SYSTEMATIC REVIEW

Dextrose 50% versus Dextrose 10% or Dextrose Titration for the Treatment of Out-of-Hospital Hypoglycemia: A Systematic Review

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Abbreviations:
BGL: blood glucose level
D10: 10% dextrose
D40: 40% dextrose
D50: 50% dextrose
EMS: Emergency Medical Services
ILCOR: International Liaison Committee on Resuscitation
IV: intravenous
JBI: Joanna Briggs Institute
PEP: Prehospital Evidence-Based Practice Program
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT: randomized controlled trial

Abstract

Introduction: Paramedics commonly administer intravenous (IV) dextrose to severely hypoglycemic patients. Typically, the treatment provided is a 25g ampule of 50% dextrose (D50). This dose of D50 is meant to ensure a return to consciousness. However, this dose may cause harm and lead to difficulties regulating blood glucose levels (BGLs) post-treatment. It is hypothesized that a lower concentration, such as 10% dextrose (D10), may improve symptoms while minimizing harm.

Methods: PubMed, Embase, CINAHL, and Cochrane Central were systematically searched on September 15, 2020. The PRISMA guidelines were followed. GRADE and risk of bias were applied to determine the certainty of the evidence. Primary literature investigating the use of IV dextrose in hypoglycemic diabetic patients presenting to paramedics or the emergency department was included. Outcomes of interest included safety, efficacy (symptom resolution), and BGL.

Results: Of 680 abstracts screened, 51 full-text articles were reviewed, with eleven studies included. Data from three randomized controlled trials (RCTs) and eight observational studies were analyzed. A single RCT comparing D10 to D50 was identified. The primary significant finding of the study was an increased post-treatment glycemic profile by 3.2mmol/L in the D50 group; no other outcomes had significant differences between groups. When comparing pooled data from all the included studies, there was greater symptom resolution in the D10 group (95.9%) compared to the D50 group (88.8%). However, the mean time to resolution was approximately four minutes longer in the D10 group (4.1 minutes [D50] versus 8.0 minutes [D10]). There was a greater need for subsequent doses with the use of D10 (19.5%) compared to D50 (8.1%). The post-treatment glycemic profile was lower in the D10 group at 6.2mmol/L versus 8.5mmol/L in the D50 group. Both treatments had nearly complete resolution of hypoglycemia: 98.7% (D50) and 99.2% (D10). No adverse events were observed in the D10 group (0/1057) compared to 13/310 adverse events in the D50 group.

Conclusion: Studies show D10 may be as effective as D50 at resolving symptoms and correcting hypoglycemia. Although the desired effect can take several minutes longer, there appear to be fewer adverse events. The post-D10-treatment BGL may result in fewer untoward hyperglycemic episodes.

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Introduction

Severe hypoglycemia, characterized by impaired consciousness, affects up to 35%-42% of those with Type I diabetes and 16.5% of those with Type II diabetes.[1,2] Hypoglycemic-induced

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impaired consciousness can lead to neurologic sequalae or death if not treated promptly.[3,4] Emergency Medical Services (EMS) are often called to provide care for the patient with severe hypoglycemia. These types of responses account for one percent to four percent of call volumes.[2]

Paramedics treat severe hypoglycemia with intravenous (IV) dextrose.[5] Current EMS standard of care is to administer 25g of 50% dextrose (D50).[6] This dose of D50 is meant to ensure expedited delivery of much needed glucose to the brain in an amount that ensures a return to consciousness. The current literature suggests other options may be as effective with fewer adverse effects. A systematic review conducted in 2008 concluded that 10% dextrose (D10) may be as effective as higher concentration solutions.[7]

Ten percent dextrose could be considered an alternative to D50 treatment.[7] Both D50 and D10 are delivered intravenously, resulting in a rapid response to medication administration. A concern regarding IV delivery of D50 is the risk of extravasation resulting in tissue necrosis. Due to D50 being administered in a hypertonic state, this can result in a high risk of damage to the surrounding tissue when compared to D10, which has more isotonic properties.[5] The 25g dose of D50 provides five-times the normal adult level of glucose.[8] This high concentration delivery can often lead to post-treatment hyperglycemia and unnecessary physiological challenges for the patient in the time following the event.[6] Furthermore, D50 is in frequent short supply and costly, at approximately US$7.00 per ampule compared to US$2.50 per 25g bag, making D10 a sensible consideration.[6,9] The 2018 United Kingdom Joint Royal Colleges Ambulance Liaison Committee (London, UK) Guidelines update and the Ambulance Victoria Guideline in Victoria, Australia include D10 as the preferred treatment choice for some of these reasons.[10,11]

It is hypothesized that alternative treatment modalities such as D10 or titrating the D50 to a complete return of consciousness may be optimal and may avoid some of the complications that arise from larger, more concentrated boluses.

