

Health and Disability

Identification of risk factors for suffering fear of hypoglycemia in type 1 Diabetes Mellitus patients

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Hypoglycemia is one of the main burdens for type I Diabetes Mellitus (DM I) patients. The consequences of hypoglycemia can be quite unpleasant due to the variety of disagreeable physical and psychological symptoms it triggers. The patient's previous experience with hypoglycemia episodes will condition his psychological reaction to future episodes, promoting behavioral modifications that associate with poor glycemic control and worse prognosis, and even with developing psychological disorders, leading to fear of hypoglycemia (FH). To be able to provide tailored prevention and treatment of patients with FH it is necessary to identify the risk factors in DM I patients. We developed and validated the FH-15 scale, a novel instrument to assess FH, which showed good concurrent and predictive validity in DM I patients. In this work we aim to identify the risk factors for suffering FH by detecting DM I patients with FH using the FH-15 scale and then analyzing the association of clinical and sociodemographic variables. We found that age, needing help to resolve an episode of hypoglycemia, and a perceived lack of social support are risk factors for suffering FH.

Key words: Fear, hypoglycemia, type 1 Diabetes Mellitus, risk factors.

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INTRODUCTION

Hypoglycemia is one of the main burdens of type I Diabetes Mellitus (DM I) (Davis & Alonso, 2004). The consequences of hypoglycemia can be quite unpleasant due to the variety of disagreeable and potentially life threatening physical and psychological symptoms it triggers (Wild, von Maltzahn, Brohan, Christensen, Clauson & Gonder-Frederick, 2007). The patient's previous experience with hypoglycemia episodes will condition his/her psychological reaction to future episodes. Indeed, it has been recently shown by Sheu, Ji, Nitiyanant *et al.* (2012) that DM I patients who suffered severe episodes had an increased risk of developing fear of hypoglycemia (FH). Moreover, psychological reaction can promote behavioral modifications leading to low therapeutic adherence and contraindicated nutritional habits. These behavioral modifications are associated with poor glycemic control and worse prognosis, and even with the development of psychological disorders in these patients (Böhme, Bertin, Cossan, Chevalier & GEODE Group, 2013). Although several studies have been carried out in patients suffering FH, its correlation with some clinical and demographic variables is still unclear (Hartung, Reise, Kloos, Müller, Wolf & Müller, 2010) and has delayed the elaboration of useful strategies for prevention and treatment of FH. We developed and validated the FH-15 scale, a novel instrument to assess FH that showed good concurrent and predictive validity (Anarte, Caballero, Ruiz de Adana *et al.*, 2011). This scale is a useful tool to identify DM I patients with FH who could be provided with personalized treatment for their fear. In this work

we aim to identify the risk factors for FH in DM I patients by applying the FH-15 scale to detect patients with FH and then analyzing the association of clinical and sociodemographic variables.

METHODS

Sample

We recruited 250 outpatients with DM I who attended the Diabetes Unit, Endocrinology and Nutrition Department, Hospital Regional Universitario, Malaga (Spain). Ethical approval was obtained from the Research and Ethics Committee of Carlos Haya Regional University Hospital, Malaga (Spain).

Inclusion criteria were: DM I diagnosis with greater than one year evolution, over 18 years of age, not pregnant, no disabling mental illness, reading and writing skills and written consent to participate in the study. Patients who did not fulfill these criteria were excluded from the study.

We performed a prospective study of 229 patients. The mean age was 34.60 (\pm 11.02) years and the mean diabetes duration was 16.11 (\pm 10.05) years. Patients were treated with multiple daily injection (MDI) therapy, continuous subcutaneous insulin infusion (CSII) or sensor augmented pump therapy with paradigm real time in 67.7%, 26.6% and 5.7% respectively. A detailed description of the sample is shown in Table 1.

