Assessment of hypoglycemic symptoms in insulin-treated adults with diabetes mellitus

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Background

Diabetes mellitus (DM) is a chronic endocrine disorder that is characterized by hyperglycemia as a result of insulin deficiency (type 1) or insulin resistance (type 2). Insulin is used for type 1 DM and it can be used for type 2 DM in addition to oral hypoglycemic medications. Appropriate insulin regimens along with life style modifications should maintain a state of euglycemia with minimal hyperglycemic or hypoglycemic episodes to protect from the development of diabetic complications. Hypoglycemia is considered more severe than hyperglycemia as the former enhances the release of glucagon and other counter regulatory hormones resulting in acute sympathetic and neuroglycopenic symptoms that may lead to coma. Fortunately, patients can feel these symptoms and thus self-treat themselves by taking a source of sugar. Adversely, frequent episodes of hypoglycemia may decrease the recognition of the hypoglycemic symptoms resulting in a condition called Impaired Awareness of Hypoglycemia (IAH).

Aims

To assess the frequency of hypoglycemic episodes, awareness of hypoglycemic symptoms, intensity of hypoglycemic symptoms, and the association between level of hypoglycemic awareness and other measurements including type of DM, duration of DM, duration of insulin therapy, and frequency of hypoglycemia among insulin-treated diabetic adults.

Methods

Study design. Insulin-treated type 1 and type 2 DM patients were recruited from the diabetic clinic of King Abdullah University Hospital in Jordan. Patients who were on oral hypoglycemic medications were excluded from the study. Patients were asked to report the number of their hypoglycaemic episodes in the past month and 6 months. The intensity of hypoglycemic symptoms was assessed using the validated Edinburgh hypoglycemia survey [1] and the awareness of hypoglycemia was assessed using Clarke's hypoglycemia survey [2].

Statistical analysis. Statistical analysis was performed using IBM SPSS statistics version 20 (Armonk, New York, USA). Data were expressed as number of participants (%), mean $\pm$ standard deviation (SD) or median (25th – 75th percentiles) as appropriate. Differences in qualitative variables were determined using Chi-square test or Fisher's exact test as appropriate (p-values < 0.05 were considered statistically significant).

Results

Data were collected from 410 insulin-treated adults (94.6% type 2 and 5.4% type 1 DM) from both genders (46.6% males and 53.4% females) with an average ($\pm$ SD) age of 57.63 ($\pm$ 13.45) years. The average ($\pm$ SD) duration of DM was 14.78 ($\pm$ 7.36) years, the median (25th-75th percentiles) duration of insulin therapy was 4.0 (2.0-7.0) years, and the average ($\pm$ SD) of glycated hemoglobin (HbA1c) was 9.32% ($\pm$ 2.17%).

Table 1: Patients' characteristics

Variable	Value
Type of DM	
Type 1	22 (5.4)
Type 2	388 (94.6)
Age (Years)	57.63 $\pm$ 13.45
Gender	
Male	191 (46.6)
Female	219 (53.4)
BMI	30.28 $\pm$ 5.37
Level of education	
Not educated	58 (14.1)
Primary school	118 (28.8)
Secondary school	154 (37.6)
High university education	80 (19.5)
Number of family members	5.0 (3.5-6.0)
Average family income (JD)	
$\leq$ 500	328 (80)
> 500	82 (20)
Duration of DM (Years)	14.78 $\pm$ 7.36
Duration of insulin therapy (Year)	4.0 (2.0-7.0)
HbA1c (%)	9.32 $\pm$ 2.17

Data are presented as number of participants (%), mean $\pm$ standard deviation (SD) or median (25th – 75th percentiles) as appropriate

48.8% of participants did not develop any hypoglycemic episode that was associated with hypoglycemic symptoms during the last month while 42.2%, 3.2%, 3.9% and 2% of them had developed 1-3 hypoglycemic episodes, one hypoglycemic episode weekly, 2-3 hypoglycemic episodes weekly and 4-5 hypoglycemic episodes weekly, respectively.

Figure 1: Frequency of blood glucose measurement < 70 mg/dL during the last month with symptoms

Results

According to Clarke's hypoglycemia survey, 81% of participants were classified as being aware of hypoglycemic symptoms and 19% were classified as having impaired awareness of hypoglycemia.

