fluid, diffusion of glucose into erythrocytes, and meal restriction during or just before HD, lead to hypoglycemia. On the contrary, increased insulin clearance by HD, shifting meals from before or during HD to post-HD, and increased counter-regulatory hormones from low blood glucose (LBG) result in hyperglycemia, especially after HD[2]. The current guidelines recommend maintaining hemoglobin A1c (HbA1c) within a range, from 6.5% for fit patients with a low risk of hypoglycemia to 8% for those with multiple comorbidities and a high risk of hypoglycemia[3,4]. In particular, even low blood sugar levels of less than 100 mg/dL in ESKD may increase mortality[5]. The incidence of hypoglycemia in patients with diabetes having ESKD and undergoing HD has been reported to be 17% to 24%, with most of them being asymptomatic[6-8]. Several interventions can prevent hypoglycemia during HD, including blood glucose monitoring, tailoring antidiabetes drugs, and avoiding glucose-free or low-glucose dialysate[6,9,10].

Carbohydrate supplementation is another practical intervention to prevent and rescue

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hypoglycemia in patients with diabetes in various settings, especially before exercise[11,12]. In HD with diabetics, which has a high incidence of hypoglycemia, carbohydrate supplementation just before or during HD is an interesting idea. However, in clinical practice, allowing oral food intake just before or during HD varies considerably across in-center dialysis facilities globally[13] owing to the concern of postprandial splanchnic vasodilation. This condition can result in a postprandial drop in blood pressure and intradialytic hypotension, especially in patients with diabetes and neuropathy[14,15]. Because of variations in clinical practice and the lack of robust evidence for carbohydrate supplementation before HD, the present study evaluated the benefits and risks of 15 g of carbohydrate supplementation before HD in patients with diabetes.

Objective

The present study aimed to determine whether diabetic patients with ESKD exhibited a different incidence of hypoglycemia and LBG, which is defined as blood glucose levels below 90 mg/dL, on days when they were administered 15 g of carbohydrates prior to dialysis versus days without carbohydrate administration. Secondary outcomes included intradialytic hypotension and patient satisfaction.

Materials and Methods

Study design and participants

A non-randomized quasi-experimental study was conducted in six HD centers in Thailand between May 2023 and May 2024. Adults, aged older than 18 years, with diabetes and ESKD receiving HD for more than three months and on stable antidiabetes treatment for more than one month were screened. Those with a capillary blood glucose (CBG) level of 80 to 200 mg/dL before HD who provided informed consent to participate in the study were enrolled. Blood glucose levels during HD were compared between an HD session without snack supplementation (control group) and an HD session with snack supplementation (intervention group). Patients who were unable to swallow the food, those who were currently on steroids, and those who had unstable ESKD conditions such as volume overload, uncontrolled blood pressure, and active infection, were excluded from the study. The present study was approved by the Maharat Nakhon Ratchasima Hospital Institutional Review Board (number 052/2023). The baseline data, including comorbidity, current diabetes medication, and blood chemistry, were collected.

Figure 1. The details of Thai rice crackers.

HD prescription

In the first HD session, and for the control group, the participants received the usual HD two to three times a week for four hours per session with a dialysate fluid that contained 100 mg/dL of glucose. The blood flow rate was set at 300 mL per minute, and the dialysate flow rate was set at 500 mL per minute using a reused high-flux dialyzer, thus a surface area of 1.8 to 2.1 m^2. Ultrafiltration was set at a dry weight that did not exceed four liters to prevent intradialytic hypotension. Meals, including food and drink, were not allowed during HD in all dialysis centers. The patients did not have any light meal, snack, or drink that contained sugar for 30 minutes before starting HD. Blood pressure was recorded every 30 minutes during dialysis. Clinical status and HD parameters, including ultrafiltration rate, were monitored during HD.

Snack supplementation

In the next HD session, for the intervention group, the patients received all dialysis prescriptions similar to those in the control group, and a light snack was added 15 to 30 minutes before HD. The snack was a 22 g Thai rice cracker, which is Thai rice 85%, black sesame 10%, vegetable oil 2%, and salt 3%, that contained 15 g of carbohydrates, 1 g of protein, 5.3 g of fat, and 0.66 g of sodium, and had a total calorific value of 112.2 kcal. The details of Thai rice crackers are shown in Figure 1. The HD prescription was the same as that of the first session, including the prohibition of any food or drink during HD.

