Dietary Practices In Treatment Of Hypoglycaemia In Elevated One-Hour Postload Glucose And Diabetes

Dietary treatment of hypoglycaemia: should the Australian recommendation be increased?

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General recommendations for self-treatment of hypoglycaemia

All recommend:

- Initial treatment with carbohydrate, preferably quickly absorbed

- Eventual follow-up with longer lasting carbohydrate.

Diabetes Australia

Diabetes UK

Diabetic Society of Singapore

ADA

DESG

Asian-Pacific Type 2 Diabetes Policy Group

Recommendations for initial treatment of hypoglycaemia

Recommended carbohydrate (g)	Recommended by:
15	• Diabetes Australia • Singapore Diabetes Association
15 - 20	• Diabetes UK • American Diabetes Association – Standards of Medical Care (2013)
15 - 30	• Diabetes Educators Study Group (European Association for the Study of Diabetes)
Unspecified	• Asian-Pacific Type 2 Diabetes Policy Group

National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults (NHMRC)

- 20 – 25 g 'readily available glucose'

- 'Promptly followed up by a food that has slower-acting carbohydrate'

Recommendation for wait-time to retreatment if hypoglycaemia persists

Time (minutes)	Recommended by:
10	• Diabetes UK
10 - 15	• Diabetes Australia
15	• American Diabetes Association – Standards of Medical Care (2013) • Singapore Diabetes Association
Unspecified	• Diabetes Educators Study Group (European Association for the Study of Diabetes) • Asian-Pacific Type 2 Diabetes Policy Group

Rationale For Recommendations

ADA - Expert opinion

DIABETES AUSTRALIA - Diabetes Australia 2011, Diabetes management in general practice 2012/2013, Diabetes Australia, ACT. -

NHMRC – Wiethop and Cryer 1993(1)

DIABETES UK - Slama G 1990(2) and Cryer PE, Fisher JN, Shamoon 1994(3),

who references: Slama G 1990(2) and Wiethop and Cryer1993(1) and Brodows R 1984(4)

SINGAPORE DIABETIC ASSOCIATION – Diabetes UK

Wiethop and Cryer 1993(1) - used intravenous insulin overnight and regular insulin during the day but no longer acting insulin

Brodows R 1984(4) - used intravenous insulin with medium acting insulin ceased 12 hours previously.

Slama G 1990(2) used intravenous insulin with medium acting insulin ceased 12 hours previously.

Mean duration of diabetes of 0.9 ±1.2 years

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1.   Wiethop BV, Cryer PE. Alanine and terbutaline in treatment of hypoglycemia in IDDM. Diabetes Care. 1993 August 1, 1993;16(8):1131-6.
2.   Slama G, Traynard P-Y, Desplanque N, Pudar H, Dhunputh I, Letanoux M, et al. The Search for an Optimized Treatment of Hypoglycemia: Carbohydrates in Tablets, Solution, or Gel for the Correction of Insulin Reactions. Arch Intern Med. 1990 March 1, 1990;150(3):589-93.
3.   Cryer PE, Fisher JN, Shamoon H. Hypoglycemia. Diabetes Care. 1994 July 1, 1994;17(7):734-55.
4.   Brodows RG, Williams C, Amatruda JM. Treatment of insulin reactions in diabetics. JAMA. 1984 Dec 28;252(24):3378-81. PubMed PMID: 6389915. Epub 1984/12/28. eng.

Aim

To determine:

- if there are optimum recommendations for dietary treatment of hypoglycaemia
- in free-living individuals
- on present-day insulin regimes.

Practicalities

- Assess 15 and 20 g carbohydrate (the most common recommendations)

- The range of recommended wait-times to repeat treatment (WTR) is 10 – 20 minutes.

- Assess 10 mins (the shortest of these)