Figure 2: Level oh hypoglycemic awareness defined by Clarke's method

Level of hypoglycemic awareness was significantly dependent on the type of DM, body mass index (BMI), duration of DM, duration of insulin therapy and frequency of hypoglycemia during the past 6 months.

Table 2: Dependence of hypoglycemia awareness on different variable

	Aware (n= 332)	Reduced awareness (n= 78)	P-value*
Type of DM			
Type 1	10 (3.0)	12 (15.4)	0.00
Type 2	322 (97.0)	66 (84.6)	
Gender			
Male	151 (45.5)	40 (51.3)	0.38
Female	181 (54.5)	38 (48.7)	
BMI			
Normal (18.5-25)	46 (13.9)	23 (29.5)	0.00
Overweight (25-30)	123 (37.0)	22 (28.2)	
Obese (> 30)	163 (49.1)	33 (42.3)	
Level of education			
Not educated	51 (15.4)	7 (9.0)	0.01
Primary school	104 (31.3)	14 (17.9)	
Secondary school	112 (33.7)	42 (53.8)	
High university education	65 (19.6)	15 (19.2)	
Average family income (JD)			
$\leq$ 500	269 (81.0)	59 (75.6)	0.35
> 500	63 (19.0)	19 (24.4)	
Duration of DM (Year)			
1-5 years	43 (13.0)	2 (2.6)	0.01
6-10 years	82 (24.7)	27 (34.6)	
> 10 years	207 (62.3)	49 (62.8)	
Duration of insulin therapy (Year)			
< 1 year	19 (5.7)	7 (9.0)	0.046
1-5 years	221 (66.6)	39 (50.5)	
6-10 years	59 (17.8)	20 (25.6)	
> 10 years	33 (9.9)	12 (15.4)	

* Chi-square test or Fisher's exact test as appropriate (p-values < 0.05 were considered statistically significant)

Sweating, drowsiness, weakness, hunger, tiredness and trembling were the most common symptoms of hypoglycemia that were usually felt by participants when they develop hypoglycemia (median Edinburgh intensity score was 6 for all of these symptoms).

Table 3: Intensity of Hypoglycemic symptoms measured by Edinburgh survey

Hypoglycemic symptoms	Edinburgh intensity of symptom (n= 410)	Hypoglycemic symptoms	Edinburgh intensity of symptom (n= 410)
Confusion	4 (2-6)	Blurred vision	3.5 (1-6)
Sweating	6 (5-7)	Hunger	6 (5-7)
Drowsiness	6 (5-7)	Nausea	1 (1-2)
Weakness	6 (5-7)	Anxiety	1 (1-3)
Dizziness	2 (1-6)	Tiredness	6 (5-6)
Warmth	2 (1-4)	Tingling lips	1 (1-4)
Difficulty in speaking	2 (1-3)	Trembling	6 (5-7)
Pounding heart	2 (1-5)	Headache	2 (1-6)
Inability to concentrate	3 (1-5)		

Data are expressed as median (25th-75th percentiles)

Discussion

This study has reported high prevalence of hypoglycemic awareness (81%) among insulin-treated diabetic adults. This is supported by the development of hypoglycemia that was associated with symptoms by around 50% of participants during the last month. Analysis of hypoglycemic symptoms intensity suggests that participants can recognize hypoglycemic episodes by feeling sweating, drowsiness, weakness, hunger, tiredness and trembling. The dependence of hypoglycemic awareness on the frequency of hypoglycemia suggests that the level of awareness may decrease when frequency of hypoglycemia is increased.

References

- [1] Price, J., Reynolds, R., Mitchell, R., Williamson, R., Fowkes, F., Deary, I., Lee, A., Frier, B., Hayes, P. and Strachan, M. (2008). The Edinburgh Type 2 Diabetes Study: study protocol. *BMC Endocrine Disorders*, 8(1), p.18.
- [2] Clarke, W., Cox, D., Gonder-Frederick, L., Julian, D., Schlundt, D. and Polonsky, W. (1995). Reduced Awareness of Hypoglycemia in Adults With IDDM: A prospective study of hypoglycemic frequency and associated symptoms. *Diabetes Care*, 18(4), pp.517-522.