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Patient Education and Counseling xxx (2005) xxx–xxx

Patient Education and Counseling

www.elsevier.com/locate/pateducou

Evaluation of a self-management-based patient education program for the treatment and prevention of hypoglycemia-related problems in type 1 diabetes

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Received 23 July 2004; received in revised form 19 January 2005; accepted 21 January 2005

Abstract

Objective: Aim of this study was to investigate the effectiveness of a patient education program for the treatment of hypoglycemia-associated problems in type 1 diabetic inpatients.
Methods: In this observational controlled pre-post study, the intervention group (IG; $N = 105$) participated in the new program, controls (control group CG; $N = 102$) received conventional patient education on hypoglycemia.
Results: Follow-up data (mean follow-up: 6.63 months) were obtained from 177 patients (85.6%). Though severe hypoglycemia also decreased in CG to some degree, the decrease in IG was higher than in CG, but fails to reach significance between groups. Hypoglycemia awareness remained constant in IG, whereas some deterioration was observed in CG ($p = 0.06$). Prevalence of hypoglycemia-related problems decreased in IG, whereas in CG it remained constant. No differential effects with regard to psychological well being, fear of hypoglycemia and late complications, and control beliefs were observed.
Conclusion: The results suggest that the new intervention program is an effective treatment. The effectiveness should be confirmed, however, in a randomized controlled trial, also incorporating outpatient settings.
Practice implications: A self-management intervention targeting the patients' health beliefs and attitudes towards hypoglycemia and their diabetes self-management, rather than knowledge-centered patient education, can help to ameliorate or even prevent hypoglycemia-associated problems.

Keywords: Type 1 diabetes mellitus; Hypoglycemia; Hypoglycemia awareness; Self-management intervention

1. Introduction

A major goal of insulin therapy in type 1 diabetes is to maintain tight glycemic control with blood glucose levels in the normal range of non-diabetics in order to prevent severe late-diabetic complications, like blindness or renal failure [1,2]. One major downside of near-normal glycemic control is the elevated risk for hypoglycemia [2,3]. Mild hypoglycemic episodes (blood glucose $\sim$ <3.3 mmol/L) are common and nearly inevitable in type 1 diabetic patients in tight glycemic control [4]. Usually, mild hypoglycemia does not cause major problems, because it is associated with characteristic "warning symptoms" (e.g. trembling, sweating, difficulties in concentrating) [5] that can easily alert the patient of being hypoglycemic and make him take action (ingestion of rapid-acting carbohydrates to normalize blood glucose levels, e.g. dextrose tablets [6]).

Impaired hypoglycemia awareness refers to a state in which the diabetic patient suffers from a reduced ability to perceive the onset of insulin-induced hypoglycemia and to treat low blood glucose in time by ingesting rapid acting

Abbreviations: IG, intervention group; CG, control group; OR, odds ratio; CI, confidence interval

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doi:10.1016/j.pec.2005.01.008

carbohydrates [7]. Impaired hypoglycemia awareness is a common side effect of near-normal glycemic control in type 1 diabetic patients with an estimated prevalence of 20–30% [7,8] and is a major risk factor for severe hypoglycemic episodes with unconsciousness or seizures [9]. Pathophysiologically, the basis of hypoglycemia unawareness lies in an adaptation of the hormonal counter-regulatory response towards low blood glucose levels [10]. This ''downshift'' of the hormonal response leads to a lowering of hypoglycemia symptom thresholds, thus inducing reduced awareness [11]. Hence, ''hypoglycemia begets hypoglycemia'' [12], patients with reduced hypoglycemia awareness being caught in a ''vicious cycle''. On the other hand, from a biopsychosocial perspective the onset of this pathophysiological mechanism is strongly associated with the individual self-care behavior and diabetes self-management [13], e.g. decisions to treat low blood glucose levels, the role of immediate treatment, or having individual blood glucose target levels being rather low because of the fear of diabetic complications.

