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Original article

Psychometric analysis of the Spanish and Catalan versions of a questionnaire for hypoglycemia awareness[☆]

Marga Jansa [a], Carmen Quirós [a], Marga Giménez [a], Merce Vidal [a], Mercedes Galindo [b], Ignacio Conget [a],*

[a] Unidad de Diabetes, Servicio de Endocrinología y Nutrición, Hospital Clínic i Universitari de Barcelona, Universitat de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Barcelona, Spain
[b] Servicio de Endocrinología y Nutrición, Hospital Clínico San Carlos, Madrid, Spain

ABSTRACT

Background and objective: Intensive insulin therapy with multiple insulin doses in subjects with type 1 diabetes mellitus (T1D) is associated with a higher risk of hypoglycaemic episodes. Repeated hypoglycemia results in a reduced ability/failure to recognise hypoglycemia symptoms and predisposes to severe episodes. In this context, it is crucial to work with specific questionnaires to diagnose and address this burden. Our study aimed to perform the psychometric analysis of Spanish and Catalan versions of Clarke et al. questionnaire for hypoglycemia awareness.
Patients and method: Psychometric analysis in patients with T1D of Spanish and Catalan versions of Clarke et al. questionnaire in three phases: (1) translation, back-translation and cultural adaptation of the English version; (2) analysis of internal, external and test–retest validity, and (3) assessing sensitivity to change in hypoglycemia perception.
Results: One-hundred and forty-four subjects with T1D answered the Clarke et al. questionnaire (mean age [SD] 36 [18] years, 46% men). We observed a Cronbach's α coefficient for internal validity of 0.75, a correlation coefficient for test–retest reliability of $r = 0.81$ and a correlation of the questionnaire score with the frequency of severe and no severe hypoglycemia events of $r = 0.47$ and $r = 0.77$, respectively. The analysis of 20 patients with T1D 24 months after the initiation of continuous subcutaneous insulin infusion showed a decrease in the frequency of non-severe hypoglycemia/week (from 5.40 [2.09] to 2.75[1.74]) and in the number of severe hypoglycaemic episodes/year (1.25 [0.44] to 0.05 [0.22]). This was associated with a decrease in scores of the translated versions of Clarke et al. questionnaire (from 5.45 [1.19] to 1.60 [2.03]).
Conclusions: Spanish and Catalan versions of Clarke et al. questionnaire display good psychometric properties and both could be considered a useful tool for evaluating hypoglycemia awareness in patients with T1D from our area.

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Análisis psicométrico de las versiones en lengua castellana y catalana de un cuestionario de percepción de la hipoglucemia

RESUMEN

Fundamento y objetivo: El tratamiento intensivo con múltiples dosis de insulina de los pacientes con diabetes mellitus tipo 1 (DT1) se asocia con la aparición de hipoglucemias. Su recurrencia condiciona la pérdida progresiva de los síntomas asociados a las mismas y predispone a la aparición de episodios graves. Es importante disponer de cuestionarios específicos y validados para identificar a los pacientes con este problema. Con este objetivo se realizó el análisis psicométrico de las versiones castellana y catalana del cuestionario de Clarke et al. destinado a valorar la percepción de hipoglucemias.

Pacientes y método: Análisis psicométrico en pacientes con DT1 de las versiones en castellano y catalán del cuestionario de Clarke et al. en 3 fases: 1) traducción, retrotraducción y adaptación cultural de la versión en inglés; 2) análisis de la consistencia interna, validez de constructo y test-retest del mismo, y 3) análisis de su sensibilidad al cambio en la percepción de hipoglucemias.

