

การศึกษาเปรียบเทียบการให้สารละลายเดกซ์โทรสเข้าหลอดเลือดดำความเข้มข้น 10% ขนาดต่ำ (15 กรัม และ 20 กรัม) กับ ความเข้มข้น 50% ขนาดมาตรฐาน (25 กรัม) สู่เป้าหมายระดับน้ำตาลในเลือดปกติในการรักษาภาวะน้ำตาลในเลือดต่ำ

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กลุ่มงานเวชศาสตร์ฉุกเฉิน โรงพยาบาลสมเด็จพระเจ้าตากสินมหาราช

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บทคัดย่อ

การให้สารละลายเดกซ์โทรสร้อยละ 50 ทางหลอดเลือดดำ ในผู้ป่วยที่มีภาวะน้ำตาลในเลือดต่ำมักส่งผลให้ระดับน้ำตาลในเลือดภายหลังการรักษาสูงกว่ากลุ่มที่ให้สารละลายเดกซ์โทรสร้อยละ 10 ซึ่งอาจก่อให้เกิดผลข้างเคียงที่ไม่พึงประสงค์ เช่น ภาวะน้ำตาลในเลือดต่ำซ้ำ และความแปรปรวนของระดับน้ำตาลในเลือดที่เพิ่มขึ้น การศึกษานี้เป็นการศึกษาแบบ prospective, cohort, non-blinded, non-randomized จัดสรรผู้ป่วยเข้ากลุ่มตามลำดับ ในผู้ใหญ่ (อายุ ≥ 18 ปี) ที่ได้รับการรักษาภาวะน้ำตาลในเลือดต่ำในห้องฉุกเฉิน หรือโดยหน่วยแพทย์ฉุกเฉิน แบ่งผู้ป่วยออกเป็น 3 กลุ่ม ได้แก่ 1) เดกซ์โทรส ร้อยละ 10 ขนาด 15 กรัม 2) เดกซ์โทรส ร้อยละ 10 ขนาด 20 กรัม และ 3) เดกซ์โทรส ร้อยละ 50 ขนาด 25 กรัม วิเคราะห์สัดส่วนของผู้ที่มีระดับน้ำตาลในเลือดปกติ (นิยามระดับน้ำตาลในเลือดปลายนิ้วอยู่ในช่วง 80-180 มก./ดล.) ที่ 15 และ 60 นาทีหลังให้เดกซ์โทรส โดยใช้การวิเคราะห์ความแตกต่างของสัดส่วน และใช้การวิเคราะห์ถดถอยพหุระดับเพื่อประเมินระดับน้ำตาลปลายนิ้ว, ภาวะน้ำเกิน, ภาวะน้ำตาลในเลือดสูง (ระดับน้ำตาลปลายนิ้ว >180 มก./ดล.) และภาวะน้ำตาลในเลือดต่ำ (ระดับน้ำตาลปลายนิ้ว <80 มก./ดล.) หลังให้เดกซ์โทรสโดยปรับอิทธิพลของตัวแปรกวน และคำนึงถึงความสัมพันธ์ระหว่างข้อมูลในแต่ละบุคคล แต่ละกลุ่มมีผู้ป่วย 55 ราย ที่ 15 นาทีหลังให้เดกซ์โทรส กลุ่ม 15 กรัมมีความแตกต่างของสัดส่วนผู้ที่มีระดับน้ำตาลปกติอยู่ที่ร้อยละ 60.0 (ความเชื่อมั่นที่ร้อยละ 95 = 45.2-74.8; $p<0.001$) และกลุ่ม 20 กรัมอยู่ที่ร้อยละ 30.9 (ความเชื่อมั่นที่ร้อยละ 95 = 13.2-48.6; $p=0.001$) ระดับน้ำตาลปลายนิ้วโดยเฉลี่ยอยู่ในเกณฑ์ปกติในกลุ่ม 15 และ 20 กรัม แต่เกินเกณฑ์ในกลุ่ม 25 กรัม ($p<0.001$) ความเสี่ยงต่อภาวะน้ำตาลในเลือดสูงลดลงร้อยละ 65.8 สำหรับกลุ่ม 15 กรัม และร้อยละ 40.4 สำหรับกลุ่ม 20 กรัม อัตราการเกิดภาวะน้ำเกินในกลุ่ม 15 กรัมไม่แตกต่างกัน ขณะที่กลุ่ม 20 กรัมต่ำกว่ากลุ่ม 25 กรัมอย่างมีนัยสำคัญทางสถิติ (ร้อยละ -4.9; $p=0.007$) ผลการศึกษานี้แสดงให้เห็นว่า การให้เดกซ์โทรสร้อยละ 10 ขนาด 15 และ 20 กรัมมีประสิทธิภาพมากกว่าเดกซ์โทรสร้อยละ 50 ขนาด 25 กรัมในการทำระดับน้ำตาลกลับเข้าสู่ภาวะปกติ และลดความเสี่ยงต่อภาวะน้ำตาลในเลือดสูง โดยไม่เพิ่มความเสี่ยงต่อภาวะน้ำเกิน

คำสำคัญ: ภาวะน้ำตาลในเลือดต่ำ; ภาวะน้ำตาลในเลือดสูง; น้ำตาลกลูโคสเข้มข้นสูง; ห้องฉุกเฉิน; โรคเบาหวาน

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Comparative study of lower-dose 10% intravenous dextrose (15 g and 20 g) versus standard 50% dextrose (25 g) in achieving euglycemia during hypoglycemia treatment