Severe hypoglycemia and hypoglycemia unawareness, can lead to substantial morbidity (e.g. accidents) [14,15]. Furthermore, hypoglycemia unawareness is a very distressful state for the patients as well as their relatives, as sense of security is often reduced by fears of hypoglycemia that could occur any time and experiencing lack of control [14,16,17]. Hence, the broader term of ''hypoglycemia-associated problems'' could be considered more appropriate than referring simply to a syndrome of hypoglycemia unawareness, as the causes and impact of hypoglycemia unawareness include psychosocial and self-management factors that also should be addressed in an intervention.

Fortunately, the described adaptation towards low blood glucose levels resulting in impaired hypoglycemia awareness is reversible. Meticulous avoidance of even mild hypoglycemic episodes has been shown to lead to a re-adaptation of glycemic thresholds and restoring hypoglycemia awareness [18,19]. On the other hand, concepts of ''awareness training'' (blood glucose awareness training, BGAT; [20]) were found to be effective, with regard to improving detection rates of low (as well as high) blood glucose levels, diabetes-related knowledge and metabolic control [21–24].

A new inpatient education program based on a self-management approach rather than training of ''symptom perception'' was developed by our center targeting at a reduction of hypoglycemia-related problems and at an improvement of hypoglycemia awareness. The aim of the present study was to evaluate the newly developed program with regard to its effectiveness.

2. Materials and methods

2.1. Patients

Patients were recruited from a clinical sample of inpatients with long-standing type 1 diabetes, a high-risk group for developing hypoglycemia-related problems [4], being treated in the Diabetes Clinic, Diabetes Center Mergentheim, Germany, for continuous subcutaneous insulin therapy [25]. Exclusion criteria comprised severely impaired vision, significant cognitive impairment, and psychiatric comorbidity. A total of $N = 207$ type 1 diabetic patients gave informed consent and were included. The number of severe hypoglycemia and the rate of hypoglycemia-associated problems were high in both groups (see Table 1), many patients being transferred to insulin pump treatment because of hypoglycemia (intervention group: $N = 31$ (29.5%); controls: $N = 29$ (28.4%)).

2.2. Design

The study was designed as a controlled pre-post trial without randomization. The study was observational insofar, as 8 months after the beginning of the study the patient education curriculum was switched from the conventional patient education scheme to the novel hypoglycemia self-management approach. The patients studied before switching the curriculum served as controls for the latter. Measurements were obtained before treatment (baseline t_0) and at 6 months follow-up after demission from the diabetes center (follow-up t_1).

2.3. Interventions

Patient groups of 8–10 patients were consecutively assigned to either the intervention or control condition. A total of $N = 105$ patients participated in a new self-management oriented treatment program (six lessons, 45 min each, intervention group, IG). The lessons focused on coping with hypoglycemia in everyday situations, mechanisms of hypoglycemia perception, causes of impaired hypoglycemia awareness, individual health beliefs, and self-care behavior. Table 1 summarizes the contents of the intervention.

Table 1
Curriculum and contents of the new program

Lesson 1: goal-setting, prior experiences with hypoglycemia, initial problem analysis and introduction of self-monitoring techniques
Lesson 2: individual problem analysis and building up motivation to change
Lesson 3: model of hypoglycemia perception and ''circulus vitiosus'' of impaired hypogylcemia awareness
Lesson 4: individual glycemic goals, fear of hypoglycemia and diabetic complications
Lesson 5: hypoglycemia in social context and coping with hypoglycemia in daily life
Lesson 6: goal attainment, feedback and strategies for maintaining behavior change

Table 2
Baseline characteristics of sample

	Baseline (t_0)				
	Controls ($N = 102$)		Intervention ($N = 105$)		
	M	S.D.	*M*	S.D.	
Age (years)	34.3	12.9	37.0	14.1	ns
Gender, *N* (%) male	41	40.2	41	39.0	ns
Duration of disease (years)	16.2	9.3	16.4	10.6	ns
HbA_{1c} (%)[a]	7.0	1.7	7.0	1.5	ns
Severe hypoglycemic episodes (number/12 months)[b]	1.33	4.5	1.4	4.7	ns
Hypoglycemia awareness (score)[c]	11.7	5.3	12.1	4.9	ns
Patients with hypoglycemia problems, *N* (%)	43	42.2	53	50.0	ns
Patients with diabetic complications, *N* (%)	44	43.1	41	39.0	ns

Shown as $M \pm$ S.D., if not stated otherwise; *t*-test or χ^2-test was performed; ns: not significant ($\alpha = 0.05$).
[a] Reference range $5.0 \pm 0.8\%$.
[b] Severe hypoglycemic events defined as hypoglycemia requiring intravenous glucose or intramuscular glucagon for treatment.
[c] Based on self-report (dichotomized visual analogue scale).