Resultados: Ciento cuarenta y cuatro pacientes con DT1 contestaron los cuestionarios en lengua castellana o catalana, según preferencias (edad media [DE] de 36 [18] años, 46% varones). Se obtuvo un coeficiente α de Cronbach para la consistencia interna de 0,75, un coeficiente de correlación para la fiabilidad test-retest de r = 0,81 y una correlación de la puntuación del cuestionario con la frecuencia de hipoglucemias no graves y graves de r = 0,47 y r = 0,77, respectivamente. El análisis de 20 pacientes con DT1 durante 24 meses tras el inicio de infusión subcutánea continua de insulina mostró una disminución de la frecuencia de hipoglucemias no graves/semana (de una media de 5,40 [2,09] a 2,75 [1,74]), así como del número de episodios de hipoglucemia grave/año (de una media de 1,25 [0,44] a 0,05 [0,22]). Esta reducción se asoció con una mejora en la percepción de la hipoglucemia, con una disminución de la puntuación del cuestionario de Clarke et al. (de 5,45 [1,19] a 1,60 [2,03]).

Conclusiones: Las versiones en lengua castellana y catalana del cuestionario de Clarke et al. tienen buenas características psicométricas y pueden ser un instrumento útil para evaluar la presencia de hipoglucemia desapercibida en pacientes con DT1 de nuestro entorno.

Introduction

Currently, intensive therapy using multiple insulin doses is the standard treatment for patients with type 1 diabetes (T1D) following diagnosis of the disease.[1,2] However, it is not free from secondary effects. One of the most important of these is its association with a three- or fourfold increase in incidence of non-serious and serious hypoglycaemia, as reported elsewhere.[1,3] In fact, this is now the principle side effect of this treatment and the main obstacle to its implementation in these patients.[4,5]

For as yet unknown reasons, in some patients recurrent episodes of non-serious hypoglycaemia condition the progressive loss of physiological, adrenergic and neuroglycopenic symptoms of response to an episode of hypoglycaemia.[6,7] In patients with T1D, episodes of so-called unnoticed or unseen hypoglycaemia multiply the risk of serious hypoglycaemia. Some studies have shown that abnormal perception of hypoglycaemia can lead to a sixfold increase in the risk of having an episode of this type.[8,9] Hence, in clinical practice, the use of specific questionnaires—validated in both the Spanish and Catalan languages—is essential if we are to identify patients with unnoticed hypoglycaemia.[9–11]

The objective of the present study was to conduct a psychometric analysis of the Spanish and Catalan versions of the Clarke et al. questionnaire to assess awareness of hypoglycaemia in patients with T1D.

Materials and methods

We chose the Clarke et al. questionnaire because it had already been validated in Spanish and Catalan.[10] It consists of eight questions about the patient's perception of hypoglycaemia, the frequency of serious and non-serious episodes, and the blood sugar level thresholds at which the patient experiences symptoms. Each answer is classified as normal (A) or abnormal (R). The total sum of R responses determines the level of awareness of hypoglycaemia: 1–2R = normal; 3R = indeterminate; >3R = abnormal. We requested and obtained authorisation to use the questionnaire from the authors of the English language version.

Our psychometric analysis of the Spanish and Catalan versions of the Clarke et al. questionnaire for patients with T1D was conducted in three stages. Stage 1 was based on a cross-sectional, observational, descriptive design. Stages 2 and 3 were longitudinal and observational.

Stage 1. Translation, back-translation and cultural adaptation of the English questionnaire for the Spanish and Catalan versions. The original version of the questionnaire was independently translated into Spanish and Catalan by three endocrinologists, two nurses specialised in diabetes and one psychologist specialised in psychometry. Subsequently, after a group discussion between the participating professionals, the different versions were merged into a single text. Both questionnaires were then independently back-translated into English by two native English translators. These were then compared with the original text and a new version of each questionnaire was produced. Twenty bilingual patients with T1D (aged 20–60 years) from our out-patient clinics (at the Endocrinology and Nutrition Service of the Hospital Clínic i Universitari de Barcelona) volunteered to participate in the study. Spanish was the mother tongue of 10 patients and Catalan the mother tongue of the other 10. All the participants answered the questionnaire to identify and modify terms and expressions that were difficult to understand or interpret. The final Spanish and Catalan versions of the questionnaire were produced using their observations.

