Effects of Insulin Therapy on the Diabetes Symptom Checklist-Revised (DSC-R): Data From a Large Insulin Clinical Trial

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Introduction

- The initiation of insulin therapy is associated with concerns of impaired quality of life,[1] and adding insulin injections to a patient's daily regimen typically requires overcoming barriers.[2-5]
- A better understanding of the effects of initiating insulin therapy on patient-reported outcomes may assist in assessing the impact of specific treatment regimens on patients.
- The Diabetes Symptom Checklist-Revised (DSC-R)[1] is a diabetes-specific instrument used to measure both the occurrence and the perceived burden of physical and psychological symptoms related to type 2 diabetes (T2D) and its possible complications.

Objective

- To examine the impact of insulin initiation on the DSC-R in patients with T2D using data from a large insulin initiation clinical trial

Methods

Study Design

- Data for these analyses were obtained from a subset of patients with T2D participating in the DURABLE (Assessing the DURAbility of Basal vs. Lispro Mix 75/25 Insulin Efficacy) clinical trial, a randomized, multicenter, open-label, two-arm, parallel study.[6]
- The DURABLE trial was designed to compare two commonly used starter insulin regimens: once-daily insulin glargine versus twice-daily insulin lispro mix 75/25, added to existing oral antidiabetic drugs (metformin, thiazolidinedione, and/or sulfonylurea).
- The current analyses included subjects with complete DSC-R data from both the baseline and 6-month visits.

Study Participants

- The DURABLE trial enrolled 2,091 insulin-naive patients from 242 centers in 11 countries between December 2005 and July 2007.
- Subjects from the United States and Puerto Rico completed patient reported-outcome measures, including the DSC-R.

The DSC-R

- The DSC-R is a T2D-specific measure that assesses the occurrence and the perceived burden of the following eight types of T2D-related symptoms[1]: hypoglycemic, hyperglycemic, cardiovascular, neuropathic/pain, neuropathic/sensory, psychological/fatigue, psychological/cognitive, and ophthalmologic/vision. Additionally, a total DSC-R score is computed from the mean of the eight subscales.
- Summary scores for each domain ranged from 0 to 100, with higher scores indicating greater symptom burden.
- We compared change in mean score (baseline to 6-month visit) for the two insulin arms combined together to assess the effects of insulin therapy in general on the DSC-R.
- Two analytic methods were used to describe the extent and significance of change:
  - Paired *t*-test, comparing 6-month and baseline scores
  - Effect size (Cohen's *d*)[7] estimates for mean change, where 0.2, 0.5, and 0.8 represent small, medium, and large degrees of change, respectively
- As a sensitivity analysis, we applied the last observation carried forward (LOCF) method to account for scores of subjects who terminated the study early, prior to the 6-month visit.

Results

- A total of 576 patients completed the DSC-R at baseline and the 6-month visit. An additional 48 patients terminated the study early, prior to 6-month visit. Our results did not differ after applying the LOCF method.
- Baseline demographic and clinical characteristics are presented in Table 1 (mean age = 57 years, 41% female, 72% Caucasian, body mass index [BMI] = 33.7 kg/m², duration of diabetes = 9.6 years).

Table 1. Demographic and Clinical Characteristics of Patients (N = 576)

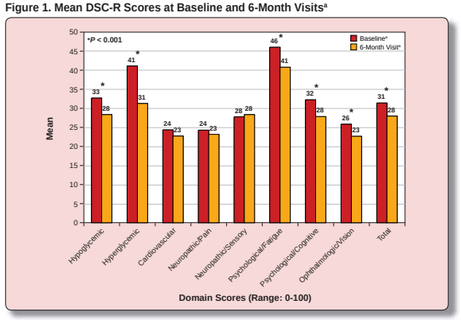
Demographic and Clinical Characteristics	Overall
Age (years), n (%)	
30 to 39	22 (3.8)
40 to 49	111 (19.3)
50 to 59	206 (35.8)
60 to 69	173 (30.0)
70+	64 (11.1)
Mean (SD)	57.0 (9.9)
Gender, n (%)	
Female	236 (41.0)
Male	340 (59.0)
Ethnicity, n (%)	
African American	55 (9.6)
Caucasian	415 (72.1)
Hispanic	71 (12.3)
Other	35 (6.1)
BMI (kg/m²), mean (SD)	33.7 (6.0)
Duration of diabetes (years), mean (SD)	9.6 (6.1)
A1c, mean (SD)	8.9 (1.2)
Language, n (%)	
US English	533 (93.4)
US Spanish	19 (3.3)
PR Spanish	19 (3.3)
Marital status, n (%)	
Single[a]	190 (33.5)
Married	378 (66.6)
Health insurance, n (%)	
Commercial	304 (55.9)
Medicaid	28 (5.2)
Medicare	78 (14.3)
Government, other	134 (24.6)
Highest education degree, n (%)	
High school degree or less	322 (57.9)
College degree	169 (30.4)
Postgraduate or professional degree	51 (9.2)
Other	14 (2.5)
Household income, n (%)	
$0 to $20,000	108 (19.6)
$20,001 to $40,000	166 (30.1)
$40,001 to $60,000	111 (20.2)
$60,001 to $100,000	112 (20.3)
> $100,000	54 (9.8)
Current employment, n (%)	
Employed	335 (59.4)
Other	143 (25.4)
Retired	86 (15.3)

SD = standard deviation.

