



Adherence to guidelines for self-treatment of mild hypoglycaemia in type 1 diabetes

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Introduction

Hypoglycaemia is an inherent risk of insulin therapy in type 1 diabetes. Mild symptomatic hypoglycaemic episodes are experienced on average twice per patient per week¹⁻⁴ and the frequency of severe hypoglycaemia is 1.0–1.6 episodes per patient per year in unselected populations of patients with type 1 diabetes.¹⁻⁷ While mild hypoglycaemic episodes are not feared by patients,¹ severe hypoglycaemia is feared by patients¹ – as much as complications such as blindness and kidney failure – and by their relatives.⁸ Appropriate self-treatment of mild hypoglycaemia is believed to be essential to prevent progression to more severe degrees of hypoglycaemia, and

Abstract

Aim: To compare self-treatment of mild symptomatic hypoglycaemia in people with type 1 diabetes with national Danish guidelines recommending 10–20 g of refined carbohydrate initially followed by unrefined carbohydrates.

Methods: A cohort of 201 patients with type 1 diabetes filled in a questionnaire including self-treatment of mild symptomatic hypoglycaemia and occurrence of mild and severe hypoglycaemia. Initial intake of less than 10 g of refined carbohydrate was defined as under treatment and intake of 20 g or more as over treatment.

Results: A total of 147 patients (73%) answered both questions about initial and follow-up self-treatment of hypoglycaemia. Fifty per cent of patients treated themselves with 10–20 g refined carbohydrates (female:male = 59%:43%; $p < 0.05$), whereas 37% over treated (female:male = 34%:39%; not significant) and 13% under treated (female:male = 6%:18%; $p < 0.05$). Initial treatment was followed by consumption of unrefined carbohydrates in 70% of the patients. Overall, 37% (female:male = 49%:28%; $p < 0.05$) of the patients adhered to guidelines. The number of severe hypoglycaemic episodes (lifetime) and amount of carbohydrate intake were positively correlated ($r = 0.2$; $p < 0.05$). Adherence to guidelines was not related to occurrence of mild and severe (in the last year) hypoglycaemia, glycated haemoglobin, or fear of hypoglycaemia.

Conclusions: Only about one-third of patients with type 1 diabetes treat mild hypoglycaemia according to guidelines. Female patients show better compliance. Patients with frequent episodes of severe hypoglycaemia over treat more often.

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Key words

Type 1 diabetes; hypoglycaemia; fear of hypoglycaemia; glycated haemoglobin; treatment

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specific guidelines for self-treatment of mild hypoglycaemia exist.⁹⁻¹¹ However, knowledge about patients' adherence to these guidelines is scarce,¹² and it is not known whether there is a relationship between adherence to guidelines and glycaemic control (including occurrence of mild and severe hypoglycaemia).

We therefore conducted a study in a cohort of patients with type 1 diabetes in order to describe self-treatment practice of mild symptomatic hypoglycaemia. Patients' practice was compared with national Danish guidelines and related to the self-reported occurrence of mild and severe hypoglycaemia, the level of glycated haemoglobin, and a fear of hypoglycaemia.

Methods

All 269 patients who were included in our previous studies of severe hypoglycaemia (1999–2001)^{2,3} who have had type 1 diabetes for more than two years were considered for participation in the study. The patients were originally recruited from the outpatient diabetes clinic at Hillerød Hospital, Denmark. Of these, three patients have died, 27 patients have moved, and five patients were excluded due to end-stage renal failure (haemodialysis) or concomitant malignant disease. Among the remaining 234 patients, 201 (86%) accepted the invitation to participate (Table 1). A total of 147 (73%) of the 201 patients answered both questions related to self-treatment of



hypoglycaemia. There were no differences between participants and non-participants in any of the clinical parameters mentioned in Table 1. Type 1 diabetes was defined by insulin treatment from the time of diagnosis and random C-peptide concentration <300 pmol/l (<600 pmol/l if venous blood glucose concentration >12 mmol/l). The study was approved by the regional medical ethics committee and written informed consent was obtained from all participants.