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Abstract

Hypoglycemic patients treated with a rapid intravenous bolus of 50% dextrose often have higher post-treatment blood glucose levels compared to those receiving 10% dextrose, potentially causing adverse effects such as rebound hypoglycemia and increased glycemic variability. This prospective, non-blinded, non-randomized cohort study with sequential group allocation compared the proportion of post-treatment euglycemia and volume overload within 24 hours among adult patients (≥ 18 years) treated for hypoglycemia in the emergency department (ED) or by the emergency medical service (EMS). Patients were divided into three groups: Group 1. 10% dextrose, 15 g; Group 2. 10% dextrose, 20 g; Group 3. 50% dextrose, 25 g. The proportions of patients achieving euglycemia (defined as capillary blood glucose [CBG] 80-180 mg/dL) at 15 and 60 minutes were analyzed using difference in proportions analysis. Multilevel multivariable regression was used to assess CBG, volume overload, and post-bolus hyperglycemia (CBG >180 mg/dL) and hypoglycemia (CBG <80 mg/dL), adjusting for confounders and intrapersonal correlations. Each group included 55 patients. At 15 minutes, the differences in the proportions of patients achieving euglycemia were 60.0% (95% CI = 45.2-74.8; $p<0.001$) for the 15 g group and 30.9% (95% CI = 13.2-48.6; $p=0.001$) for the 20 g group. The mean CBG levels were euglycemic for the 15 g and 20 g groups but hyperglycemic for the 25 g group ($p<0.001$). Hyperglycemia risk was reduced by -65.8% for the 15 g group and -40.4% for the 20 g group. Volume overload was similar for the 15 g, while the 20 g groups had statistically significant lower than the 25 g group (-4.9%; $p=0.007$). These findings suggest that using 10% dextrose (15 g and 20 g) was more effective than 50% dextrose (25 g) at achieving euglycemia and reducing hyperglycemia, without increasing volume overload.

Keywords: hypoglycemia; hyperglycemia; hypertonic glucose solutions; emergency departments; diabetes mellitus

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Introduction

Severe hypoglycemia has traditionally been treated with an intravenous bolus of 50% dextrose. Recently, there has been an increasing trend toward using lower-concentration solutions, such as 10% and 20%, with recommended doses ranging from 10 to 25 g¹⁻⁴. Studies have suggested that 10% dextrose may be as effective as 50% dextrose in reversing hypoglycemia. However, treatment with 50% dextrose is linked to higher post-treatment blood glucose levels, which may increase the risk of rebound hypoglycemia due to increased insulin release³⁻⁶.

Maintaining euglycemia after treatment is crucial because glycemic variability has been linked to oxidative stress, endothelial dysfunction, and apoptosis, contributing to higher mortality and longer hospital stays in critically ill patients^{7,8}. It is also an independent risk factor for diabetic complications beyond HbA1c levels⁹. Therefore, hypoglycemia management should aim to restore blood glucose to the euglycemic range while avoiding both hyperglycemia and recurrent hypoglycemia. Current guidelines vary in recommending dextrose concentrations from 10% to 50% with doses of 10-25 g^{1,10,11}. While 50% dextrose poses a higher risk of tissue injury from extravasation due to its osmolarity⁴, 10% dextrose is safer but requires larger volumes, which may be problematic for patients with fluid restrictions such as those with chronic kidney disease or heart failure.

Previous studies have compared different glucose concentrations and doses,

focusing either on recovery of mental status^{5,12} or on broader outcomes such as admission rates, length of stay, and mortality⁶. However, to date, no study has directly assessed their effectiveness in achieving euglycemia and the associated risk of volume overload, particularly when larger volumes of 10% dextrose are administered. Therefore, the primary aim of this study was to compare the effectiveness of administering 15 g and 20 g of 10% dextrose versus 25 g of 50% dextrose in restoring euglycemia. Secondary outcomes included the evaluation of mean capillary blood glucose levels after treatment and the incidence of volume overload within 24 hours.

Materials and Methods

Study design

This was a prospective, non-blinded, non-randomized therapeutic cohort study with sequential group allocation that included adult patients (aged ≥18 years old) who received an intravenous bolus of dextrose for hypoglycemic episodes, either at the Emergency Department (ED) of Somdejphrajoataksinmaharaj General Hospital, Thailand (with an annual ED census of approximately 48,000 visits) or by the hospital's Emergency Medical Service (EMS) team before being transferred to the hospital's ED. Randomization was not chosen because it was felt that it could have caused confusion among the healthcare providers, who needed to select between the three regimens for treating hypoglycemia, a medical emergency, and as we believed such confusion might have led to deviations from the treatment protocol.

Therefore, we opted for a sequential group allocation approach, completing data collection for one group before proceeding to the next. This method ensured better adherence to the protocol and facilitated a smoother workflow for the healthcare providers. The study period was from December 2023 to September 2024. Ethical approval was obtained from the hospital's ethics committee and the study was registered with the Thai Clinical Trials Registry (no. TCTR20240404005).

Sample size

The sample size was calculated using data from a pilot study conducted in the hospital's ED to investigate post-treatment euglycemia across three regimens, with 10 patients per group. The pilot study showed a post-treatment euglycemia rate of 40% in the 50% dextrose group, compared to 70% in both 10% dextrose groups (15 g and 20 g). A 1:1 ratio was used, with power set at 80% and a significance level of 5%. The calculated sample size was 49 patients per group. To account for potential dropouts, the sample size was increased by 10%, resulting in 55 patients required per group and a total of 165 patients overall. At 60 minutes, the pilot study showed a post-treatment euglycemia rate of 60% in all groups. No cases of volume overload were observed in the pilot study.

Participants

The inclusion criteria were: 1. Adults (≥ 18 years old), with or without diabetes, who presented with hypoglycemia defined as a capillary blood glucose (CBG) < 70 mg/dL. 2. Patients with altered consciousness or those

recommended for intravenous glucose treatment by the treating physician, even if conscious. The exclusion criteria were: 1. Patients in cardiac arrest. 2. Patients suspected by the treating physician or EMS team of having impending or ongoing respiratory failure due to volume overload at the time of hypoglycemia diagnosis. 3. Fully conscious patients in the EMS setting with CBG < 70 mg/dL who did not receive an immediate intravenous glucose bolus, as per EMS protocol.