Measures

The sociodemographic variables were assessed through a structured interview that included age, gender, marital status, education level and subjective support regarding diabetes in the following areas: family, partner, friends, workplace and health care provider. The latter variable was collected with the question: *Do you feel supported regarding your diabetes? If yes, specify by whom.*

Table 1. Demographic and clinical characteristics (n = 229)

Variables	Mean ± SD	%
Gender		
Men		42.36
Women		57.64
Age		
Age of the participants	34.60 ± 11.02	
Age at diagnosis of diabetes	18.48 ± 10.47	
Diabetes duration (years)	16.11 ± 10.05	
Frequency of hypoglycemic episodes previous week (n = 144)	2.36 ± 2.49	
Hypoglycemic episodes previous week (n = 144)		
Yes		78.5
No		21.5
HbA _{1c} (%) (n = 165)	7.45 ± 1.27	
HbA _{1c} (mmol/mol) (n = 165)	58 ± 10	
Daily self-monitoring controls of blood glucose	4.58 ± 1.93	
Diabetes Treatment		
MDI		67.7
CSII		26.6
Sensor augmented pump therapy with paradigm real time		5.7
FH-15 scale	27.88 ± 9.66	
Fear yes (≥ 28)		45.4
No (< 28)		54.6
Marital status		
Single		44.5
Married		47.2
Separated		3.1
Divorced		3.5
Widowed		1.3
Educational level		
Basic (reading and writing)		2.6
Primary school studies		35.8
High school studies		21.8
Vocational training		10
Undergraduate degree		13.1
Graduate degree		16.6

The clinical data collection was conducted through a structured script completed by the physician during the medical check-up. The variables were: diabetes duration (years); type of diabetes treatment, glycemic control (HbA_{1c}); frequency of hypoglycemic episodes in the previous week; whether the patient often perceived diabetes hypoglycemia (always/not always); help needed to overcome an episode of hypoglycemia in the previous 6 months (yes/no); number of hypoglycemic episodes requiring help in the previous 6 months; and daily self-monitoring controls of blood glucose.

Glycemic control was expressed as HbA_{1c} levels measured by high performance liquid chromatography (HPLC) using Kyoto Daiichi Kagaku equipment. It was recoded as a qualitative variable as *Good* (HbA_{1c} < 7%) or *Bad* (HbA_{1c} > 7%).

Patients with FH were identified with the fifteen-item scale (FH-15) as in Anarte *et al.* (2011). The scale registers 15 negative items measured on a five-point Likert scale (1-5) and three factors (Fear, Avoidance and Interference) yielding a total score ranking from 15 to 75. High FH-15 scores are associated with FH. The cut-off score was set at 28 and patients with a score equal to or greater than 28 were classified as *suffering FH*.

The participants were free to ask the psychologist questions about the scale items.

Procedure

Recruitment occurred during the first trimester of 2009. Physicians informed the patients about the study during their check-up and those who agreed to participate followed the nurse to an office next door

where the psychologist proceeded with the study. Patients participated voluntarily, completed the questionnaire after signing the informed consent and were not compensated by any means.

Physicians recorded clinical variables through a structured script during the check-up. Psychologists recorded the sociodemographic variables and data to complete the FH-15 scale through a structured interview.

Statistical analysis

Statistical analysis was performed using SPSS 17.0 for Windows (Chicago, IL: SPSS). Descriptive statistics were used to characterize the sample. To analyze correlations among variables, Pearson's correlation coefficient was applied. Significance was found using the unpaired *t*- and ANOVA tests when two or more than two groups were compared, respectively, with a CI of 95%. Logistic regression analysis was performed to calculate the odds-ratio (OR) to analyze the correlation among FH (or *not suffering* FH) as the dependent variable and the clinical and sociodemographic variables.

To identify risk factors for FH, a categorical (demographic or clinical) variable was considered to be the independent variable. In addition, a multivariate adjusted logistic regression analysis was performed with FH as the dependent variable and the previously identified risk factors as the independent variables (age was recoded as ≤ 40 or > 40 years).

RESULTS

The analysis of correlation among continuous variables and FH by Pearson's correlation coefficient and *t*- and ANOVA tests showed correlation only for the variables *number of hypoglycemic episodes needing help from others* and *daily self-monitoring controls of blood glucose* (Table 2). Moreover, we found that FH correlates with age >40 years, *Good* glycemic control, *number of hypoglycemic episodes needing help from others*, *help needed to overcome an episode of hypoglycemia in the previous 6 months* and *more than 5 daily self-monitoring controls of blood glucose*. Interestingly, we found that FH correlates with female gender and, in addition, with not always *perceiving hypoglycemia*, and with no support from friends, workplace or health-care provider (Table 3).