Methods

Study Design

This is a systematic review and meta-analysis of the evidence on the effectiveness and harms of D50 compared to D10 or titrated dextrose for the EMS management of hypoglycemia. The Prehospital Evidence-Based Practice (PEP) program is a knowledge translation program, maintained by the Dalhousie Department of Emergency Medicine, Division of EMS (Halifax, Nova Scotia, Canada). The Division of EMS supported this systematic review. The Cochrane Handbook for Systematic Reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist guided the review and reporting, respectively.[12] The protocol was registered on PROSPERO, registration number: CRD42019138770 on August 16, 2019. This review did not include collection of patient data and thus did not require ethics approval.

Search Strategy

Databases searched included PubMed (National Center for Biotechnology Information, National Institutes of Health; Bethesda, Maryland USA), Embase (Elsevier; Amsterdam, Netherlands), CINAHL (EBSCO Information Services; Ipswich, Massachusetts USA), and The Cochrane Central Register of Controlled Trials (The Cochrane Collaboration; London, United Kingdom). A search strategy was created with the aid of a health sciences librarian using the medical sub-headings of "Dextrose," "D50," "D10," and "Hypoglycemia." A full search strategy is available in Appendix A (available online only). Databases were searched from inception to September 15, 2020. A targeted grey literature and on-going trial search were also conducted by author JS from June 17, 2019 through June 18, 2019. This search was conducted using the databases: Cochrane Library (The Cochrane Collaboration; London, United Kingdom); Australian New Zealand Clinical Trials Registry (ANZCTR; Camperdown, New South Wales, Australia); ClinicalTrails.gov (US National Library of Medicine; Bethesda, Maryland USA); Health Canada's clinical trials database (Health Canada; Ottawa, Ontario, Canada); European Union clinical trials register (EU; Brussels, Belgium); and the PEP. Reference lists from included studies were hand searched.

Study Selection

Studies were considered eligible for inclusion by *a priori* criteria if the patient population studied received IV dextrose for the treatment of suspected hypoglycemia. Hypoglycemia treatments of interest included the standard 25g ampule diluted to D50 solution, D10, and any other variations of IV dextrose concentrations or titrations. Only studies on adult patients (>18 years of age) with hypoglycemia of any etiology were to inform a range of situations in which dextrose treatment would be considered. The original study setting criteria were limited to only patients treated in the prehospital environment. However, the criteria were later expanded upon to include treatment within the emergency department to be more inclusive.

At least one of the a *priori* outcomes of interest must have been reported by the included studies. These outcomes were based on previous work on treatment of hypoglycemia completed by the International Liaison Committee on Resuscitation (ILCOR; world-wide organizations).[13] The primary outcomes of interest were: resolution of symptoms, time to resolution of symptoms, and blood glucose level (BGL) post-treatment. Level of consciousness may be measured by a formal scale (eg, Glasgow Coma Scale [GCS]) or by clinician impression. Secondary outcomes of interest were: need for subsequent doses, adverse events, resolution of hypoglycemia, and time to resolution of hypoglycemia. Adverse events considered included treatment failure to return consciousness, reverting to standard of care after a failure of initial treatment, or tissue damage. Subsequent doses may be considered as part of the same acute event while attempting to obtain symptom resolution.

Randomized controlled trials (RCTs), cohort studies, observational studies, case series, and case reports were eligible for inclusion. Case studies were specifically considered to capture any report of low incidence adverse events. From the preliminary investigation of this topic, there was an anticipated paucity of prospective and randomized studies, and given the nature of this treatment, it was decided that observational studies would be included. Incomplete or unpublished studies, abstracts, trial protocols, studies on animals, and studies conducted in a laboratory setting were excluded. All languages were included where an English title was available during screening.

All potentially eligible studies were independently screened by two appraisers at the title and abstract level by MH and JS using Covidence software (Melbourne, Victoria).[14] Disagreements were resolved by third author adjudication (JAG). Full-text review for inclusion was conducted by MH and JS with third party review by JAG.