A total of $N = 102$ patients served as control group (CG) and received conventional patient education on the subject of hypoglycemia (two lessons, 45 min each). Lessons consisted of basic hypoglycemia-related knowledge (causes and treatment of hypoglycemia). Other than the hypoglycemia-specific lessons, other courses (e.g. on insulin therapy) and strategies of medical diabetes care were identical in the CG and IG. Baseline characteristics did not differ significantly between the groups (Table 2).

The lessons in both CG and IG were delivered by a postgraduate psychologist experienced in diabetes care and patient education.

2.4. Target criteria and measures

2.4.1. Primary target criteria

As primary target criteria, parameters directly related to hypoglycemia-related problems were chosen. The primary target criteria were assessed via questionnaire as well as clinical interviews (at t_1 via telephone) for verification. In case questionnaires were not returned at follow-up, phone interviews were also used to complete the dataset with regard to the primary target criteria.

A hypoglycemia-related problem was defined as the occurrence of severe hypoglycemia and/or impaired hypoglycemia awareness (assessed via self-report questionnaire). This combined definition was chosen in order to be able to identify patients with a history of ''manifesting'' severe hypoglycemia, which can be regarded as a clinical end point of impaired hypoglycemia awareness, as well as patients who are merely unaware of hypoglycemia.

Number of severe hypoglycemic episodes (coma, i.e. requiring intravenous glucose or intramuscular glucagon for treatment) were assessed by clinical interview retrospectively (12 months before treatment), and prospectively by questionnaire and verification via telephone interview. This verification method was chosen to further check for reliability of the patients' self-reports, as patients' reports are prone to be unreliable [26].

Hypoglycemia awareness was assessed via patients' self-report using a visual analogue scale (length: 18.5 cm; [27,28]). In addition to using the scale's raw score (0: totally absent awareness to 18.5: ''perfect'' hypoglycemia awareness), the score was dichotomised with patients with score in the lower third (score < 6.25) classified as having subjectively reported impaired hypoglycemia awareness.

As a marker for glycemic control, HbA_{1c} levels were assessed to ensure that a potential decrease in hypoglycemia was not associated with a deterioration in glycemic control. The baseline values are based on a high liquid pressure chromatography assay (A1CHA8140 HPLC, Menarini Diagnostics, Firenze, Italy, reference range in the non-diabetic population 4.2–5.8%), follow-up HbA_{1c} was assessed via patients' report and general practitioners' data, respectively.

2.4.2. Secondary target criteria

Secondary target criteria comprised psychological well-being, fear of hypoglycemia and late complications, and diabetes-specific control beliefs. Psychological well-being was operationalized using standardized depressiveness and anxiety measures (depression: Zerssen-d-Scale [29]; anxiety: State Trait Anxiety Inventory, state version [STAI-Trait] [30]). Data on fear of hypoglycemia and fear of late-diabetic complications were acquired, using visual analogue scales [4,14]. In the domain of health beliefs, diabetes-specific control beliefs were assessed with the IPC-D1 questionnaire. The IPC-D1 is a diabetes specific version of the IPC questionnaire [31], consisting of the four subscales ''internal control'' (range of scores: 8–48; higher scores reflecting higher levels of experienced control), ''external control'' (range of scores: 7–42), ''unpredictability'' (range of scores: 9–54), and ''luck and chance'' (range of scores: 5–30). Control beliefs and fear of hypoglycemia/late complications were included among the target criteria because of their probable association with impaired hypoglycemia awareness and severe hypoglycemia, e.g. in the sense of loss of control or a decrease of fear of hypoglycemia associated with a decrease in hypoglycemic events.