Patient recruitment

For patients managed by the EMS team, recruitment was conducted by the team leader (a registered nurse or paramedic). According to the offline EMS protocol, an intravenous glucose bolus was indicated only for patients with CBG < 70 mg/dL and altered consciousness. Fully conscious patients with CBG < 70 mg/dL were generally not given a bolus; some received only glucose-containing intravenous fluids, while in other cases the team leader may consult the online medical command for authorization. Such patients were excluded because the bolus was not administered immediately after CBG measurement.

For patients presenting directly to the ED, recruitment was carried out by the treating physician. In the ED, an intravenous glucose bolus was administered to patients with CBG < 70 mg/dL and altered consciousness, while fully conscious patients with CBG < 70 mg/dL received a bolus based on the clinical judgment of the treating physician.

Interventions

Patients were divided into three groups across three consecutive study periods. In the first period, patients received 10% dextrose, 150 mL (15 g). In the second period, patients received 10% dextrose, 200 mL (20 g). In the final period, patients received 50% dextrose, 50 mL (25 g) (Refer to Figure 1 for the study flow diagram).

After establishing intravenous access, blood samples were drawn for assessing the patients' plasma glucose, BUN, and creatinine levels. For the 10% dextrose groups (15 g and 20 g), the dextrose solution was prepared using 10% dextrose in half-strength normal saline (10%D/N/2) at 1,000 mL per bag. A 50 mL syringe with a three-way stopcock and extension tubing was used to administer the IV bolus (150 mL or 200 mL). Following the bolus, the same bag was used for continuous IV infusion. For the 50% dextrose group (25 g), the solution was drawn directly from a 50 mL vial using a 50 mL syringe for the bolus. After the bolus, patients received a continuous drip of 10%D/N/2 solution (1,000 mL per bag) which was administered with or without an infusion pump, depending on availability and clinical judgment. The infusion rate was

determined by the treating physician. Finger CBG levels were measured at 15 and 60 minutes after the dextrose bolus. A member of the medical team performed the finger prick and recorded the results, including the infusion rates of the 10%D/N/2 solution, on the record form.

Data collected included the patients' demographics (gender, age, weight), medical history (underlying diseases, comorbidities, type of diabetes medication), baseline plasma glucose level, and creatinine clearance from the electronic medical records. Additional information on the use of intravenous diuretics and emergency hemodialysis was gathered to assess volume overload based on predefined criteria.

Variable definitions

1. Post-bolus euglycemia: defined as CBG between 80 and 180 mg/dL. 2. Post-bolus hypoglycemia: Defined as CBG <80 mg/dL. 3. Post-bolus hyperglycemia: Defined as CBG >180 mg/dL. 4. Volume overload within 24 hours: Defined as the need for intravenous diuretics or emergency hemodialysis (outside of routine cycles) within 24 hours following the IV bolus of dextrose, or at discharge if it occurs earlier.