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Data Extraction and Assessment
Authors MH and JS each independently extracted data from all studies. Where required, data were estimated from the graphs provided. In cases of missing data, corresponding authors were contacted or attempts to contact were made. All data collection was audited by JAG and disagreements were resolved by consensus.

Variables
Data related to study design, dates, setting/location, and sample demographics including but not limited to sample size and setting were extracted. Patient conditions (eg, initial level of consciousness, initial BGL, and history of diabetes) were collected. Intervention and comparison characteristics (eg, drug, concentration, dose, and route) were collected. Results from each reported outcome in the *a priori* list were collected for analysis.

Risk of Bias
Risk of bias for each study was assessed independently by MH and JS using the Joanna Briggs Institute (JBI; Adelaide, Australia) Critical Appraisal checklists appropriate for each study design.[15] The final score was discussed between authors (MH, JS, and JAG), and upon agreement, the final risk of bias score was recorded being very high risk of bias, high risk of bias, medium risk of bias, or low risk of bias. Appendix B (available online only) shows full risk of bias within each study.

Data Synthesis
Study results were compared, where appropriate. Descriptive statistics were reported including mean differences and 95% confidence intervals (CI). Results were pooled across outcomes for both D10 and D50. Graphical representations were used, where appropriate. Formal meta-analysis was not possible due to inconsistent comparison groups rendering statistical synthesis inappropriate.

Results

Study Selection
Six-hundred-eighty studies were identified for inclusion. Full-text review was performed on 51, of which 11 were included for analysis (Figure 1). One non-English language study was translated from German to English by a volunteer. Five identified studies were ultimately excluded because corresponding authors were unable to provide the missing data required to include each study at the full-text phase. Reviewer kappa was 0.55619 for title and abstract screening between authors (MH and JS). For full-text screening, the senior author (JAG) double checked all inclusion decisions and the kappa at this stage was 1.00 between (JS and JAG) and 0.74194 between (MH and JAG).

Study Characteristics
The review included 11 studies: three RCTs[16–18] and eight observational studies[5,19–25] with a total of 1,462 patients. Of the 11 studies, eight were conducted in the prehospital setting[17,19,20,22–25] and originated from six countries (Denmark, United States, Wales, England, Germany, and Scotland; Table 1).

Three studies investigated the effects of D10,[5,17,25] nine studies investigated D50,[16–20,22–25] and one study investigated a 40% dextrose (D40) solution.[21] Two studies compared D10 directly to D50:[17,25] Moore was an RCT where both interventions were used, and the dose could be titrated to the clinician's discretion in response to drug effect;[17] Weant was an observational before-and-after study where a new protocol supported clinician discretion on dextrose concentration selection.[25] The remaining studies did not have a comparator[5,20,21,23,24] or used another standard hypoglycemia treatment as the comparator (one milligram of intramuscular glucagon; Table 1).[16,18,22]

Hypoglycemia was defined as point-of-care capillary measurement of less than 3.0 millimole/liter (mmol/L) at the lowest threshold[16] and up to 4.4mmol/L at the higher threshold,[23,24] or by the paramedic's "empiric impression" in one study (Hoffman). All studies that recorded history of diabetes reported 100% diabetes etiology, except Moore, which reported 84% (43/51) of patients had insulin dependent diabetes.[17] One study reported tissue extravasation.[19]

Data for each outcome of interest were extracted. Ten studies investigated symptom resolution;[5,16–18,20–25] six investigated time to symptom resolution;[16–18,21,22,25] glycemic profile post-treatment was investigated by five studies;[5,16–18,25] need for subsequent doses by four studies;[5,18,24,25] adverse events by seven studies;[5,16,17,19,23–25] resolution of hypoglycemia by five studies;[5,16–18,23] and time to resolution of hypoglycemia was reported in two studies[16,18] (Table 2).

Risk of Bias within Studies
Using the JBI risk of bias assessment tools, two studies were identified as high risk: one RCT and one retrospective case series.[18,20] The Patrick study was deemed high risk due to lack of clarity in reporting of its methods, resulting in concerns regarding valid randomization strategy, blinding and appropriate design execution.[18] The second high risk of bias study to be assessed was the Hoffman retrospective case series. This study was deemed high risk due to its limited reporting of patient results, patient test group similarities, and patient condition prior to treatment.[20] The remaining studies were all assessed as low risk of bias, included the RCT comparing D10 directly to D50 (Appendix A; available online only).[5,16,17,19,21–25]