The logistic regression analysis to identify risk factors for suffering FH showed that *age* (both as a continuous and a categorical variable), *needing help to resolve an episode of hypoglycemia in the previous six months*, or *not perceiving social support from family, friends or health care provider* are risk factors (Table 4). We next performed a multiple adjusted logistic regression analysis with the variables *needing help to resolve an episode of*

Table 2. Correlations between observed continuous variables and the FH-15 scale

	n	Correlation	
		R	p
Age	229	0.103	0.119
Diabetes duration (years)	229	0.065	0.326
Frequency of hypoglycemic episodes previous week (number of episodes)	144	0.080	0.339
HbA _{1c}	165	-0.031	0.695
Number of hypoglycemic episodes needing help from others	229	0.172	0.009**
Daily self-monitoring of blood glucose	229	0.254	< 0.001**

Note: **p < 0.01.

Table 3. Differences in observed variables using the FH-15 scale

	Score on the FH-15		
	Mean ± sd	n	p
Gender			
Male	25.505 ± 7.919	97	0.001**
Female	29.628 ± 10.457	132	
Age			
> 40 years old	30.043 ± 10.579	70	0.024*
≤ 40 years old	26.931 ± 9.106	159	
Time with diabetes			
< 10 years	26.803 ± 9.374	72	0.507
10–20 years	28.141 ± 8.709	71	
> 20 years	28.570 ± 10.686	86	
Frequency of hypoglycemic episodes previous week (number of episodes)			
Hypoglycemia Yes	28.283 ± 9.839	113	0.861
Hypoglycemia No	27.936 ± 9.504	31	
Diabetes treatment			
MDI	28.019 ± 9.574	155	0.186
CSII	26.656 ± 9.544	61	
Sensor augmented pump therapy with paradigm real time	32.000 ± 10.801	13	
HbA _{1c} < 7%	29.397 ± 10.809	63	0.048*
HbA _{1c} ≥ 7%	26.294 ± 7.520	102	
Help needed to overcome an episode of hypoglycemia in the previous 6 months			
Yes	32.254 ± 10.719	55	< 0.001**
No	26.600 ± 8.901	174	
Number of hypoglycemic episodes needing help from others			
None	26.710 ± 9.124	176	0.003**
One	30.667 ± 9.412	24	
Two or more	32.690 ± 11.327	29	
Perceive hypoglycemia			
Always	26.703 ± 9.043	155	0.007**
Not always	30.351 ± 10.493	74	
Family support			
Yes	27.514 ± 9.575	210	0.055
No	31.947 ± 9.980	19	
Partner support			
Yes	27.248 ± 8.899	149	0.176
No	29.062 ± 10.910	80	
Friends' support			
Yes	23.775 ± 9.215	169	0.003**
No	31.000 ± 10.284	60	
Workplace support			
Yes	26.672 ± 9.038	122	0.043*
No	29.262 ± 10.200	107	
Health care provider support			
Yes	26.694 ± 8.633	183	0.003**
No	32.609 ± 11.968	46	
Daily self-monitoring			
More than 5 times	29.981 ± 10.570	88	0.009**
Up to 5 times	26.570 ± 8.841	141	

Note: * $p < 0.05$; ** $p < 0.01$.

hypoglycemia in the previous six months and not perceiving social support from family, friends or health care provider, adjusting the model for the two age categories (≤ 40 or > 40 years). As shown in Table 5, the risk factors for suffering FH varied according to age. In patients 40 years old or younger the risk factor for suffering FH was the perception of lack of support from friends, whereas in those older than 40 years, both the perception of lack of family support and the need for help to