Stage 2. Reliability: internal consistency, testing, re-testing and construct validity. This stage involved volunteer patients with T1D aged >18 years, receiving multiple insulin doses (MDI) or continuous subcutaneous insulin infusions (CSII), attending the Endocrinology and Nutrition out-patient clinics at the Hospital Clínic i Universitari de Barcelona and the Hospital Clínico de Madrid. This group included patients who the authors agreed were classified as being at high-risk of having unnoticed hypoglycaemia: patients with >10 years T1D, with a frequency of ≥3 episodes of non-serious hypoglycaemia per week during the previous 4 weeks and/or ≥1 episode of serious hypoglycaemia during the previous year (based on American Diabetes Association guidelines). Those patients who did not satisfy these criteria were classified as low-risk unnoticed hypoglycaemia patients. After receiving orientation about the study and signing the corresponding informed consent documents, patients completed the Clarke et al. questionnaire in the translated version of their individual language preference (51% Spanish). All participants provided sociodemographic data (age, gender, level of education) and clinical data (years of T1D progression, type of treatment, glycosylated haemoglobin [HbA$_{1c}$, determined by means of high-performance liquid chromatography using the Tosoh G8 Automated HPLC Analyser, Tosoh Bioscience Inc., South San Francisco, CA, USA, calibrated with the standard values of the Diabetes Control and Complications Trial; reference values 4–6%]) for the previous month, as well as data on the frequency of non-serious episodes of hypoglycaemia in the previous 4 weeks and serious episodes of hypoglycaemia in the previous year. All patients were provided with a second copy of the questionnaire and a post-paid envelope for them to complete and return this

within a maximum of one week. Both questionnaires had the same alphanumeric code so that they could be merged in the statistical analyses. When the second questionnaire had been returned, we checked to determine whether or not it was within the stipulated period. If the deadline had already passed, the data was excluded.

Stage 3. Sensitivity to change. This stage involved patients with T1D ($\geq$18 years old) who had started CSII treatment at the Diabetes Unit of the Endocrinology and Nutrition Service at the Hospital Clínic i Universitari de Barcelona between 2006 and 2008, as a consequence of high incidence of non-serious and serious episodes of hypoglycaemia. As in stage 2, sociodemographic and clinical data were collected. Awareness of hypoglycaemia was evaluated using the Spanish and Catalan versions of the Clarke et al. questionnaire at the beginning of the study and at 6, 12 and 24 months after initiating CSII treatment.

Statistical analysis

Data are expressed as mean [SD]. Means were compared using the Student's *t*-test. The correlation between variables was calculated with Pearson's correlation coefficient. Cronbach's α coefficient was used to assess the internal consistency of the questionnaire. We considered $p \leq 0.05$ to be significant. Statistical analysis was with SPSS® 17.0 (SPSS Inc., Chicago, IL, USA). The study sample size was not determined.

Results

Stage 1. After translating the questionnaires from English into Spanish and Catalan, and the subsequent back-translation into English, 16 words were modified in the Spanish version and 20 in the Catalan version. Two other words and a verb tense were changed after their cultural adaptation by patients. The final Spanish and Catalan versions were produced using all available observations (Tables 1–3).

Stage 2. Of the total number of patients invited to participate, 30 were excluded (new readers, language barrier, type 2 diabetes, unwillingness to participate). In total, 144 patients completed the questionnaire in Spanish or Catalan, as they preferred (mean age [SD] 36 [18] years; 46% men; level of education: primary 18%, secondary 37%, university 45%; 41% received CSII and the rest, MDI; mean HbA$_{1c}$ was 7.5% [1.4%]). Cronbach's α coefficient for internal consistency was 0.75. Test–retest reliability showed a correlation coefficient of $r = 0.81$; $p < 0.001$. The correlation between the questionnaire score (R) and the frequency of non-serious episodes of hypoglycaemia was $r = 0.47$ ($p < 0.05$); and the frequency of serious episodes of hypoglycaemia was $r = 0.77$ ($p < 0.001$) (construct validity).