Results of Individual Studies
Resolution of Symptoms—All studies reported on symptom resolution after dextrose treatment. Evidence from nine pooled studies (three RCTs and six observational studies), enrolling 367 hypoglycemic patients treated with IV D50, reported symptom resolution in 88.8% (95% CI, 88.7%-89.1%) of patients (Figure 2).[16–20,22–25] Evidence from three studies (one RCT and two observational), enrolling 1,057 patients treated with IV D10, reported 95.9% resolution of symptoms (95% CI, 95.8%-95.9%).[5,17,25] The RCT comparing D10 to D50 reported a non-statistically significant difference in symptom resolution of four percent favoring D50 (-12 to +22%; P = .360).[17] Symptom resolution was 96% (25/26 patients) in the D50 arm and 92% (23/25) the D10 arm.[17] When the results for symptom resolution were pooled across studies, both D10 and D50 had high resolution success with a non-clinically significant difference of 7.1% favoring D10.[16–20,22–25] One single case reported a patient received a D40 infusion and recovered to normal level of consciousness.[21]

Time to Symptom Resolution—Evidence from four studies (three RCTs and one observational), enrolling 60 patients treated with D50, had a mean symptom resolution time of 4.1 minutes (95% CI, 3.46-4.78 minutes; Figure 3).[16–18,21] Evidence from one RCT, enrolling 51 patients treated with dextrose, reported a median time to resolution of 8.0 minutes in the D10 arm (n = 25) and 8.0 minutes in the D50 arm (n = 26; P = .733).[17] The mean difference between these treatments may be clinically meaningful at 3.9 minutes. One single case reported a patient received a D40 infusion had symptom resolution within two minutes.[21]

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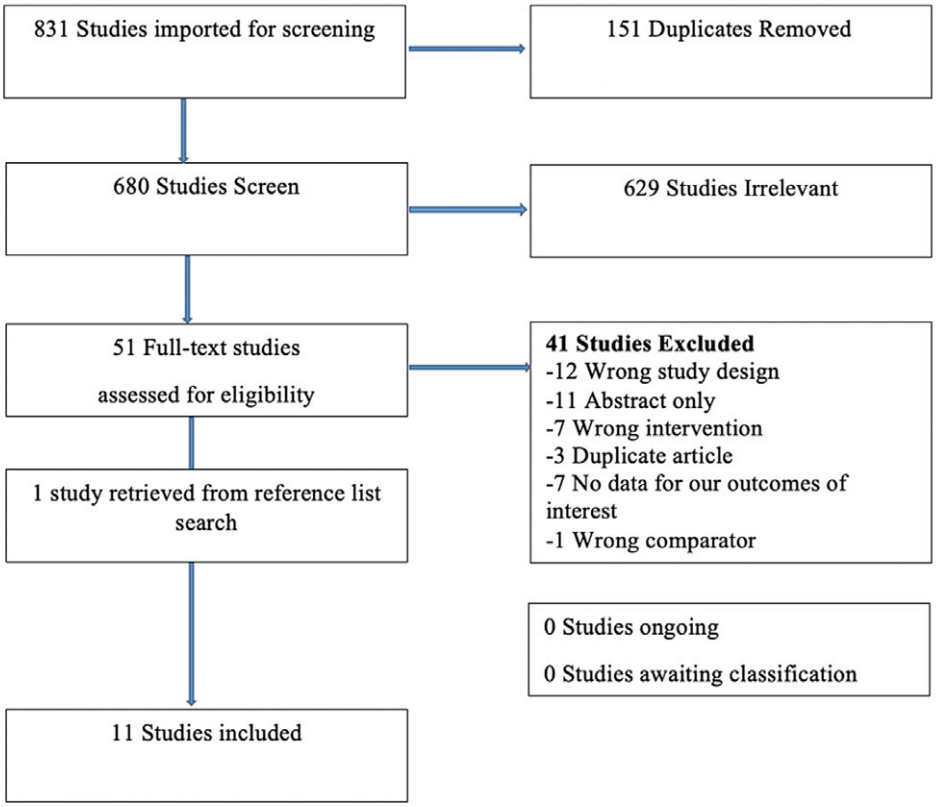