All subjects filled completed a questionnaire evaluating their self-treatment of mild symptomatic hypoglycaemia, worries about hypoglycaemia, and the occurrence of mild and severe hypoglycaemic episodes. The questionnaire was a brief version

of one that had previously been used in our multicentre survey of hypoglycaemia and awareness of hypoglycaemia.⁴ Mild hypoglycaemic episodes were reported for the previous week and were defined as subjective symptoms of hypoglycaemia, manageable by the patient. Severe hypoglycaemic episodes were defined as those in which assistance from other people was needed to recover, irrespective of whether or not consciousness was lost, as significant neuroglycopenia had evidently occurred. These episodes were reported for the preceding year as well as for lifetime with diabetes. We have previously demonstrated that recall of mild¹ and severe^{1,13} hypoglycaemic episodes during a week and a

year, respectively, are well preserved in people with type 1 diabetes. Patients' worries about mild and severe hypoglycaemia were rated on a seven-point Likert scale ranging from 'not at all' (0) to 'very often' (6).

The key question about self-treatment of hypoglycaemia 'How do you usually treat low blood sugar?' was subdivided into three questions: 'What is the first thing you take?', 'How much?', and 'Do you take anything else?' Predefined categories of answers, e.g. grams of sugar taken, were deliberately avoided in order not to bias patients' immediate answers. The answers were classified into intake of refined (sugar) and unrefined (starch) carbohydrates. Intake of

	Females	Males	Females vs males p-value	Total
Patients (%)	85 (42%)	116 (58%)	–	201 (100%)
Age (years)	49 ± 13	50 ± 12	NS	50 ± 13
Duration of diabetes (years)	25 ± 12	24 ± 11	NS	24 ± 12
C-peptide (pmol/l)	65 ± 101	64 ± 86	NS	64 ± 93
HbA _{1c} (%)	8.3 ± 1.0	8.2 ± 0.9	NS	8.3 ± 1.0
≥4 daily insulin injections no. (%)	70 (82%)	101 (87%)	NS	171 (85%)
Patients answering all questions about adherence to self-treatment of mild hypoglycaemia no. (%)	61 (72%)	86 (74%)	–	147 (73%)
Awareness (%)				
normal	23 (38%)	37 (43%)	NS	60 (41%)
impaired	29 (47%)	34 (40%)	NS	63 (43%)
unaware	9 (15%)	15 (17%)	NS	24 (16%)
Threshold for hypoglycaemic symptoms mg/dl (mmol/l)	52 ± 2 (2.9 ± 0.1)	49 ± 2 (2.7 ± 0.1)	NS	50 ± 2 (2.8 ± 0.1)
Dominant hypoglycaemic symptoms (%)				
autonomic	17 (28%)	24 (28%)	NS	41 (28%)
mixed	14 (23%)	13 (15%)	NS	27 (18%)
neuroglycopenic	30 (49%)	49 (57%)	NS	79 (54%)
Retinopathy	35 (43%)	72 (63%)	p=0.02	107 (54%)
Peripheral neuropathy	19 (24%)	41 (36%)	NS	60 (31%)
Nephropathy	15 (19%)	29 (26%)	NS	44 (23%)
Autonomic neuropathy	6 (14%)	11 (14%)	NS	17 (14%)
Macrovascular complications	4 (5%)	11 (9%)	NS	15 (7%)
NS: not significant; figures are percentage or mean ± SD when indicated				

Table 1. Clinical characteristics of the study population



refined carbohydrates was quantified using a standard scheme from the Danish Diabetes Association (Table 2).¹⁴ The calculated intake of refined carbohydrates was compared with the recommended intake of 10–20 g refined carbohydrates as stated in the national Danish guidelines.¹¹ These guidelines also recommend follow-up treatment with unrefined carbohydrates (no quantity specified). Initial intake of less than 10 g of refined carbohydrates was defined as under treatment and intake of 20 g or more as over treatment.

Glycated haemoglobin (HbA_{1c}) was measured by DCA-2000 (Bayer, Leverkusen, Germany) with a normal range of 4.1–6.4%. C-peptide was determined by a radioimmunoassay (AutoDELFA, Wallac Oy, Turku, Finland).

Standard descriptive statistics were used to characterise the study population, and comparisons were made by parametric (linear regression analysis) or non-parametric (Chi-square test) methods when appropriate. The level of statistical significance was chosen as $p < 0.05$ (two-sided).