Stage 3. Twenty patients with T1D (mean age 34.0 [7.5] years; 12 women; mean disease progression 16.2 [6.6] years; mean HbA$_{1c}$ 6.7% [1.1%]) were assessed. Before initiating treatment with CSII, 19 of the 20 patients were classified as having an *abnormal perception of a situation of hypoglycaemia* (mean score 5.45 [1.19]). The remaining patient was classified as having an *indeterminate perception*.

The use of CSII was associated with a fall in the number of non-serious episodes of hypoglycaemia per week (mean between 5.40 [2.09] and 4.60 [2.33], 3.07 [1.39] and 2.75 [1.74] at 6, 12 and 24 months, respectively; $p < 0.001$). Similarly, the number of episodes of serious hypoglycaemia decreased from 1.25 [0.44] per patient/year to 0.05 [0.22] at the end of the study ($p < 0.001$). We observed a progressive reduction in the questionnaire score, indicating a progressive improvement in perception of hypoglycaemia (mean 3.7 [1.65], 2.74 [1.06] and 1.60 [2.03] at 6, 12 and 24 months, respectively). After 24 months, only 3 of the 20 patients were still

Table 1
Spanish language version of the questionnaire Clarke.

1. Escoja la categoría que mejor le describe (solo una)
  a) Siempre tengo síntomas cuando mi azúcar en sangre está bajo
  b) Algunas veces tengo síntomas cuando mi azúcar en sangre está bajo
  c) Ya no tengo síntomas cuando mi azúcar en sangre está bajo

2. ¿Ha perdido alguno de los síntomas que solía presentar ante una bajada de azúcar (hipoglucemia)?
  a) Sí
  b) No

3. En los últimos 6 meses, ¿con qué frecuencia ha tenido episodios de HIPOGLUCEMIA GRAVE SIN PÉRDIDA DE CONOCIMIENTO? (episodios en los que se ha sentido confundido, desorientado, cansado y sin posibilidad de tratar usted mismo la situación de hipoglucemia)
  a) Nunca
  b) Una/2 veces
  c) Una vez cada 2 meses
  d) Una vez al mes
  e) Más de una vez al mes

4. En el último año, ¿con qué frecuencia ha tenido episodios de HIPOGLUCEMIA GRAVE CON PÉRDIDA DE CONOCIMIENTO? (episodios acompañados de pérdida de conciencia o convulsiones que hayan requerido la administración de glucagón o glucosa intravenosa)
  a) Nunca
  b) Una vez
  c) 2 veces
  d) 3 veces
  e) 5 veces
  f) 6 veces
  g) 7 veces
  h) 8 veces
  i) 9 veces
  j) 10 veces
  k) 11 veces
  l) 12 veces o más

5. En el último mes, ¿con qué frecuencia ha tenido lecturas inferiores a 70 mg/dl con síntomas?
  a) Nunca
  b) De una a 3 veces
  c) 2 o 3 veces/semana
  d) 4 o 5 veces/semana
  e) Casi cada día

6. En el último mes, ¿con qué frecuencia ha tenido lecturas inferiores a 70 mg/dl sin síntomas?
  a) Nunca
  b) De una a 3 veces
  c) 2 o 3 veces/semana
  d) 4 o 5 veces/semana
  e) Casi cada día

7. ¿Hasta cuánto ha de bajar su azúcar en sangre para notar síntomas?
  a) 60-69 mg/dl
  b) 50-59 mg/dl
  c) 40-49 mg/dl
  d) Inferior a 40 mg/dl

8. ¿Hasta qué punto puede decir por sus síntomas que su azúcar en sangre es bajo?
  a) Nunca
  b) Casi nunca
  c) Algunas veces
  d) Casi siempre
  e) Siempre

classified as having an *abnormal perception of a situation of hypoglycaemia*.

Discussion

Psychometric analysis of English into Spanish and English into Catalan translations of a hypoglycaemia awareness questionnaire shows that this instrument could be useful in the detection of patients with T1D and unnoticed hypoglycaemia, in our context.

Without doubt, the occurrence of repeated episodes of hypoglycaemia is currently one of the most substantial obstacles to

Table 2
Catalan version of the questionnaire Clarke.