Figure 1. PRISMA Flow Diagram of Included and Excluded Studies.
Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Blood Glucose Level Post-Treatment—Evidence from four pooled studies (three RCT and one observational), enrolling 196 total patients treated with D50, resulted in a mean post-treatment glycemic profile of 8.45mmol/L (95% CI, 8.4-8.5mmol/L; Figure 4).[16–18,25] Evidence from three pooled studies (one RCT and two observational), enrolling 1,057 patients treated with D10, had a mean post-treatment glycemic profile of 6.2mmol/L (95% CI, 6.24-6.16mmol/L).[5,17,25] A statistically significant difference of 3.2 minutes (P = .003) was reported by the RCT comparing D50 directly to D10.[17] This RCT reported a median post-treatment BGL of 9.40mmol/L in the D50 arm and 6.20mmol/L in the D10 arm.[17]

Need for Subsequent Doses—Evidence from three pooled studies (one RCT and two observational), enrolling 259 patients treated with D50, reported 8.1% (95% CI, 7.9%-8.3%) of patients needed subsequent treatment (Figure 5).[18,24,25] Results from two observational studies, reporting on 1,032 patients treated with D10, found 19.5% (95% CI, 19.4%-19.6%) required additional D10 treatment.[5,25]

Resolution of Hypoglycemia—Evidence from pooled four studies (three RCTs and one observational), enrolling 78 patients treated with D50, reported 98.7% (95% CI, 98.4%-99.0%) resolution of hypoglycemia (Figure 6).[16–18,23] Evidence from two pooled studies (one RCT and one observational), enrolling 896 patients treated with D10, reported 99.2% (95% CI, 99.2%-99.2%) resolution from hypoglycemia.[5,17] The RCT comparing D50 to D10 reported 100% resolution in both groups: 26 of 26 and 25 of 25 patients, respectively.[17]

Time to Resolution of Hypoglycemia—Time to resolution of hypoglycemia was reported on in two RCTs investigating D50 administration in 20 patients.[16,18] The RCT by Patrick enrolling 14 patients receiving D50 reported a BGL of approximately12.5mmol/L at the first check five minutes post-treatment.[18] The RCT by Carstens enrolling six patients receiving D50 reported a BGL of approximately 9.5mmol/L at the first check 10 minutes post-treatment. No data were available for this outcome using D10 treatment.[16]

Adverse Events—Seven studies, including 1,367 total patients, investigated adverse events (Table 3 and Table 4). Evidence from six studies (two RCTs and four observational studies), enrolling 310 patients treated with D50, reported a 4.2% (13/310) adverse event rate.[16,17,19,23–25] These consisted of three patients reporting mild hypoglycemia requiring only self-treatment, eight rebound calls to 911 within 48 hours, one patient who did not recover who was later diagnosed in-hospital with encephalopathy as the cause of the hypoglycemia, and one case of extravasation. There were no (0/1,057) adverse events reported in the three studies investigating adverse events for D10 treatment.[5,17,25] The RCT reported no adverse events in either treatment group (0/25 D10 group and 0/26 D50 group).[17] One observational study reported an overall 27.0% (84/311) of patients had hyperglycemia upon hospital arrival with no statistical difference between the D50 and D10 groups. Hyperglycemia had not been considered as an adverse

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Study Author/ Year	Study Design	Setting	Mean Age (years)	Treatment Group	% Male Patients	Intervention	Outcomes
Carstens, 1998[16]	Randomized Controlled Trial	Emergency Department, Denmark	46.9 years	n = 6	64%	D50 50ml IV	Symptom Resolution Time to Symptom Resolution BGL Post-Treatment Adverse Events Resolution of Hypoglycemia Time to Resolution of Hypoglycemia
Chinn, 2017[19]	Case Report	Prehospital, Milwaukee USA	57 years	n = 1	100%	D50 50ml IV	Adverse Events
Hern, 2016[5]	Prospective Cohort	Prehospital, Oakland USA	65 years	n = 871	53.8%	D10 100ml IV	Symptom Resolution BGL Post-Treatment Adverse Events Resolution of Hypoglycemia Need for Subsequent Doses
Hoffman, 1992[21]	Retrospective Cohort	Prehospital, Los Angeles USA	Not reported	n = 29	Not reported	D50 IV (dose not reported)	Symptom Resolution
Hohenstein, 2006[22]	Case Report	Emergency Department, Stuttgart Germany	36 years	n = 1	100%	D40 20ml IV	Symptom Resolution Time to Symptom Resolution
Howell, 1997[23]	Prospective Cohort	Prehospital, Bristol UK	Not reported	n = 14	Not reported	D50 25g IV	Symptom Resolution Time to Symptom Resolution
Lerner, 2003[24]	Prospective Cohort	Prehospital, Buffalo USA	47 years	n = 36	53%	D50 IV	Symptom Resolution Adverse Events Resolution of Hypoglycemia
Mechem, 1998[25]	Prospective Cohort	Prehospital, Philadelphia USA	56.7 years	n = 95	54.4%	Amp of D50 IV	Symptom Resolution Need for Subsequent Doses Adverse Events
Moore, 2005[17]	Randomized Controlled Trial	Prehospital, Cardiff Wales	55 years	n = 25	60%	D10 (5g 50ml IV aliquots)	Symptom Resolution Time to Symptom Resolution BGL Post-Treatment Adverse Events Resolution of Hypoglycemia