Results

Adherence to guidelines is shown in Table 3. Fifty per cent of the patients initially treated themselves according to guidelines. Female patients were significantly more compliant than males ($p < 0.05$). Over treatment was more frequent than under treatment ($p < 0.0001$) and men under treated more often than women ($p < 0.05$). Follow-up treatment was only performed by 70% of the patients, and again women tended to be more compliant ($p = 0.052$). A total of 147 (73%) of the patients answered both questions regarding initial and follow-up self-treatment of hypoglycaemia. Overall, 54 (37%) of these patients adhered to the recommendations by consuming 10–20 g refined sugar, followed by an intake

- 2 teaspoonful of sugar, 4 glucose tablets, or 3 pieces of lump sugar
- 1 small orange, 1 apple, or 1/2 banana
- 200 ml milk, or 100 ml chocolate milk
- 100 ml juice, 100 ml diluted fruit syrup, or 100 ml (non-light) soft drink
- 1/4 – 1/6 chocolate bar (e.g. 1/4 Mars bar or 1/6 Ritter bar)

Table 2. Classification of 10 g refined carbohydrates¹⁴

of unrefined carbohydrates. Women were more compliant than men (49% versus 28%; $p < 0.05$).

A total of 138 (72%) of the 191 patients had experienced severe hypoglycaemia during their life with diabetes, and the frequencies of mild and severe hypoglycaemia were 2.0 episodes per patient per week and 0.77 episodes per patient per year, respectively (Table 4). Men had experienced more severe episodes within the last year, but not during their lifetime with diabetes.

We found a positive correlation between the number of severe hypoglycaemic episodes (lifetime) and the amount of carbohydrate intake in response to warning symptoms ($r = 0.2$; $p < 0.05$). There was no significant relationship between self-treatment and mild hypoglycaemia in the preceding week.

Subjects with a normal awareness more frequently under treated, compared to those with reduced awareness (20% versus 4.6%; $p < 0.005$), but follow-up treatment was not affected by their state of awareness.

There was no correlation between adherence to self-treatment of hypoglycaemia and HbA_{1c} in any group. Patients were more worried about severe rather than mild hypoglycaemia (3.6 ± 2.1 versus 1.8 ± 1.8 on a Likert scale; $p < 0.001$) with no difference between genders. Worries about mild and severe hypoglycaemic episodes were not correlated

with the patient's overall adherence to treatment of hypoglycaemia.

Discussion

Self-reported overall adherence to guidelines for treating mild symptomatic hypoglycaemia was only observed in about one-third of the patients; in about half of the women and a quarter of the men studied. Female patients were more compliant with recommendations concerning both initial and follow-up treatment, while men generally under treated. The differences between women and men can not be explained by differences in glycaemic control, or by a greater fear of mild or severe hypoglycaemia among women than men. Since data on self-treatment of mild hypoglycaemia were self-reported, we cannot tell whether women are more adherent or less truthful when filling in the questionnaire.

The Edinburgh group recently assessed how people self-treat mild symptomatic hypoglycaemia in a mixed cohort of 101 type 1 (73%) and insulin-treated patients with type 2 diabetes.¹² In results very similar to our own, they found that only 40% adhered to guidelines, but – in contrast to our findings – as many as 47% of the patients under treated whereas 13% over treated hypoglycaemia.

A positive correlation was observed between the number of severe hypoglycaemic episodes (lifetime) and the amount of carbohydrate intake during warning symptoms. Men had an almost two-fold higher occurrence of severe hypoglycaemia during the last year. An obvious hypothesis is that men under treat mild hypoglycaemia. However, the design of our study does not assess this hypothesis. Moreover, it is of note that lifetime occurrence of severe hypoglycaemia did not differ between genders.