[a]Single defined as never married, widowed, or separated/divorced.

- The mean score at baseline ranged from 24.2 (neuropathic/pain) to 45.9 (psychological/fatigue) (Figure 1 and Table 2).
- The mean score at 6-month visit ranged from 22.6 (ophthalmologic) to 40.7 (psychological/fatigue) (Figure 1 and Table 2).

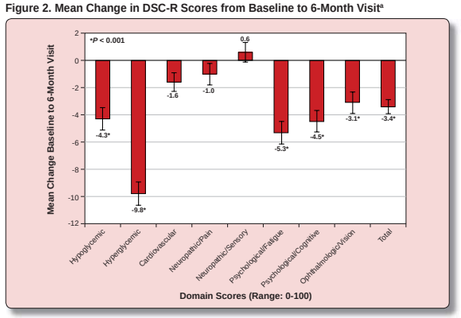
Figure 1. Mean DSC-R Scores at Baseline and 6-Month Visits[a]



[a]Higher score indicates greater symptom burden.

- Absolute changes in the mean domain score from baseline to the 6-month visit ranged from +0.6 (neuropathic/sensory) to –9.8 (hyperglycemic) (Figure 2 and Table 2). Negative change corresponds to improvement in the DSC-R domain scores.

Figure 2. Mean Change in DSC-R Scores from Baseline to 6-Month Visit[a]



[a]Negative change corresponds to improvement in the DSC-R domain scores.

- Mean changes from baseline to the 6-month visit, although small, were statistically significant for the hypoglycemic, hyperglycemic, psychological/fatigue, psychological/cognitive, and ophthalmologic/vision subscales and the total DSC-R score ($P < 0.001$) (Table 2).
- A small to moderate effect size was observed for hyperglycemic symptom domain at 0.38 (Table 2). Domains resulting in small effect sizes (~0.20) included psychological/fatigue and psychological/cognitive. All other effect sizes were less than 0.20.

Table 2. DSC-R Domain Scores from Baseline to 6-Month Visit

		Descriptive Statistics		Baseline to 6-Month Change		
Subscale	**N**	**Baseline Mean (SD)**	**6-Month Mean (SD)**	**Difference Mean (SD)**	**Difference Effect Size**	***P* Value**
Hypoglycemic	576	32.6 (23.3)	28.3 (22.3)	–4.3 (19.5)	0.18	**< 0.001**
Hyperglycemic	576	41.0 (26.1)	31.2 (23.6)	–9.8 (20.5)	**0.38**	**< 0.001**
Cardiovascular	574	24.3 (19.3)	22.7 (19.3)	–1.6 (16.4)	0.08	0.02
Neuropathic/Pain	566	24.2 (22.5)	23.1 (22.3)	–1.0 (19.2)	0.05	0.20
Neuropathic/ Sensory	574	27.7 (22.6)	28.3 (22.3)	0.6 (17.3)	0.02	0.45
Psychological/ Fatigue	576	45.9 (25.2)	40.7 (24.1)	–5.3 (20.7)	**0.21**	**< 0.001**
Psychological/ Cognitive	574	32.2 (21.9)	27.8 (21.2)	–4.5 (18.6)	**0.20**	**< 0.001**
Ophthalmologic/ Vision	575	25.8 (21.4)	22.6 (20.8)	–3.1 (19.2)	0.15	**< 0.001**
Total	574	31.3 (17.9)	27.9 (17.7)	–3.4 (13.4)	0.19	**< 0.001**

Limitations

- Current analyses were conducted in a setting of a randomized controlled trial. There could be differences in patients' assessments of insulin therapy in a real-world setting. Information from patients who refused screening for the study was not collected.
- We were unable to assess the long-term effects of insulin therapy on patient-reported outcomes. However, since the DURABLE trial is an ongoing, 2-year trial, a longitudinal assessment of insulin therapy on patient-reported outcomes is forthcoming.

Conclusions

- Initiation of insulin therapy was associated with a small to moderate improvement in the hyperglycemic symptoms domain.
- Mean changes with small effect size were also observed in psychological/fatigue and psychological/cognitive domains.
- After initiation of insulin, our results suggest that most T2D-specific symptom domains improved, as assessed by the DSC-R. And, importantly, we did not observe any significant deterioration among specific symptom domains.

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