  plus 5 minute WTR. (based on a substantial effect of glucose on BGL at 5 minutes)
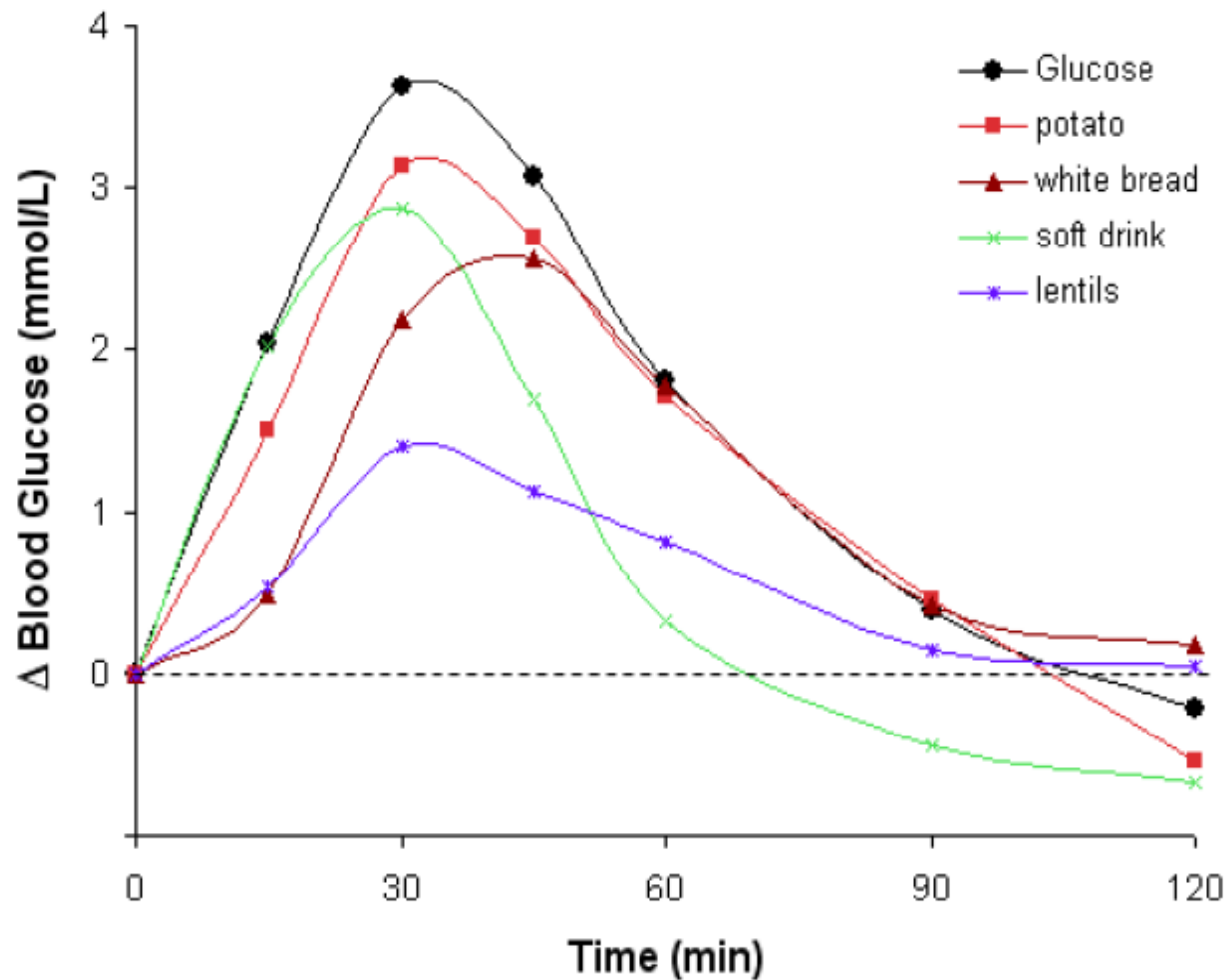
Brand-Miller J, McMillan-Price J, Steinbeck K, Caterson I. Carbohydrates--the good, the bad and the whole grain. Asia Pac J Clin Nutr. 2008;17 Suppl 1:16-9.

Sample Size

- The study was not based on a hypothesized effect size
- No power calculations.
- The rate of incidental hypoglycaemic events in participants reporting for scheduled appointments to our clinics was of the order of 1 – 3/wk
- A 12 month audit (about 80 participants) judged sufficient to answer the study questions.

Objectives

1. To determine if there was a significant difference in the need for repeat treatment of hypoglycaemia following initial treatment with 15 g or 20 g of fast acting carbohydrate in people suffering spontaneous hypoglycaemia in the free-living situation.

2. To determine if WTR could be reduced to either 5 or 10 minutes without significantly increasing the need for repeat dietary treatment.

3. The effect of treating carbohydrate quantity on subsequent hyperglycaemia was also investigated.

Participants

- 92 free-living people (50 male, 42 female)

- > 18 years

- Insulin-treated diabetes (subcutaneous insulin injection (SII) or continuous subcutaneous insulin infusion (CSII))

- Attending their scheduled outpatient diabetes clinic appointment

- Found to have hypoglycaemia on routine blood testing.

- Consent, insulin treatment and hypoglycaemia were the only inclusion criteria.

Identification of Hypoglycaemia

- Identification of hypoglycaemia was by blood glucose monitoring

- A level of less than 3.5 mmol/L defined as hypoglycaemia.

- This level has been suggested as indicating 'clinical' hypoglycaemia

1. Amiel SA, Dixon T, Mann R, Jameson K. Hypoglycaemia in Type 2 diabetes. Diabet Med. 2008 Mar;25(3):245-54.
2. Frier BM. Defining hypoglycaemia: what level has clinical relevance? Diabetologia. 2009 Jan; 52(1):31-4
3. Swinnen SG, Mullins P, Miller M, Hoekstra JB, Holleman F. Changing the glucose cut-off values that define hypoglycaemia has a major effect on reported frequencies of hypoglycaemia. Diabetologia. 2009 Jan;52(1):38-41.