Table 3
Return at follow-up

	Controls ($N = 102$)		Intervention ($N = 105$)		
	M	S.D.	*M*	S.D.	
Follow-up (months)	6.75	3.2	6.51	3.5	ns
	N	%	*N*	%	
Follow-up completed					
Questionnaire	66	64.7	68	64.7	
Interview only	26	25.5	17	16.3	
Total	92	90.2	85	81.0	ns

2.5. Data analysis

Data analysis was performed using the software package Systat 10.2 (Systat, Chicago, IL, USA [32]). For analysis, χ^2-tests were to be used for the categorical first primary target criterion (occurrence of hypoglycemia-related problems). Descriptive logistic regression was to be performed to obtain a measure of the effect achieved (i.e. change in relative risk by receiving the intervention). Non-parametric procedures (Mann–Whitney *U*-tests between groups IG and CG on difference score $t_0 - t_1$; descriptive Wilcoxon tests for each group to test for t_0 versus t_1 changes) were to be employed for continuous parameters, because deviance from the normal distribution could be expected with the variables assessed. As the first primary target variable (occurrence of hypoglycemia-related problems) is considered to be the crucial criterion, α levels were set at 0.05 for all subsequent testing without adjustment for alpha inflation.

3. Results

3.1. Return

Follow-up data for the primary target criteria were obtained from 92 CG patients (90.2%) and 85 IG patients (81.0%) with a mean follow-up period of 6.75 ± 3.2 versus 6.51 ± 3.5 months (ns; Table 3).

3.2. Dropout analysis

To investigate a potential effect of selective dropout, hierarchical logistic regression was performed (criterion: dropout, coded as '1'). Two baseline parameters were included in the final model (log likelihood = −51.7; $p = 0.003$; MacFadden's $\rho^2 = 0.115$): baseline HbA_{1c} ($t = 3.04$; $p < 0.01$; OR = 1.76; CI: 1.22–2.53) and the subscale "luck and chance" of the IPC-D1 ($t = -1.66$, $p < .01$, OR = 0.85; CI: 0.77–1.02). This indicates a higher chance of participants with higher HbA_{1c} (i.e. "worse" glycemic control) to dropout, as well as patients with higher attributions of treatment outcome on "luck and chance" being more likely to respond to some degree. No further significant differences in any of the medical and psychosocial measures were observed using descriptive *t*-tests.

3.3. Primary target criteria

3.3.1. Hypoglycemia-related problems

Prevalence of hypoglycemia-related problems decreased in IG, whereas prevalence in CG remained constant (Table 4). At t_1, 24 IG patients (28.2%) who suffered from hypoglycemia-related problems at t_0, ceased to have problems, compared with 15 patients in CG (16.3%). Three IG patients (3.5%) developed problems during follow-up, whereas in CG there are 15 patients (16.3%) with newly manifested problems. Furthermore, exploratory logistic

Table 4
Prevalence of hypoglycemia-related problems, controls (panel a) vs. intervention (panel b), t_0 vs. t_1

		Hypoglycemia problem t_1				Total	%
		No, *N*	%	Yes, *N*	%		
(a) Controls ($N = 92$)							
Hypoglycemia problem t_0	No, *N* (%)	39	42.4	15	16.3	54	58.7
	Yes, *N* (%)	15	16.3	23	25.0	38	41.3
	Total, *N* (%)	54	58.7	38	41.3	92	100.0
(b) Intervention ($N = 85$)							
Hypoglycemia problem t_0	No, *N* (%)	41	48.2	3	3.5	44	51.8
	Yes, *N* (%)	24	28.2	17	20.0	41	48.2
	Total, *N* (%)	65	76.5	20	23.5	85	100.0

Hypoglycemia-related problems defined as occurrence of severe hypoglycemia and/or impaired hypoglycemia awareness (self-report, dichotomized analogue scale). t_0: baseline and t_1: 6-months follow-up. Mantel–Haenszel $\chi^2 = 5.45$; $p < 0.01$.