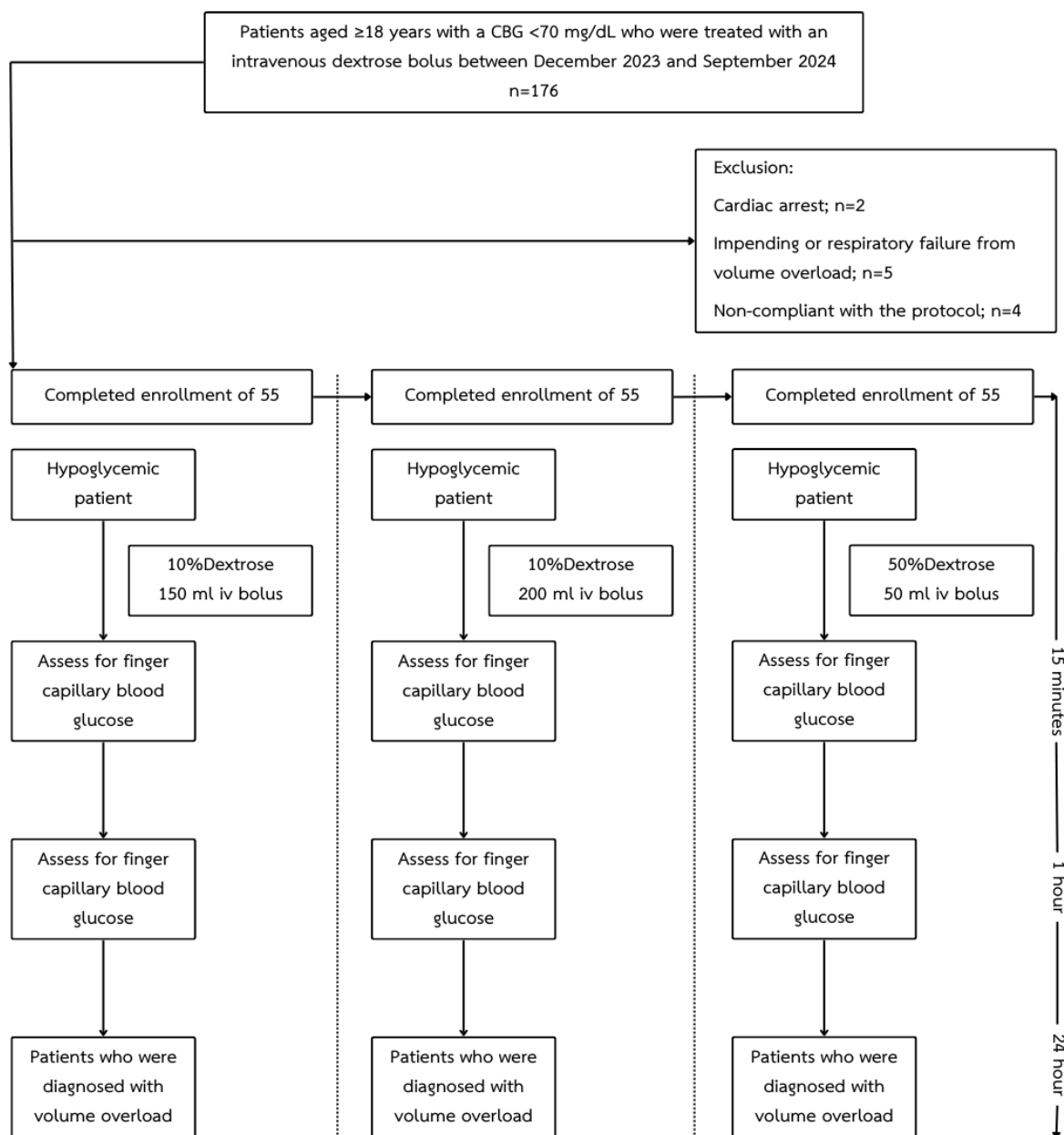


Figure 1 Study flow diagram

Outcomes

The primary outcome was the proportion of patients achieving post-bolus euglycemia at 15 and 60 minutes after treatment. Secondary outcomes included the proportions of patients with post-bolus

hyperglycemia and post-bolus hypoglycemia at 15 and 60 minutes post-treatment, the mean capillary blood glucose levels at these time points, and the proportion of patients diagnosed with volume overload within 24 hours.

Statistical analysis

Descriptive and inferential statistics were used to summarize baseline characteristics. Categorical data were reported as frequencies and percentages, normally distributed continuous variables as mean with standard deviation, and non-normally distributed variables as median with interquartile range (IQR). The proportions of patients achieving euglycemia, hyperglycemia, and hypoglycemia at 15 and 60 minutes were compared between groups (10% dextrose 15 g vs. 50% dextrose 25 g, and 10% dextrose 20 g vs. 50% dextrose 25 g). Capillary blood glucose levels at 0, 15, and 60 minutes were analyzed using linear mixed-effects regression with random intercepts and slopes at the patient level, adjusting for baseline CBG and potential confounders. The diagnosis of volume overload within 24 hours, as well as post-treatment hyperglycemia and hypoglycemia, were assessed using generalized linear models with Gaussian family and identity link, applying robust standard errors and adjusting for potential confounders. Intrapersonal correlations were accounted for in the analysis of repeated CBG outcomes.

Results

During the study period, a total of 176 patients received intravenous dextrose bolus treatment, and were considered for inclusion but 11 patients were excluded in line with the exclusion criteria. The 10% dextrose (15 g) group had more male patients, while the 10% dextrose (20 g) and 50% dextrose (25 g) groups

had a slightly higher proportion of female patients. The mean age was approximately 65 years old, and the mean weight was around 60 kilograms across all groups. Around 80% of the patients had diabetes mellitus, with a slightly higher proportion in the 10% dextrose (20 g) group. End-stage renal disease (ESRD) was observed in 9% across all groups. The most common comorbidities included infection/sepsis, acute renal failure, and alcohol-related hypoglycemia. The most frequently used diabetes medication was sulfonylurea (around 50%), with about one-third of the patients receiving home insulin or biguanides. Approximately 80% of the patients presented with altered consciousness. The mean baseline plasma glucose was similar across all the groups, averaging around 35 mg/dL, and the mean baseline capillary blood glucose was also similar, averaging around 40 mg/dL. The median creatinine clearance for all the groups indicated chronic kidney disease stage 3. The infusion rate of 10% D/N/2 during the first 0-15 minutes after the treatment was similar across all the groups, but the infusion rate during the 15-60 minutes period was the highest in the 10% dextrose (15 g) group, followed by the 10% dextrose (20 g) and 50% dextrose (25 g) groups (Table 1).

Without adjusting for confounding factors, the mean CBG levels at both 15 and 60 minutes post-treatment were increased according to the dextrose dosage: the highest levels were observed in the 50% dextrose (25 g) group, followed by the 10% dextrose (20 g) group, and lastly the 10% dextrose (15 g)

group. Conversely, the proportion of patients achieving euglycemia was the highest in the 10% dextrose (15 g) group, followed by the 10% dextrose (20 g) group, and the lowest in the 50% dextrose (25 g) group at both time points. The proportion of patients diagnosed with volume overload did not differ significantly between the groups (Table 2).

After adjusting for confounding factors, the mean CBG in the 50% dextrose (25 g) group was within the hyperglycemic range (CBG >180 mg/dL), while the mean CBG values for the 10% dextrose (15 g and 20 g) groups were within the euglycemic range (80-180 mg/dL) at 15 minutes. By 60 minute post-treatment, the adjusted mean CBG had decreased to the euglycemic range in all the groups (Figure 2).