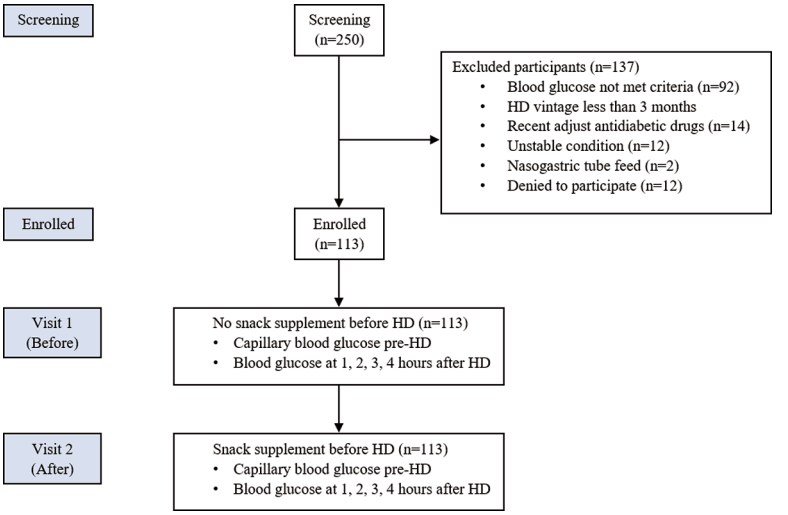

Figure 2. Flow chart of patient enrollment.

Glucose measurement

The CBG level in the blood at the fingertip was measured using Contour® plus (Ascensia Diabetic Care Holdings AG, Switzerland) before starting dialysis (0 hour). The blood glucose was measured at fixed hourly intervals as the end of 1, 2, and 3 hours and the end of the dialysis (4 hours) using a glucometer (Contour® plus; Ascensia Diabetic Care Holdings AG, Switzerland) from the venous blood during HD.

Outcomes

The primary outcome of hypoglycemia incidence during dialysis was defined as a blood glucose level of less than 70 mg/dL at 1, 2, 3, or 4 hours. The secondary outcomes included the incidence of LBG, with blood glucose of less than 90 mg/dL during HD. Moreover, the blood pressure was measured every 30 minutes during dialysis, and the incidence of intradialytic hypotension was defined as a decline in systolic blood pressure during HD greater than 20 mmHg from predialysis systolic blood pressure. The outcomes for patient satisfaction were collected using a 5-point Likert scale questionnaire and patient-reported symptoms during dialysis.

Statistical analysis

Descriptive data were presented as the mean and standard deviation for variables with a normal distribution and as the median and interquartile range for those with a skewed distribution. Categorical variables were analyzed using the chi-square test, whereas continuous variables were assessed using either the paired t-test or Wilcoxon signed rank test. The incidence rates of hypoglycemia, LBG, and intradialytic hypotension were compared between the control and the intervention groups using McNemar's test. All statistical analyses were performed using Stata Statistical Software, version 17 (StataCorp LLC, College Station, TX, USA). A p-value of less than 0.05 was considered statistically significant.

Results

During the study period, 250 patients were screened, of which 113 were enrolled in the study. One hundred thirty-seven were excluded because of the following reasons: 92 had CBG level that did not meet the criteria, five had been on HD for less than three months, 14 had recently adjusted their diabetes treatment, 12 had unstable ESKD condition, two were on the nasogastric tube, and 12 refused to participate (Figure 2).

The baseline characteristics and blood biochemistry are shown in Table 1. The mean age was 56 years, with a body mass index (BMI) of 24 kg/m2 and a mean dialysis vintage of 33 months. The patients had diabetes for a mean of 13 years, with 45% having diabetic retinopathy and 22% having diabetic neuropathy. The mean HbA1c was 6.5%, and 44% did not receive any antidiabetic medication.

The mean CBG at 0 hour, before starting dialysis, was comparable between the HD sessions without snack supplementation, or the control group, and those with snack supplementation, or the intervention group, at 147.3±32.5 versus 149.2±32.1 mg/dL (p=0.66). The mean blood