Initial Procedure

- Treatment - 15 g or 20 g of glucose
  WTR - 5 or 10 minutes — **4 groups**
- Each protocol - 16 weeks (or until 20 participants had been audited).
- Participants identified as hypoglycaemic were given fluid containing 15 g (groups 1 and 2) or 20 g (groups 3 and 4) of glucose.
- Retested in 5 minutes (groups 1 and 3) or 10 minutes (groups 2 and 4).
- If BGL < 3.5 mmol/L they were treated again with the same quantity of glucose.
- This procedure was continued until BGLs ≥ 3.5 mmol/L.
- Hypoglycaemic symptoms were recorded on a checklist at the time hypoglycaemia was identified and at each retest.

Procedure Post-resolution Hypoglycaemia

- Ongoing assessment BGLs every 30 mins while participants remained in clinic.

- Post clinic visit participants were requested to blood test every 30 mins to 4 h post resolution of hypoglycaemia on their own blood glucose meter

- Record results, food and exercise on a standard form

- Post the form back to clinic in a provided SAE.

- Follow their normal procedure with meals and insulin.

Statistical Analysis

- Demographics - descriptive statistics
- Shapiro–Wilk test - to determine normality,
- Between-group differences - Kruskal–Wallis test for non-normally distributed continuous variables.
- The χ^2 test - compare categorical variables.
- Mann–Whitney *U-test* - determine independent group differences.
- Analysis PASW v18

Results - Characteristics

Table 1 Characteristics of participants by hypoglycaemia treatment group

Variables	Treatment group†				P-value
	15 g/5 min	15 g/10 min	20 g/5 min	20 g/10 min	
n	25	19	20	28	
Age (years)	47.5±17.8	50.2±16.2	45.3±17.8	52.5±16.8	0.52‡
Gender (male/female)	13/12	9/10	9/11	19/9	0.36§
Diabetes duration (years)	14.8±11.5	20.6±15.8	17.8±13.5	22.6±15.5	0.24‡
Diabetes treatment (SII/CSII)	24/1	16/3	18/2	25/3	—
Haemoglobin A1c (%)	8.8± 2.0	8.1± 1.9	8.8± 2.1	8.7± 2.2	0.63‡
Body mass index (kg/m^2)	28.0± 5.8	26.9± 4.6	25.4± 5.2	26.2± 8.1	0.63‡
Presenting BGL (mmol/L)	2.8± 0.5	2.7± 0.4	2.8± 0.5	2.9± 0.5	0.59‡

†Treatment group – carbohydrate quantity/wait-time to retreatment. ‡Independent samples Kruskal–Wallis test. §χ^2 test. BGL, blood glucose level; CSII, continuous subcutaneous insulin infusion; SII, subcutaneous insulin injection.

Results - Symptoms

- Hypoglycaemic symptoms were reported by 38% of participants

- In those who were symptomatic:

    * 71.8% - symptoms resolved concurrently with resolution

        of hypoglycaemia

    * 28.6% - remained symptomatic for 10 minutes after their

        BGL attained normal levels

- Distribution of presenting BGLs were the same across both groups (p = 0.59).

Results –Resolution of Hypoglycaemia

Table 2 Number of dietary treatments required to resolve hypoglycaemia

Treatment group†	15 g/5 min	15 g/10 min	20 g/5 min	20 g/10 min
n	25	19	20	28
Resolved with one treatment	32.0%	63.2%	55%	89.3%
Resolved after two treatments	44%	31.6%	30%	10.7%
Required >2 treatments	24%	5.2%	15%	0%

†Treatment group – carbohydrate quantity/wait-time to retreatment.

There was a significant association between treatment group and resolution of hypoglycaemia with one treatment $(\chi^2\ P < 0.01)$

Results – Hyperglycaemia at 30 minutes Post-resolution of Hypoglycaemia

- BGLs were recorded for 45 participants at 30 min post-resolution of hypoglycaemia.
- There was no significant difference between this group and nonrecorders for age, gender, duration, HbA1c or BMI ($P > 0.05$).
- BGL > 10 mmol/L was arbitrarily defined as hyperglycaemia
- 2/45 participants were hyperglycaemic at 30 min, but results were insufficient to compare treatment groups.

Results - Hyperglycaemia to 4 h Post-resolution of Hypoglycaemia

- BGLs were recorded for 34 participants to 4h post-resolution of hypoglycaemia

- There was no significant difference between this group and nonrecorders for age, gender, duration, HbA1c or BMI ($P > 0.1$)

- 14 recorded at least one BGL >10 mmol/L unrelated to food intake 90 – 240 min post-resolution hypoglycaemia.

- There was no significant association between initial treating carbohydrate quantity and subsequent hyperglycaemia (p = 0.41).

Conclusions

- 20 g of fast-acting carbohydrate will resolve hypoglycaemia within 10 minutes in 89.3% of free-living individuals on current insulin regimes, compared to 15 g which resulted in only 63.2% resolving in 10 minutes.

- Decreasing the WTR to 5 minutes increased those needing repeat treatments with both 15 and 20 g treatments

- 2/45 hyperglycaemic at 30 mins (when you would expect treating carbohydrate quantity to have an effect) numbers insufficient to statistically assess.

- 14/34 hyperglycaemic at 90 – 240 mins. Unsurprisingly this was not significantly associated with quantity of treating carbohydrate and is probably best attributed to counter regulatory mechanisms