	Total n=201 (%)	Females n=85 (%)	Males n=116 (%)	Females vs males p-value
Adherence to initial treatment				
No. answering	155	64	91	NS
Adequate treatment (10–20 g CH)	77 (50%)	38 (59%)	39 (43%)	0.043
Over treatment (>20 g CH)	58 (37%)	22 (34%)	36 (39%)	NS
Under treatment (<10 g CH)	20 (13%)	4 (6%)	16 (18%)	0.038
Adherence to follow-up treatment				
No. answering	172	72	100	NS
+ follow-up	120 (70%)	56 (78%)	64 (64%)	NS
- follow-up	52 (30%)	16 (22%)	36 (36%)	–
Overall adherence				
No. answering	147	61	86	NS
Adequate sugar + follow-up	54 (37%)	30 (49%)	24 (28%)	0.014
Adequate sugar - follow-up	21 (14%)	6 (10%)	15 (17%)	NS
Over treatment + follow-up	38 (26%)	16 (26%)	22 (26%)	NS
Over treatment - follow-up	18 (12%)	6 (10%)	12 (14%)	NS
Under treatment + follow-up	12 (8%)	3 (5%)	9 (10%)	NS
Under treatment - follow-up	4 (3%)	0 (0%)	4 (5%)	NS

NS: not significant; CH: carbohydrate

Table 3. Adherence to guidelines

Patients with frequent episodes of severe hypoglycaemia more often over treat themselves, but the same tendency is not seen in patients with many mild hypoglycaemic episodes in the preceding week. Patients with a reduced awareness rarely under treat. This might contribute to reduce the risk of severe hypoglycaemia.

National Danish guidelines recommend that people with type 1 diabetes should respond to hypoglycaemic warning symptoms by an initial intake of 10–20 g refined sugar.¹¹ Guidelines from the American Diabetes Association recommend at least 15 g is eaten or taken in liquid form in the event of a hypoglycaemic reaction,¹⁰ whereas recommendations from Diabetes UK⁹ are similar to the Danish guidelines. All three recommendations are partly arbitrary and partly based on experimental studies in patients with type 1 diabetes subjected to insulin-induced mild symptomatic hypoglycaemia.^{15,16} Thus, following experi-

mental attainment of a nadir blood glucose concentration of 55 mg/dl (3 mmol/l) subjects taking 15–20 g glucose respond with a rise in blood glucose to approximately 100 mg/dl (5.5 mmol/l) within 15–20 minutes.

In our clinic all newly diagnosed patients with type 1 diabetes are educated in handling hypoglycaemia according to the Danish guidelines, and exposed to provoked (or spontaneous) hypoglycaemia within the first days after initiation of insulin treatment. Follow-up education along the course of diabetes is tailored individually to the patient, and is expected to include handling of hypoglycaemia.

Reasons for poor adherence are not apparent from the study. Given that current guidelines for self-treatment of hypoglycaemia are relevant (as indicated in experimental studies^{15,16} and clinical survey¹⁷), the diabetes team might face a considerable task educating patients in order to improve adherence and

to correct inappropriate habits that easily develop during a life with diabetes. Alternatively the poor adherence could be explained by patients' relevant adjustments of their self-care along the course of diabetes and therefore be a reflection of qualified individual judgement.

In conclusion, only about one-third of patients with type 1 diabetes treat mild hypoglycaemia in accordance with the recommendations. Female patients showed better compliance. Patients with frequent episodes of severe hypoglycaemia more often over treat themselves. However, the degree of adherence to self-treatment of hypoglycaemia was not related to self-reported occurrence of mild hypoglycaemia, the level of glycosylated haemoglobin, a fear of hypoglycaemia.

Further studies are needed to evaluate the glycaemic consequences of non-adherence in order to provide evidence to facilitate changes in recommendations and in clinical practice.



	Total n=201 (%)	Females n=85 (%)	Males n=116 (%)	Females vs males p-value
<i>Mild hypoglycaemia (last week)</i>				
Number answering	185	77	108	NS
Number of patients with episodes	140 (76%)	61 (79%)	79 (73%)	NS
Number of episodes	363	162	201	
Episodes per patient per week	2.0	2.1	1.9	
<i>Severe hypoglycaemia (last year)</i>				
Number answering	190	82	108	NS
Number of patients with episodes	65 (34%)	21 (26%)	44 (41%)	0.029
Number of episodes	146	43	103	
Episodes per patient per year	0.77	0.52	0.95	
<i>Severe hypoglycaemia (lifetime)</i>				
Number answering	191	81	110	NS
Number of patients with 1 episode	138 (72%)	56 (69%)	82 (75%)	NS
NS: not significant				

Table 4. Occurrence of mild and severe hypoglycaemia

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Conflict of interest statement:

None

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