Table 1. Baseline characteristics

	n=113
Male; n (%)	63 (55.7)
Age (years); mean±SD	56.7±11.1
Duration of diabetes (years); mean±SD	13.7±7.6
Hemodialysis vintage (months); mean±SD	33.7±28.0
Weight (kg); mean±SD	65.0±13.1
BMI (kg/m^2); mean±SD	24.3±4.0
Diabetic retinopathy; n (%)	51 (45.1)
Diabetic neuropathy; n (%)	25 (22.1)
Myocardial infarction; n (%)	8 (7.0)
Cerebrovascular disease; n (%)	8 (7.0)
Previous symptoms of hypoglycemia; n (%)	65 (57.5)
Previous admission for hypoglycemia; n (%)	11 (9.7)
Antihyperglycemic medication; n (%)	
Insulin	45 (39.9)
Oral hypoglycemic agent	25 (22.1)
Diet control	50 (44.3)
Biochemistry; mean±SD	
Hb (g/dL)	9.7±1.5
Hct (%)	30.3±4.8
BUN (mg/dL)	57±17.7
Creatinine (mg/dL)	9.2±2.6
HbA1c (%)	6.5±1.3
Albumin (g/dL)	3.9±0.4
Potassium (mmol/L)	4.4±0.8
iPTH (pg/mL)	395.2±306.6

SD=standard deviation; BMI=body mass index; Hb=hemoglobin; Hct=hematocrit; BUN=blood urea nitrogen; HbA1c=hemoglobin A1c; iPTH=intact parathyroid hormone

glucose level decreased from the start to the end of the HD session by 40.5±30.6 mg/dL (27.5%) and 38.8±32.7 mg/dL (26%) in HD without and with snack supplementation, respectively, as illustrated in Figure 3. The blood glucose levels at 1, 2, and 3 hours in the intervention group were significantly higher than those in the control group, as presented in Figure 3. In comparison, the blood glucose level at the end of dialysis, at 4 hours, was not significantly different between the two groups.

There was no incidence of hypoglycemia during dialysis in the control group and one episode in the treatment group. The incidence of LBG during

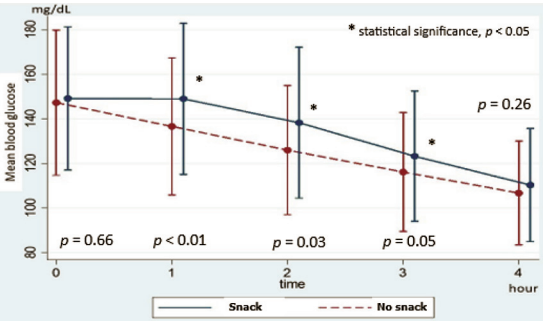

Figure 3. The mean blood glucose before and during hemodialysis.

dialysis was 33 out of 113 cases (29.2%), with three patients reporting hypoglycemic symptoms in the control group, and 23 out of 113 cases (20.4%), with one patient reporting hypoglycemic symptoms in the treatment group. Snack supplementation before dialysis tended to reduce the incidence of LBG during HD compared with the lack of snack supplementation (risk difference 0.08, 95% CI −0.02 to 0.2, p=0.12), as shown in Table 2.

The safety outcome is presented in Table 3. The incidence of intradialytic hypotension was 5.3% and 11.5% in the control and the intervention groups, respectively, with no significant difference (p=0.11). The details of blood pressure predialysis and during dialysis are demonstrated in Table 4. There were two time points in the control group and 12 time points in the intervention group with a blood glucose level greater than 200 mg/dL during dialysis.

For patient satisfaction, 92.7% of the participants had the highest scale in satisfaction for snack supplementation before dialysis. None of the patients reported any gastrointestinal symptoms during dialysis and believed no harm from snack supplementation before dialysis.

Discussion

The present study found that 15 g carbohydrate snack supplementation before HD can maintain the blood glucose level during dialysis, especially 1, 2, and 3 hours after starting HD, better than without

Table 2. Incidence of hypoglycemia and low blood glucose

	No snack supplement (n=113); n (%)	Snack supplement (n=113); n (%)	Risk difference (95% CI)	p-value
Hypoglycemia	0 (0.0)	1 (0.8)	-	-
Low blood glucose	33 (29.2)	23 (20.3)	0.08 (–0.02 to 0.2)	0.12
Symptoms of hypoglycemia	3 (2.6)	1 (0.8)	0.17 (–0.01 to 0.05)	0.31

CI=confidence interval

Table 3. Safety outcomes

	No snack supplement (n=113)	Snack supplement (n=113)	p-value
Intradialytic hypotension; n (%)	6 (5.3)	13 (11.5)	0.12
Hyperglycemia*; n	2	12	-