Table 4. Risk factors for suffering fear of hypoglycemia in the sample analyzed

Variable (possible risk category)	n	OR	OR (95% CI)	p
Gender (Female)	229	1.443	0.849–2.452	0.175
Age (year)	229	1.030	1.005–1.056	0.016*
Age (> 40 years old)	229	2.347	1.321–4.169	0.004**
Diabetes duration (years)	228	1.015	0.989–1.042	0.250
Frequency of hypoglycemic episodes previous week	144	1.034	0.906–1.180	0.618
Hypoglycemia (Yes)	144	1.344	0.606–2.980	0.467
Diabetes treatment (Sensor augmented pump therapy with paradigm real time)	229	2.866	0.856–9.592	0.088
HbA _{1c}	165	1.079	0.846–1.376	0.541
Glycemic control (HbA _{1c} ≥ 7%)	165	1.475	0.784–2.774	0.228
Help needed to overcome an episode of hypoglycemia in the previous 6 months (Yes)	229	2.663	1.421–4.989	0.002**
Number of hypoglycemic episodes needing help from others	229	1.102	0.943–1.288	0.221
Perceive hypoglycemia (Not always)	229	1.673	0.958–2.922	0.071
Family support (Not perceived)	229	2.833	1.037–7.741	0.042*
Partner support (Not perceived)	229	1.053	0.610–1.817	0.852
Friends' support (Not perceived)	229	2.449	1.338–4.484	0.004**
Workplace support (Not perceived)	229	1.467	0.869–2.476	0.151
Health care provider support (Not perceived)	229	2.190	1.131–4.242	0.020*
Daily self-monitoring of blood glucose	229	1.077	0.938–1.235	0.292

Note: * $p < 0.05$; ** $p < 0.01$.

resolve an episode of hypoglycemia in the previous 6 months were the risk factors.

Of the whole study sample, 45.4% (95% CI: 38.9–51.9) experienced fear of hypoglycemia (as measured with the FH-15 scale), and 78.5% (95% CI: 71.7–85.3) of the 144 patients evaluated for the number of weekly hypoglycemia episodes had had an episode of hypoglycemia the week before the study.

DISCUSSION

The repercussions of FH on both the evolution of the disease and the psychosocial status of DM I patients have been clearly shown in previous works. However, the risk factors for suffering such fear remain unclear (Andebro, Amsberg, Adamson *et al.*, 2010; Beléndez & Hernández-Mijares, 2009). This study considered two main objectives with the aim of following up on those works: to find empirical evidence of the association between FH and some sociodemographic and clinical variables, and to identify the risk factors for FH in DM I patients.

We found that FH correlates with an age of >40 years, Good glycemic control, having had hypoglycemic episodes needing help from others and more than 5 daily self-monitoring

Table 5. Risk factors for suffering fear of hypoglycemia in the multivariate analysis ($n = 229$)

Variable (possible risk category)	≤ 40 years old			> 40 years old		
	OR	OR (95% CI)	<i>p</i>	OR	OR (95% CI)	<i>p</i>
Help needed to overcome an episode of hypoglycemia in the previous 6 months (Yes)	2.086	0.966–4.504	0.061	5.548	1.394–22.091	0.015*
Family support (not perceived)	6.059	0.560–65.521	0.138	5.742	1.127–29.245	0.035*
Friends' support (not perceived)	2.237	1.045–4.788	0.038*	1.834	0.529–6.358	0.339
Health care provider support (not perceived)	1.551	0.628–3.832	0.341	2.932	0.650–13.217	0.161

Note: * $p < 0.05$.

controls of blood glucose. In addition, FH correlates with female gender. Finally several risk factors for suffering FH were identified: the perceived lack of social support and the need for help to overcome a hypoglycemic episode in patients over 40 years of age.

The results of this work identify two risk profiles that will enable clinicians to design prevention and treatment protocols according to the characteristics of the patients with each profile. The relevance of the perception of social support for these patients is one of the main contributions of this study. The perception of social support is an important variable to consider at the onset of FH in DM I patients and should be tackled in the therapy programs according to the patient's profile as shown in Table 4.

These results should be useful tools to elaborate and implement prevention and treatment programs. Further research will be needed to analyze the impact of these programs on the disease progression, well-being and psychosocial status of DM I patients.

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