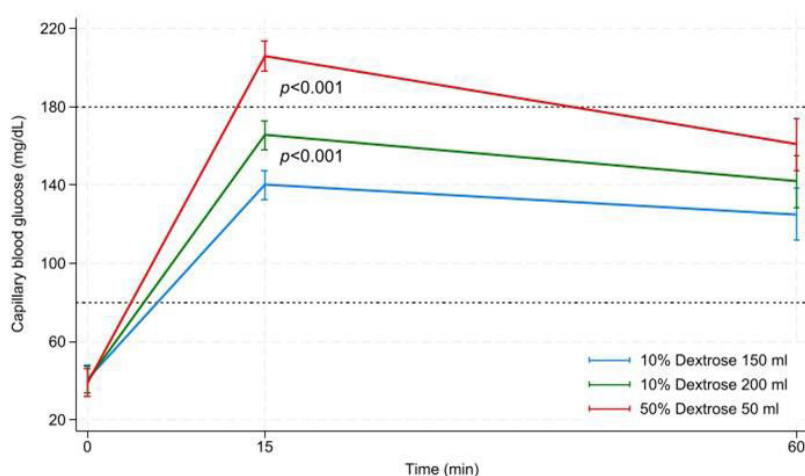


Figure 2 Adjusted mean capillary blood glucose levels at 0, 15, 60 minutes after administration of the dextrose solutions

After adjusting for confounding factors using multilevel multivariable regression models, the mean capillary glucose levels at both 15 and 60 minutes post-treatment were significantly lower in the 10% dextrose (15 g and 20 g) groups compared to the 50% dextrose (25 g) group. Additionally, the 10% dextrose groups had a lower proportion of patients diagnosed with volume overload than in the 50% dextrose (25 g) group (Table 3).

The adjusted proportion of patients achieving post-treatment euglycemia at both 15 and 60 minutes was the highest in the 10% dextrose (15 g) group, followed by the 10% dextrose (20 g) group, and the lowest in the 50% dextrose (25 g) group (Figure 3). Compared to treatment with 50% dextrose (25 g), treatment with 10% dextrose slightly increased the risk of post-treatment hypoglycemia for both the 15 g and 20 g groups. However, the risk of post-treatment hyperglycemia was markedly reduced in both groups (Table 4).

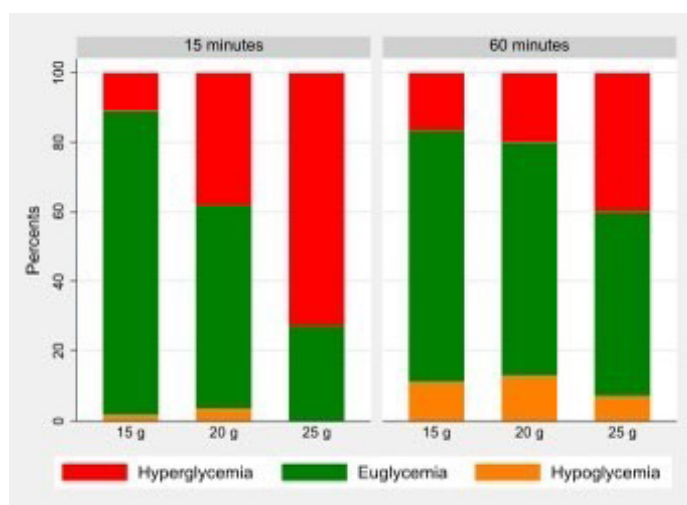


Figure 3 Proportions of patients in the various glycemic ranges (hyperglycemia, euglycemia, hypoglycemia) across the different glucose doses (15 g, 20 g, 25 g) at 15 and 60 minutes post-treatment

Table 1 Baseline characteristics of the patients

Baseline characteristics	10% Dextrose 15 g n=55, n (%)	10% Dextrose 20 g n=55, n (%)	50% Dextrose 25 g n=55, n (%)	p-value
Male	32 (58.2)	27 (49.1)	25 (45.5)	0.381
Age (years), mean±SD	63.9±14.1	65.8±11.3	65.1±11.4	0.725
Weight (kilograms), mean±SD	58.3±15.4	59.9±12.8	58.7±11.6	0.812
Underlying diseases				
Diabetes mellitus	44 (80.0)	47 (85.5)	43 (78.2)	0.677
ESRD ^a	5 (9.1)	5 (9.1)	5 (9.1)	1.000
Chronic liver disease	2 (3.6)	4 (7.3)	0 (0)	0.167
Chronic heart failure	2 (3.6)	4 (7.3)	0 (0)	0.167
Active cancer	1 (1.8)	3 (5.5)	0 (0)	0.325
Comorbid				
Sepsis/infection	13 (23.6)	22 (40.0)	8 (14.6)	0.010
Alcohol-related hypoglycemia	5 (9.1)	3 (5.5)	11 (20.0)	0.061
Acute renal failure	15 (27.3)	17 (30.9)	8 (14.6)	0.120
Acute stroke	1 (1.8)	0 (0)	1 (1.8)	1.000
Acute liver failure	1 (1.8)	0 (0)	2 (3.6)	0.774
Acute heart failure	0 (0)	1 (1.8)	0 (0)	1.000
Volume overload	0 (0)	3 (5.5)	0 (0)	0.107

Table 1 Continued

Baseline characteristics	10% Dextrose 15 g n=55, n (%)	10% Dextrose 20 g n=55, n (%)	50% Dextrose 25 g n=55, n (%)	p-value
Type of DM medication				
Insulin	20 (36.4)	20 (36.4)	23 (41.8)	0.862
Sulfonylureas	30 (54.6)	29 (52.7)	25 (45.5)	0.684
Biguanides	16 (29.1)	17 (30.9)	21 (38.2)	0.650
Thiazolidinediones	13 (23.6)	13 (23.6)	9 (16.4)	0.588
DDP-4	1 (1.8)	2 (3.6)	3 (5.5)	0.872
None	11 (20.0)	12 (21.8)	13 (23.6)	0.971
Consciousness				
Conscious and orientated	13 (23.6)	9 (16.4)	11 (20.0)	0.115
Abnormal conscious*	25 (45.5)	34 (61.8)	21 (38.2)	
Unconscious**	17 (30.9)	12 (21.8)	23 (41.8)	
PG [§] (mg/dL), mean±SD	34.8±12.8	33.3±11.8	35.1±13.9	0.723
CBG [§] (mg/dL), mean±SD	41.3±12.7	38.7±13.9	40.4 ±13.1	0.565
CrCl [†] (mL/min), median [IQR]	38.9 [17.3, 76.2]	38.9 [23.2, 56.9]	41.8 [24.9, 76.1]	0.681
IVF15 ^{‡‡} (mL/h), mean±SD	89.1±14.3	82.9±17.0	85.1±15.5	0.113
IVF60 ^{‡‡} (mL/h), mean±SD	90.0±16.4	81.8±17.3	74.4±20.7	<0.001