Table 1. Characteristics of Included Studies (*continued*)

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Study Author/ Year	Study Design	Setting	Mean Age (years)	Treatment Group	% Male Patients	Intervention	Outcomes
Patrick, 1990[18]	Randomized Controlled Trial	Emergency Department, Edinburgh Scotland	47.5 years	n = 14	76%	D50 50ml IV	Symptom Resolution Time to Symptom Resolution BGL Post-Treatment Need for Subsequent Doses Resolution of Hypoglycemia Time to Resolution of Hypoglycemia
Weant, 2019[27]	Prospective Cohort	Prehospital and Emergency Department, Charleston USA	58.7 years	n = 311	52.4%	D10 25mg IV	Symptom Resolution BGL Post-Treatment Need for Subsequent Doses Adverse Events

Table 1. *(continued).* Characteristics of Included Studies
Abbreviations: IV, intravenous; BGL, blood glucose level; D10, 10% dextrose; D40, 40% dextrose; D50, 50% dextrose.

Resolution of Symptoms	Time to Resolution of Symptoms	BGL Post-Treatment	Need for Subsequent Doses	Adverse Events	Resolution of Hypoglycemia	Time to Resolution of Hypoglycemia
Carstens	Carstens	Carstens	Hern	Chinn	Carstens	Carstens
Hern	Hohenstein	Hern	Mechem	Carstens	Hern	Patrick
Hoffman	Howell	Moore	Patrick	Hern	Lerner	
Hohenstein	Moore	Patrick	Weant	Lerner	Moore	
Howell	Patrick	Weant		Mechem	Patrick	
Lerner				Moore		
Mechem				Weant		
Moore						
Patrick						
Weant						

Table 2. Studies Investigating Each Outcome of Interest
Abbreviation: BGL, blood glucose level.

event in this review, but an untoward effect of IV dextrose administration accounted for in the post-treatment BGL results.[25] Mortality had not been listed as an *a priori* outcome but, of note, the Weant study reported a non-significant difference for in-hospital mortality of 4.7% in the D50 group versus 6.2% in the D10 group (P = .623).[25]

Discussion

Summary of Evidence

This review sought to report on the current evidence for the use of D50 and D10 in emergently reversing the immediate impact of hypoglycemia. The aim was to determine if these treatments were equivalent or if one was superior for several patient-related important outcomes. There have been several concerns related to the delivery of the hypertonic D50. A primary concern is neurologic sequala should treatment not be prompt or adequate.[4,26] Outcomes of interest were based on the ILCOR guidelines on treatment of hypoglycemia.[13] Because of this approach, neurologic sequalae and death were not considered outcomes related to the inclusion criteria. None of the included studies reported on these outcomes. There is the additional concern related to tissue necrosis should the solution become extravasated and post-treatment challenges in blood glucose regulation.[19,25] It was for these reasons that there was motivation to identify an

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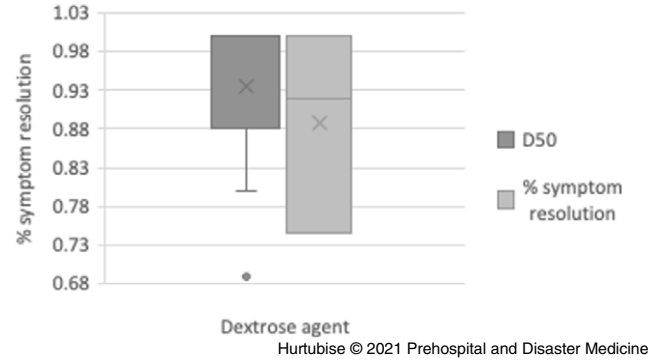

Figure 2. Symptom Resolution.
Abbreviation: D50, 50% dextrose.