1. Escull la categoria que millor el descriu (només una)
 a) Sempre tinc símptomes quan el meu sucre en sang està baix
 b) A vegades tinc símptomes quan el meu sucre en sang està baix
 c) Ja no tinc símptomes quan el meu sucre en sang està baix

2. Ha perdut algun dels símptomes que solia presentar davant una baixada de sucre?
 a) Sí
 b) No

3. En els últims 6 mesos, amb quina freqüència ha tingut episodis d'HIPOGLUCÈMIA GREU SENSE PÈRDUA DE CONEIXEMENT? (episodis en els que s'ha sentit confós, desorientat, cansat i sense possibilitat de tractar vostè mateix la situació d'hipoglucèmia)
 a) Mai
 b) Una/2 vegades
 c) Una vegada cada 2 mesos
 d) Una vegada al mes
 e) Més d'una vegada al mes

4. Al darrer any, amb quina freqüència ha tingut episodis d'HIPOGLUCÈMIA GREU AMB PÈRDUA DE CONEIXEMENT? (episodis acompanyats de pèrdua de conciència o convulsions i que varen requerir l'administració de glucagó o glucosa intravenosa)
 a) Mai
 b) Una vegada
 c) 2 vegades
 d) 3 vegades
 e) 5 vegades
 f) 6 vegades
 g) 7 vegades
 h) 8 vegades
 i) 9 vegades
 j) 10 vegades
 k) 11 vegades
 l) 12 vegades o més

5. A l'últim mes, amb quina freqüència ha tingut lectures inferiors a 70 md/dl amb símptomes?
 a) Mai
 b) Entre una i 3 vegades
 c) Una vegada/setmana
 d) De 2 a 3 vegades/setmana
 e) De 4 a 5 vegades/setmana
 f) Gairebé cada dia

6. A l'últim mes, amb quina freqüència ha tingut lectures inferiors a 70 md/dl sense cap símptoma?
 a) Mai
 b) Entre una i 3 vegades
 c) Una vegada/setmana
 d) De 2 a 3 vegades/setmana
 e) De 4 a 5 vegades/setmana
 f) Gairebé cada dia

7. Fins a quant ha de baixar el seu nivell de sucre a la sang, abans de notar símptomes?
 a) 60-69 mg/dl
 b) 50-59 mg/dl
 c) 40-49 mg/dl
 d) Inferior a 40 mg/dl

8. Fins a quin punt pot dir, pels seus símptomes, que el nivell de sucre en sang és baix?
 a) Mai
 b) Gairebé mai
 c) Algunes vegades
 d) Gairebé sempre
 e) Sempre

Table 3
Score calculation.

Question 1, b or c = R
Question 2, a = R
Question 3, b, c, d, e (any of them) = R
Question 4, b, c, d, e, f, g, h, i, j, k, l (any of them) = R
Questions 5 and 6, answer to question 5 < answer to question 6 = R
Question 7, c or d = R
Question 8, a, b or c = R

The total sum of R responses determines the level of the patient's awareness of hypoglycaemia:
 1–2R = normal perception
 3R = indeterminate perception
 >3R = abnormal perception of an episode of hypoglycaemia (unnoticed hypoglycaemia)

life. In this context, and if improved hypoglycaemia awareness and the prevention of serious hypoglycaemia episodes are our targets, then it is undoubtedly essential we have access to a questionnaire in the patients' mother tongue. In addition to the original study by Clarke et al.,[10] we have previously demonstrated the questionnaire's capacity to identify patients with unnoticed hypoglycaemia.[14] To do so, we compared the results obtained with the questionnaire with the gold standard, defined as the achievement of symptoms triggered by an episode of controlled-induced hypoglycaemia. Our comparison with the percentage increase in the symptoms score (Edinburgh's scale) between hypoglycaemia and euglycaemia demonstrated that using the questionnaire enables us to identify patients with high sensitivity. Moreover, we found a negative correlation between the increased symptoms score and the score obtained in the Clarke et al. questionnaire. Additionally, we were able to prove that the questionnaire score was higher in patients with a higher percentage of interstitial glucose: <70 mg/dl obtained by continuous monitoring.[14]

As we see it, the results pertaining to the questionnaire's capacity to detect changes are especially interesting. As the stage 3 patients had a decreasing number of episodes of non-serious and serious hypoglycaemia, the questionnaire score fell concurrently, i.e. their perception of hypoglycaemia gradually improved. That is to say, the questionnaire can detect changes associated with an intervention procedure aimed at avoiding hypoglycaemia and thus improving perception of it.