ESRD^α: end-stage renal disease; Abnormal conscious*: conscious but disorientated/confused/aggressive; Unconscious**: unconscious/seizure/very aggressive; PG[§]: plasma blood glucose; CBG[§]: capillary blood glucose before treatment; CrCl[†]: creatinine clearance; IVF15^{‡‡}: 10% dextrose IV fluid rate, 0-15 min post-bolus; IVF60^{‡‡}: 10% dextrose IV fluid, >15-60 min post-bolus.

Table 2 Crude mean and proportional differences in treatment outcomes after an intravenous dextrose bolus at 15 and 60 minutes post-treatment

Outcome	50% D 25 g n=55 mean±SD	10% D 15 g n=55 mean±SD	Difference (95%CI) 15 g vs. 25 g	p-value	10% D 20 g n=55 mean±SD	Difference (95%CI) 20 g vs. 25 g	p-value
CBG* post-bolus, mg/dL							
at 15 minutes	207.2±44.0	140.6±35.3	-66.6 (-81.5, -51.7)	<0.001	163.6±50.2	-43.6 (-61.2, -25.9)	<0.001
at 60 minutes	162±50.6	125.5±46.0	-36.5 (-54.6, -18.5)	<0.001	140.0±49.8	-22.0 (-40.7, -3.3)	0.021
Eugly ^δ , n (%)							
at 15 minutes	15 (27.3)	48 (87.3)	60.0 (45.2, 74.8)	<0.001	32 (58.2)	30.9 (13.2, 48.6)	0.001
at 60 minutes	29 (52.7)	40 (72.7)	20.0 (2.2, 37.8)	0.028	37 (67.3)	14.5 (-3.7, 32.8)	0.119
Hypogly [‡] , n (%)							
at 15 minutes	0 (0)	1 (1.8)	1.8 (-1.7, 5.4)	0.317	2 (3.6)	3.6 (-1.4, 8.6)	0.153
at 60 minutes	4 (7.3)	6 (10.9)	3.6 (-7.2, 14.5)	0.510	7 (12.7)	5.5 (-5.8, 16.7)	0.343

Table 2 Continued

Outcome	50% D 25 g n=55 mean±SD	10% D 15 g n=55 mean±SD	Difference (95%CI) 15 g vs. 25 g	p-value	10% D 20 g n=55 mean±SD	Difference (95%CI) 20 g vs. 25 g	p-value
Hypergly ^α , n (%)							
at 15 minutes	40 (72.7)	6 (10.9)	-61.8 (-76.3, 47.3)	<0.001	21 (38.2)	-34.5 (-52.1, -17.0)	<0.001
at 60 minutes	22 (40.0)	9 (16.4)	-23.6 (-40.0, -7.3)	0.005	11 (20.0)	-20.0 (-36.9, -3.1)	0.020
Vol24 ^δ , n (%)	2 (3.6)	1 (1.8)	-1.8 (-8.0, 4.3)	0.561	4 (7.3)	3.6 (-4.9, 12.2)	0.404

CBG*: capillary blood glucose; Eugly^δ: capillary blood glucose 80-180 mg/dL; Hypogly[†]: capillary blood glucose below 80 mg/dL; Hypergly^α: capillary blood glucose over 180 mg/dL; Vol24^δ: diagnosis of volume overload within 24 hours post-bolus.

Table 3 Adjusted mean and proportional differences in clinical outcomes after an intravenous glucose bolus at 15 and 60 minutes post-treatment

Outcome	Difference (95%CI) 15 g vs. 25 g	p-value	Difference (95%CI) 20 g vs. 25 g	p-value
CBG*, mg/dL				
at 15 minutes	-65.8 (-76.5, -55.1)	<0.001	-40.4 (-51.1, -29.8)	<0.001
at 60 minutes	-35.7 (-54.5, -16.9)	<0.001	-18.9 (-37.6, -0.1)	0.048
Volumeload24 ^β , n (%)	-1.7 (-4.5, -1.2)	0.252	-4.9 (-8.4, -1.3)	0.007

CBG*: capillary blood glucose.

Adjusted post-treatment CBG, considering infection, alcohol-related hypoglycemia, baseline capillary blood glucose, and the infusion rate of 10% dextrose in half-strength normal saline over 15 to 60 minutes. Volumeload24^β: diagnosis of volume overload within 24 hours post-bolus.

Adjusted proportion of volume overload within 24 hours, considering end-stage renal disease, chronic liver and heart failure, infection, acute renal and heart failure, volume overload, creatinine clearance, and the infusion rate of 10% dextrose in half-strength normal saline at 0-15 minutes and >15-60 minutes.

Table 4 Adjusted risk difference of clinical outcomes after an intravenous glucose bolus at 15 and 60 minutes post-treatment

Outcome	Risk difference (95%CI) 15 g vs. 25 g	p-value	Risk difference (95%CI) 20 g vs. 25 g	p-value
Hypoglycemia, mg/dL				
15 minutes	1.8 (1.1, 2.6)	<0.001	3.6 (2.9, 4.4)	<0.001
60 minutes	3.6 (0.8, 6.4)	0.011	5.4 (2.7, 8.2)	<0.001

Table 4 Continued

Outcome	Risk difference (95%CI) 15 g vs. 25 g	p-value	Risk difference (95%CI) 20 g vs. 25 g	p-value
Euglycemia, mg/dL				
15 minutes				
60 minutes				
Hyperglycemia, mg/dL				
15 minutes	-61.8 (-65.7, -57.9)	<0.001	-34.5 (-38.5, -30.6)	<0.001
60 minutes	-23.6 (-27.7, -19.6)	<0.001	-20.0 (-24.1, -15.9)	<0.001

Adjusted, considering infection, alcohol-related hypoglycemia, baseline capillary blood glucose, and the infusion rate of 10% dextrose in half-strength normal saline over 15 to 60 minutes.