Table 5
Primary and secondary target criteria, intervention vs. control, t_0 vs. t_1

	Intervention ($N = 92$)				Controls ($N = 85$)				IG t_0 vs. t_1[a]	CG t_0 vs. t_1[a]	IG vs. CG[b]
	t_0		t_1		t_0		t_1		p	p	p
	M	S.D.	M	S.D.	M	S.D.	M	S.D.			
Hypoglycemia awareness (score)	12.0	4.8	11.7	5.1	11.5	5.6	10.0	4.7	ns	**	0.06
Severe hypoglycemic episodes with coma (number)[c]	1.1	4.5	0.1	0.5	1.3	4.5	0.9	5.3	**	ns	0.26
HbA_{1c} (%)	6.8	1.6	6.3	0.9	6.8	1.5	6.2	1.3	**	*	0.67
Depressive symptoms (score)[d]	7.9	6.1	6.8	6.1	6.5	6.2	7.9	6.8	ns	ns	0.09
Anxiety (score)[a]	36.5	10.1	38.1	11.5	36.2	8.5	36.5	10.5	ns	ns	0.83
Control beliefs (score)[d]											
Internal control	38.4	7.0	38.2	5.7	37.7	6.0	38.7	7.1	ns	**	0.12
External control	23.1	7.1	21.7	8.2	22.5	7.0	19.5	7.4	ns	**	0.26
Unpredictability	26.7	7.7	28.1	7.8	25.2	8.1	24.4	8.2	ns	*	0.41
Luck and chance	7.9	3.3	8.8	4.3	7.8	4.0	7.5	3.4	ns	**	0.43
Fear of hypoglycemia (score)[d]	6.0	6.1	5.3	3.9	5.1	4.2	4.3	3.7	ns	*	0.83
Fear of diabetic complications (score)[d]	13.5	2.5	8.2	3.9	13.9	1.6	9.8	5.2	**	**	0.17

IG: intervention group; CG: control group; ns: not significant ($\alpha = 0.05$); t_0: baseline; t_1: 6 months follow-up.
[a] Significance testing based on Wilcoxon tests, t_0 vs. t_1, within each group.
[b] Significance testing based on Mann–Whitney U-tests on difference scores between groups, t_0 vs. t_1.
[c] Data on number of severe hypoglycemia at t_2 (6-months follow-up) are extrapolated for 12 months in order to be comparable to t_0 data (12 months retrospective assessment).
[d] Questionnaire data based on reduced data set (see Table 3).
* $p < 0.05$.
** $p < 0.01$.

regression reveals a significant relative risk reduction to suffer from hypoglycemia problems at t_1 for IG ($t = -2.492$; $p = 0.013$; OR = 0.437; CI: 0.228–0.838; controls coded as '0').

3.3.2. Hypoglycemia awareness

Hypoglycemia awareness remained constant in IG, whereas some deterioration was observed in CG (Table 5).

3.3.3. Severe hypoglycemia

There was a marked decrease in the number of severe hypoglycemia in the IG. No difference between-group effects were observed (Table 5).

3.3.4. Glycated hemoglobin (HbA_{1c})

HbA_{1c} decreased significantly in both groups, indicating an improvement in glycemic control, with no differences between IG and CG (Table 5). There is no evidence for deterioration of glycemic control in IG, thus, a reduction in hypoglycemia cannot be attributed to the fact, that by avoiding hypoglycemic episodes glycemic control deteriorated in IG.

3.4. Secondary target criteria

Neither between nor within-group effects with regard to psychological well-being (depression, anxiety) were observed (Table 5). Control beliefs only changed in CG significantly towards more internal control, less external control, less unpredictability and less ''luck and chance'' with no significant between-group effects. Fear of diabetic complications decreased significantly in both groups, fear of hypoglycemia only in CG with no between-group effects in both measures. Control beliefs, anxiety, and depression were within the published norms.