However, our study and its results are not without their limitations. The validation can only be considered partial; internal consistency, test–retest reliability of the instrument, construct validity and sensitivity to change have been established. There is also an arbitrary cut-off point that classifies patients and compares the questionnaire with a diagnostic test, although its final objectives are exclusively targeted at identifying those patients at highest risk of future serious episodes of hypoglycaemia. We should also bear in mind that the sample used for sensitivity-to-change analysis could be considered small, although the specific characteristics of the patients actually included reflect the difficulties entailed in the selection process.

To summarise, the results of our study show that the Spanish and Catalan versions of the Clarke et al. questionnaire can be a useful instrument in assessing the presence of unnoticed hypoglycaemia in patients with T1D in our context. Using the questionnaire is the step prior to any intervention targeted at detecting, preventing and improving the treatment of existing cases of hypoglycaemia, with the overall aim of eradicating the occurrence of episodes of hypoglycaemia, if possible.

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improving blood sugar level control in patients with T1D, using conventional and non-conventional insulin-intensified treatment.[12,13] The repetition of episodes leads to a progressive loss of the symptoms of a normal response to hypoglycaemia in up to 20% of patients.[13] This loss of warning symptoms in response to hypoglycaemia (unnoticed hypoglycaemia) leads to repeated non-serious episodes and, particularly, to serious episodes, thus increasing the patient's vulnerability and significantly diminishing their quality of

Conflicts of interest

The authors declare that there are no conflicts of interest.

Acknowledgements

Appendix.

Tables 1-2 English version of the Clarke questionnaire.

1. Choose the category that better describes you (only one)
a) I always have symptoms when my blood sugar levels are low
b) I sometimes have symptoms when my blood sugar levels are low
c) I do not have symptoms any more when my blood sugar levels are low

2. Have you lost any of the symptoms you usually had in case of low blood sugar levels (hypoglycaemia)?
a) Yes
b) No

3. During the last 6 months, with what frequency have you experienced episodes of SERIOUS HYPOGLYCAEMIA WITHOUT LOSS OF CONSCIOUSNESS? (episodes where you were confused, disoriented, tired and without the ability to treat the episode of hypoglycaemia by yourself)
a) Never
b) Once/twice
c) Once every 2 months
d) Once a month
e) More than once a month

4. During the last year, with what frequency have you experienced episodes of SERIOUS HYPOGLYCAEMIA WITH LOSS OF CONSCIOUSNESS? (episodes accompanied by loss of consciousness or seizures that have required the administration of intravenous glucagon or glucose)
a) Never
b) Once
c) Twice
d) 3 times
e) 5 times
f) 6 times
g) 7 times
h) 8 times
i) 9 times
j) 10 times
k) 11 times
l) 12 times or more

5. During the last month, with what frequency have you had levels lower than 70 mg/dl with symptoms?
a) Never
b) 1 to 3 times
c) 2 or 3 times a week
d) 4 or 5 times a week
e) Almost every day

Tables 1-2 (*Continued*)

6. During the last month, with what frequency have you had levels lower than 70 mg/dl without symptoms?
a) Never
b) 1 to 3 times
c) 2 or 3 times a week
d) 4 or 5 times a week
e) Almost every day

7. How much did your blood sugar levels have to decrease for you to notice any symptoms?
a) 60-69 mg/dl
b) 50-59 mg/dl
c) 40-49 mg/dl
d) Lower than 40 mg/dl

8. To what extent do your symptoms indicate that your blood sugar levels are low?
a) Never
b) Almost never
c) Sometimes
d) Almost every time
e) Always

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