Discussion

In this study, 50% dextrose (25 g) was selected as it aligns with the Thai Endocrine Society's recommendation¹³. This was compared with 10% dextrose (15 g and 20 g), administered using a commercially available 10% D/N/2 solution in a 1 liter bag, the only form of 10% dextrose available in the hospital. The first post-treatment CBG measurement was taken at 15 minutes, based on guideline recommendations^{1,10,13}. The recommended glycemic range for diabetic patients includes a preprandial CBG of at least 80 mg/dL and a postprandial CBG up to 180 mg/dL¹¹. In critically ill patients, the target range is typically 140-180 mg/dL, while non-diabetic patients may use a lower range of 80-140 mg/dL if close monitoring is feasible^{7,8}. Based on these considerations, the target post-treatment euglycemic range in this study was set at 80-180 mg/dL.

In the present study, the mean CBG in the 10% dextrose (15 g and 20 g) groups was within the euglycemic range at 15 minutes post-treatment, whereas the mean CBG in the

50% dextrose (25 g) group reached the hyperglycemic range. The mean CBG increased with higher dextrose doses but declined to the euglycemic range in all groups by 60 minutes post-treatment. A previous study in healthy volunteers who received a 50% dextrose (25 g) bolus showed a significant rise in blood glucose at 5 and 15 minutes, returning to baseline at 30 minutes¹⁴. This suggests that the mean CBG at 15 minutes reflects the immediate impact of the intravenous dextrose bolus, while the mean CBG at 60 minutes is influenced by both the elevated CBG levels at 15 minutes and the continuous infusion rate of 10% D/N/2.

After adjusting for confounders, the mean difference in CBG at 15 minutes was 65.8 mg/dL lower in the 10% dextrose (15 g) group and 40.4 mg/dL lower in the 10% dextrose (20 g) group, compared to the 50% dextrose (25 g) group. Two previous RCTs comparing 10% and 50% dextrose for treating hypoglycemic patients with altered consciousness found that the 10% dextrose dose required less total dextrose to resolve symptoms, while the 50% dextrose group had higher post-

treatment CBG levels^{5,12}. One of these RCTs reported a mean CBG of 169.4 mg/dL after administering 25 g of 50% dextrose⁵, which was lower than the mean CBG in this study's 50% dextrose group, where it exceeded 180 mg/dL. The higher mean CBG in this study may be due to differences in the patients' baseline blood glucose levels: the above-mentioned RCT⁵ included only patients with unresponsive hypoglycemia and reported a lower baseline CBG of 25.2 mg/dL, compared to 40.4 mg/dL in this study. Additionally, a prehospital study found no difference in the total intravenous bolus dose required to treat hypoglycemia between the 10% and 50% dextrose groups, with an average dose of around 20 g in both groups, but it confirmed that the 50% dextrose group had a higher mean CBG after treatment⁶.

The 10% dextrose, 15 g and 20 g groups had a higher proportion of patients achieving euglycemia at both 15 and 60 minutes, with a lower incidence of hyperglycemia compared to the 50% dextrose, 25 g group. However, this difference was reduced at 60 minutes. Hyperglycemia following the bolus may increase the risk of rebound hypoglycemia due to inhibited gluconeogenesis, suppressed glycogenolysis, and increased insulin secretion⁴. Given that about 95% of people with diabetes in Thailand have type 2 diabetes¹³, and approximately 50% of this study population used sulfonylureas (which promote insulin release), the risk of rebound hypoglycemia may be heightened.

In the prehospital study of adults treated for hypoglycemia with intravenous

glucose, both the 10% and 50% dextrose groups typically received around 20 g of glucose. The incidence of hyperglycemia was 27%, with a mean blood glucose level of 289.8 mg/dL among those who had developed hyperglycemia, and no significant differences were observed between the two groups⁶. In contrast, this study examined three dosing regimens: 10% dextrose at 15 g, 10% dextrose at 20 g, and 50% dextrose at 25 g. An increasing trend in hyperglycemia was observed at 15 minutes post-treatment, with proportions of 10.9%, 38.2%, and 72.7%, respectively, for the three groups. The incidence of hyperglycemia for the 20 g dose group in this study (38.2%) was higher than in the prehospital study (27%). This difference may be due to the timing of blood glucose assessment: the prehospital study measured blood glucose upon hospital arrival (approximately 30 minutes after the first assessment of CBG), whereas our study measured it at 15 minutes post-bolus. As previously mentioned in the study in healthy subjects, blood glucose levels were increased significantly at 5 and 15 minutes after an intravenous dextrose bolus but had returned to baseline by 30 minutes¹⁴. This may explain the higher incidence of hyperglycemia observed at the 15 minute mark in our study. Lastly, the mean body weight in this study was approximately 60 kilograms, compared to 75 kilograms in the prehospital study⁶. As a result, the dose of dextrose per kilogram of body weight was higher in our study, potentially contributing to the increased incidence of hyperglycemia.