* Event of blood glucose >200 mg/dL at any time point during hemodialysis

Table 4. Mean arterial blood pressure before and during hemodialysis

Mean arterial blood pressure	No snack supplement (n=113) mean±SD	Snack supplement (n=113) mean±SD
Before hemodialysis (mmHg)	97±13	98±12
1 hour after dialysis initiation (mmHg)	96±13*	94±11*
2 hours after dialysis initiation (mmHg)	95±11*	94±11*
3 hours after dialysis initiation (mmHg)	95±12*	95±11*
4 hours after dialysis initiation (mmHg)	96±11*	95±11*

SD=standard deviation

* p>0.05 compared with before hemodialysis

snack supplementation before dialysis. Moreover, there was no obvious adverse effect in terms of intradialytic hypotension, and the patient reported the outcome of snack supplementation before HD. The blood glucose level decreased from the beginning to the end of the dialysis session by 26.5%, even when 100 mg/dL of glucose was used in the dialysate solution, which was observed in the present study. Interestingly, this study also found that LBG was common during HD in patients with diabetes, which had an incidence of 24%, and a few of them reported hypoglycemic symptoms although the blood glucose did not reach the hypoglycemic level. Numerous studies have reported that those with uncontrolled diabetes and older patients face symptoms of hypoglycemia even when their blood glucose levels are greater than 70 mg/dL, thereby protecting against a hypoglycemic episode[16,17]. Therefore, patients with diabetes undergoing HD who have blood glucose levels of less than 90 mg/dL at any point of time during HD should be aware of hypoglycemic symptoms and be closely monitored.

Snack supplementation before dialysis could maintain blood glucose levels during HD and prevent low glucose levels during dialysis, although it did not show statistical significance in the primary outcome due to a very low incidence of hypoglycemia in both groups. A light carbohydrate snack supplementation 15 to 30 minutes before dialysis is convenient and practical, with high patient satisfaction. Eating during dialysis is another option that provides calories and could prevent hypoglycemia during the process. Nevertheless, the concerns regarding eating during HD are low blood pressure or intradialytic hypotension, especially eating more than 200 kcal in patients with diabetes who have autonomic dysfunction[15], risk of choking, inconvenience in preparing a meal, and cleanliness issues. There are still variations in the policy on eating during dialysis in each HD center around the globe[13]. However, light snack supplementation before dialysis is more practical and can be implemented in every dialysis unit to maintain blood glucose levels during dialysis.

The present study used predialysis snack supplementation, which is more convenient and practical to implement than eating during dialysis. Several studies have demonstrated the benefits and risks of eating during HD[18-20]. However, none of the studies have tested the hypothesis of snacking just before starting dialysis in terms of hypoglycemia prevention in patients with diabetes undergoing HD. The present study not only reported the clinical outcome of hypoglycemia and blood glucose level but also showed the patient preference for the intervention, which is important to the patient-centered care approach.

Nonetheless, the present study had limitations. First, the blood glucose level was measured at five cross-sectional time points before and during HD, not continuous glucose monitoring. Second, the incidence of hypoglycemia was very low compared with the previous studies[6-8]. Therefore, the present study was underpowered to detect the difference in the primary outcome between the two groups. Third, data on compliance with antidiabetic drugs, especially insulin, on dialysis days were not available. Some of the participants might have refrained from taking the antidiabetic drug or reduced its dosage on the day of HD based on their own judgment to prevent hypoglycemia, resulting in a very low incidence of hypoglycemia. The present study employed a non-randomized crossover design. Therefore, the potential for selection bias and carryover effects should be acknowledged as inherent limitations.

The 15 g carbohydrate snack supplementation just before HD shows a trend toward preventing LBG levels during HD in patients with diabetes without significant effects on hyperglycemia or intradialytic hypotension. The implementation of carbohydrate snack supplementation before dialysis is practical for every patient with well-controlled diabetes, especially in HD centers where patients are not allowed to eat during dialysis and offers excellent

patient satisfaction without any serious adverse events. Additional adequately powered randomized studies are warranted to confirm and strengthen these recommendations.

What is already known about this topic?

There are interventions and approaches to preventing hypoglycemia during HD in diabetic patients, including blood glucose monitoring, adjusting anti-diabetes drugs, and avoiding glucose-free or low-glucose dialysate, but asymptomatic hypoglycemic episodes are still reported.

What does this study add?

The 15 g carbohydrate snack supplementation before dialysis could maintain blood glucose levels during HD and prevent low blood glucose levels during dialysis without serious complications.

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Conflicts of interest

The authors declare no conflict of interest.

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