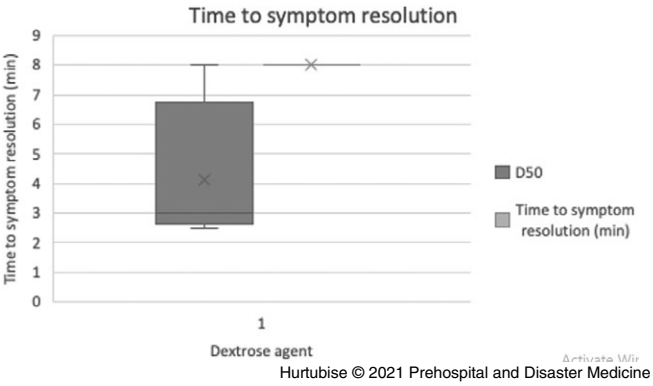

Figure 3. Time to Symptom Resolution.
Abbreviation: D50, 50% dextrose.

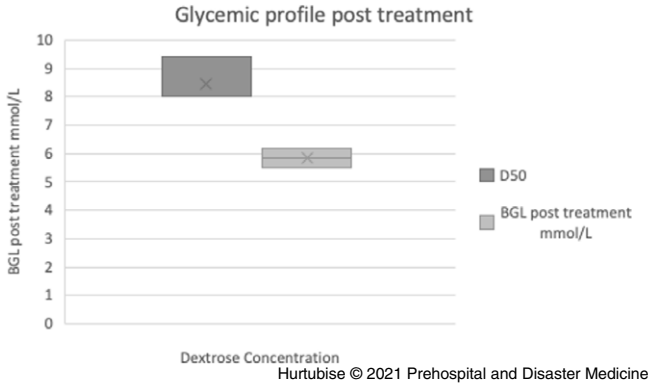

Figure 4. Blood Glucose Post-Treatment.
Abbreviations: BGL, blood glucose level; D50, 50% dextrose.

efficient evidence-based alternative for patients requiring emergent IV dextrose therapy. The primary outcome of resolution of symptoms was well-reported on and both treatments achieve high levels of success recovering patients to full consciousness. The instances where the cause of failure to rouse the patient were identified; the causes were unrelated to the drug but to the underlying patient's condition (eg, drugs, alcohol, and serious urinary tract infection).[17] The time to resolution of symptoms had a notable difference between the two treatments. This difference is thought to be related to the administration modality

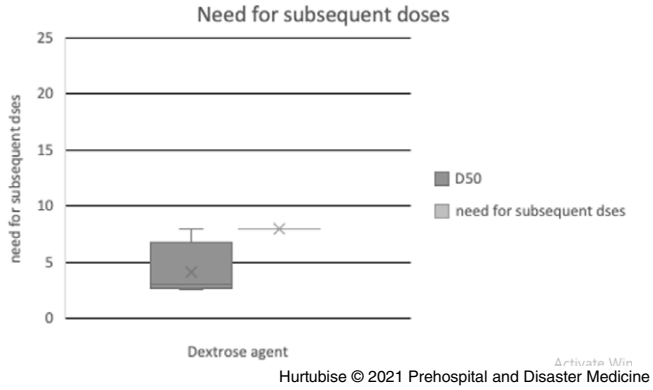

Figure 5. Need for Subsequent Doses.
Abbreviation: D50, 50% dextrose.

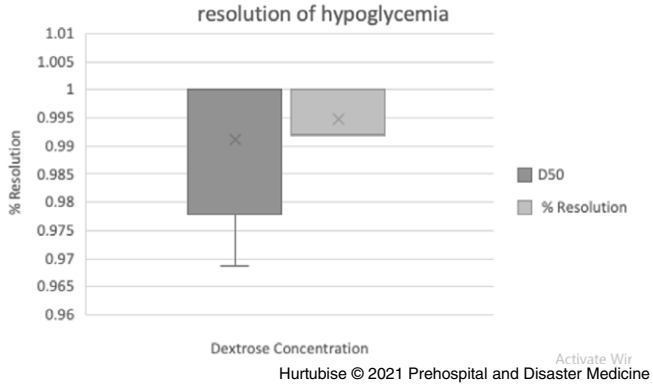

Figure 6. Resolution of Hypoglycemia.
Abbreviation: D50, 50% dextrose.