4. Discussion and conclusion

4.1. Discussion

In this observational controlled pre-post study, the effects of a self-management-based intervention program on hypoglycaemia-related problems were compared with standard patient education. A benefit of the self-management-based intervention could be observed with regards to the target criteria severe hypoglycemia and hypoglycemia-related problems without a deterioration of glycemic control observable. These results are in line with the results published on Blood Glucose Awareness Training [20,22]. The dropout analysis suggested the dropout observed was not selective with regard to this target criterion. Patients with higher HbA_{1c} levels being more likely to dropout infact might suggest that the treatment effect is underestimated, because high HbA_{1c} levels as opposed to tight glycemic control are associated with a lower risk of hypoglycemia [2], the dropouts not differing from the patients who completed follow-up with regard to any other measures at baseline.

The results also suggest a potential preventive effect of the program, in addition to ameliorating hypoglycemia-related problems: in the intervention group only three participants manifested a hypoglycemia-associated problem

during follow-up, compared with 15 patients in the control group. The possible preventive effect clearly warrants further research, as momentarily hypoglycemia-specific interventions rather focus on patients that have already manifested problems or experienced severe hypoglycemia, especially when taking into consideration the substantial morbidity and health-care cost (e.g. emergency care) caused by severe hypoglycemia.

No effects with regard to the secondary target criteria (well-being, fear of hypoglycemia and late complications, control beliefs) were observable. This could be explained by the lower return rate in case of these criteria relying merely on questionnaires. Hence, the results on secondary target criteria have to be interpreted with caution. The results presented here do not allow for hypotheses on how the observed effects for the primary criteria were achieved—e.g. they cannot be attributed to a change in health-care beliefs. Interestingly, fears of hypoglycemia and diabetic complications decrease in both groups, which could possibly be due to the fact of knowledge transfer and optimization of insulin regimens resulting in more stable glycemic control in both groups. Concerning the controls, this is in line with the observed changes in control beliefs. One has to keep in mind, though, that significance test on secondary target criteria measure are descriptive in nature.

Some methodical limitations have to be considered, though, especially concerning validity of the results. The interventions took place in an inpatient care setting (specialised hospital for diabetes mellitus), where the amount of patients with ''problematic'' diabetes and multiple late-diabetic complications can be assumed to be higher compared to the general diabetic population. Especially, the rate of patients with hypoglycemia-associated problems was high. Thus, the possibility for transfer of the results obtained in an inpatient setting to ambulatory care settings has to be discussed (e.g. with regard to outpatient care, contact and density of lessons usually is lower for logistics reasons and patient education programs rather have curricula distributing lessons over several weeks). Regarding internal validity of the results, it has to be mentioned that the patients were not randomized to treatment conditions. Furthermore, all the patients underwent a major change in insulin therapy, i.e. the transferral to insulin pump treatment. Thus, the effects of the intervention are possibly confounded with the effects of the change in insulin regimen. As well, it cannot be ruled out that the observed beneficial effect of the new intervention was – at least partly – due to the intervention's intensity, i.e. duration, the controls receiving sessions for one third of the time spent with the intervention group.

On the other hand, with hypoglycemia being a major obstacle for achieving durably near-normal glycemic control in type 1 diabetes, a self-management-based program could offer a substantial contribution, giving opportunities of treatment as well as prevention of hypoglycemia problems, though a randomized study should be carried out for further investigation to gain further evidence.

4.2. Conclusion

The results suggest the new intervention program is an effective treatment, though no evidence was found for the underlying mechanisms leading to a reduction in the prevalence of hypoglycemia-associated problems, e.g. a shift in control beliefs towards more internal control or more predictability could not be observed here. The effectiveness should be confirmed, however, in a randomized controlled trial also incorporating outpatient settings, e.g. comparing the new program with other specific interventions like the Blood Glucose Awareness Training.

4.3. Practice implications

Hypoglycemia-related problems and impaired hypoglycemia awareness are a common condition in insulin-treated diabetes mellitus, when trying to achieve near-normal glycemic control. Structured education and intervention based on a self-management-based approach targeting the patients' health beliefs and attitudes towards hypoglycemia and their diabetes self-management, rather than conventional knowledge-centered patient education, can help to ameliorate or even prevent hypoglycemia-associated problems.

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