The 10% dextrose groups (15 g and 20 g) showed a slightly increased risk of post-bolus hypoglycemia compared to the 50% dextrose group. The highest risk difference for hypoglycemia was around 5%, as observed in the 10% dextrose 20 g group at 60 minutes. Additionally, this study found a markedly lower proportion of patients with post-treatment hypoglycemia than those reported in previous studies^{3,6}. One possible explanation for this difference is that the lowest recommended dose of 10 g was not used in this study, as a prior study reported that 23% of patients required additional dextrose boluses before reaching the hospital³. However, the prehospital study using approximately 20 g of both 10% and 50% dextrose still found that more than 20% of the patients needed additional boluses. Notably, it was unclear whether those patients had received continuous intravenous dextrose infusions after the initial bolus⁶. In contrast, this study ensured that all the patients received a continuous infusion of 10% D/N/2 following the initial bolus, in accordance with the Thai Clinical Practice Guideline. This guideline recommends administering a continuous dextrose infusion (5%-10%) after an IV dextrose bolus in patients with severe hypoglycemia, starting at a rate of 2 mg of glucose per kilogram of body weight per minute and adjusting it based on capillary blood glucose (CBG) levels to maintain a target range of 80-180 mg/dL¹³. This continuous infusion likely contributed to preventing recurrent hypoglycemia.

In terms of safety, there was a concern whether the higher volume required for administering the same amount of glucose would have an adverse effect on patients at risk of fluid overload. The prehospital study comparing 10% and 50% dextrose included about 8% of patients with end-stage renal disease requiring hemodialysis. Both groups received approximately 20 g of dextrose (50% dextrose = 40 ml and 10% dextrose = 200 ml), with no differences observed in hospital length of stay or mortality rates⁶. In this study, the 10% dextrose, 15 g regimen showed a lower risk of volume overload, though this was not statistically significant. Conversely, the 10% dextrose, 20 g regimen demonstrated a statistically significant 4.9% reduction in risk compared to the 50% dextrose, 25 g regimen within 24 hours. This reduced risk, despite the higher fluid volumes, may be due to unmeasured confounders affecting the volume overload, such as the total fluid intake from blood products, intravenous fluids, and vasopressors, for which data were not collected. Based on these findings, using 10% dextrose, which requires a 100-150 ml greater volume than 50% dextrose, appeared to be safe in patients without obvious signs of volume overload, though further studies are needed to confirm this.

To the best of our knowledge, this is the first study to evaluate the effectiveness of 10% dextrose compared to 50% dextrose specifically for achieving post-treatment euglycemia, with a standardized timing of CBG measurements across all patients. Additionally,

data on the infusion rate of continuous 10% D/N/2 in all the patients were collected, and the risk of volume overload associated with administering larger volumes of less concentrated dextrose was also compared. Previous studies primarily focused on the effectiveness of 10% dextrose versus 50% dextrose in terms of symptom resolution, time to symptom resolution, blood glucose levels post-treatment, the need for additional doses, or tissue damage from extravasation¹⁵. Only one study addressed post-treatment hyperglycemia, but the timing of blood glucose measurement differed in that study, as it was recorded upon the patient's arrival at the hospital⁶.

Limitation Data on food or beverage intake before and after an intravenous dextrose bolus as well as data on intravenous drugs diluted in dextrose solutions within the first 60 minutes were not collected, which could affect post-treatment CBG levels. Additionally, infusion pumps were used in some patients, but not consistently across all cases, so the actual infusion rate could have differed from the prescribed rate. Meanwhile, guidelines recommend starting with oral food or beverages containing sugar for patients who are conscious and able to eat^{1,4,10,13}. In this study, 20% of the patients had normal consciousness. The primary reasons for using intravenous dextrose bolus in these cases were a lack of appetite, nausea, vomiting, or critical illness (e.g., sepsis). This subgroup of patients may have had a higher baseline CBG compared to those with impaired consciousness, which could explain the higher

proportion of post-bolus hyperglycemia observed in this study.

Unlike capillary blood glucose, which is an objective measure and unlikely to be affected by the non-blinded study design, the assessment of volume overload might have been subject to potential bias due to the study's non-blinded nature, and this should be noted. Specifically, since the study team was aware of the treatment group, the treating physicians may have intentionally adjusted the infusion rate to minimize the risk of volume overload. This study did not enforce a standardized infusion rate for all patients; instead, the infusion rates were adjusted based on real-world clinical practice. Physicians typically considered both the patient's body weight and pre-treatment CBG levels when making decisions. For example, patients with significantly lower CBG levels were more likely to receive a higher initial infusion rate than those with relatively higher CBG levels. However, the primary objective of adjusting the infusion rate was to achieve euglycemia, rather than to prevent volume overload. Although there was an initial concern about potential bias, the actual data did not support this issue. As shown in Table 1, the IV continuous infusion rates during the first 15 minutes were not significantly different among the three study groups. Furthermore, when analyzing infusion rates from 15 to 60 minutes, the group receiving the lowest continuous infusion rate was not the 10% dextrose bolus group, but rather the 50% dextrose group. This was likely because, at the 15 minute CBG

measurement, most patients in the 50% dextrose group had glucose levels exceeding 180 mg/dL, leading physicians to reduce the infusion rate accordingly. Finally, the non-randomized, sequential group assignment may have introduced residual confounding and temporal bias. Baseline imbalances (e.g., sepsis/infection) were present, and despite adjustment for measured confounders, unmeasured or time-related factors may still have influenced the outcomes.

Conclusions

Treating hypoglycemia with 10% dextrose at doses reduced to 15 g and 20 g lowered the risk of post-treatment hyperglycemia compared to 50% dextrose (25 g), without increasing the risk of volume overload. Although 10% dextrose at 20 g resulted in a higher post-bolus CBG than the 15 g dose, it remained within the euglycemic range. Since all the participants in this study were Thai and the research was conducted at a single center, the findings may not be generalizable to other ethnic groups and should be validated through further studies.

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