itself; D10 is typically delivered via an IV drip contrasted to an ampule that is "pushed" delivering the medication intravenously. While this several-minute delay until symptoms are visible diminishing has debatable clinical relevance and long-term outcomes should be formally investigated. However, this slower delivery may allow the clinician greater ability to monitor the patient's response and titrate the medication to desired effect. The clinicians in the Moore trial were instructed by study protocol to titrate both treatments to desire effect.[17] This may be the advantage that led to the more desirable post-treatment glycemic profile in the D10 data. Post-treatment hyperglycemia is a documented undesirable effect of emergent dextrose administration which may result in negative neurological impact.[27,28]

Secondary outcomes related to need for subsequent doses and resolution of hypoglycemia had similar results across treatments. Time to resolution of hypoglycemia was only reported for studies investigating D50 where the resolution was reported to be within two minutes. This measure is determined by the interval which the clinicians recheck the BGL and thus may be unreliable. None the less, the patients' blood glucose meets or exceeds normal levels very quickly post-D50-administration. Notably, there were no adverse events in 1,057 patients reported in the D10 group. There were, however, 13 events considered adverse amongst the patients treated with D50. The most remarkable adverse event was the single case of extravasation resulting in

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	D50	#Studies	Treatment Group (n)	D10	#Studies	Treatment Group (n)
Symptom Resolution	88.8%	9	367	95.9%	3	1057
Time to Symptom Resolution	4.1min	4	60	8min	1	25
Need for Subsequent Doses	8.1%	3	259	19.5%	2	1032
BGL Post-Treatment	8.5mmol/L	4	207	6.2mmol/L	3	1046
Resolution of Hypoglycemia	98.70%	4	78	99.20%	2	896
Time to Resolution of Hypoglycemia	2.0min	2	20	N/A	N/A	N/A
Adverse Events	4.2%	6	310	0.00%	3	1057

Table 3. Results for Each Intervention by Outcome
Abbreviation: BGL, blood glucose level.

Study	D50 (n)	Events	Details	D10 (n)	Events
Carstens[16]	6	1	Mild hypoglycemia 30 minutes post-treatment	–	–
Lerner[24]	32	3	2 (one pregnant) self-treated within 48 hours, 1 other had diagnosis of hypoglycemic encephalopathy	–	–
Mechem[25]	95	8	Rebound calls within 48 hours	–	
Moore[17]	26	0	n/a	25	0
Hern[5]	–	–	n/a	871	0
Weant[27]	150	0	No extravasation	161	0
Chinn[19]	1	1	Extravasation resulting in surgical compartment syndrome	–	–
Total	**310**	**13**		**1057**	**0**

Table 4. Adverse Events

surgical compartment syndrome.[19] Eleven events were related to rebound hypoglycemia. Three of these cases were considered mild and resulted in self-treatment; two of these three patients were pregnant. Pregnancy is an important factor to note when developing treatment guidelines for hypoglycemia, especially when a treat-and-release policy is present in an EMS service. The other eight rebound hypoglycemic events were serious enough to initiate another 911 call within 48 hours. Overall, these events are manageable and infrequent. Procurement of D50 preloaded ampules has been a challenge for some EMS services; D10 may be mixed as needed, circumventing the preload shortage concern.

Limitations

Measures were taken to reduce investigator-level bias, and although recommended methodology were followed, the resulting data had some inherent limitations. Primarily the lack of head-to-head comparisons of the interventions of interest. The RCT by Moore was low risk of bias and well-reported, however it remained under-powered.[17] Furthermore, the protocol for administration within the Moore trial left room for potential dose inconsistency because both drugs were subjectively titrated to effect.[17] Two studies (one RCT and one observational) were scored as high risk of bias primarily due to reporting quality. Many (9 of 11) of the included studies had relatively small sample sizes. There is a paucity of current research as much (7 of 11) of the included data were published prior to 2006. A formal meta-analysis was not possible due to the heterogenous nature of the data, especially in terms of dose and drug comparisons.

Conclusions

High and moderate quality evidence was identified with primarily low risk of bias stating that D10 may be equivalent to D50, for the primary outcome and for some outcomes, potentially a more desirable concentration of dextrose for the treatment of emergent hypoglycemia. Because D10 produces a lower post-treatment glycemic profile, it may mitigate patient's personal challenges moderating blood glucose. No adverse events, including rebound hypoglycemia, were reported with the use of D10. Although symptom response to D10 is delayed by approximately four minutes compared to D50, D10 appears safer and as effective for the critical outcome of returning consciousness. The two case studies, while well-reported, have inherent risks of bias due to design; these inform on extravasation and D40. More research is needed to determine if the response delay has longer term neurological sequalae on patients.

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Supplementary Materials

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