Optimizing Insulin Glargine Plus One Injection of Insulin Glulisine in Type 2 Diabetes in the ELEONOR Study

Similar effects of telecare and conventional self-monitoring of blood glucose on patient functional health status and treatment satisfaction

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OBJECTIVE—To determine the functional health status and treatment satisfaction in patients with type 2 diabetes from the Evaluation of Lantus Effect ON Optimization of use of single dose Rapid insulin (ELEONOR) study that investigated whether a telecare program helps optimization of basal insulin glargine with one bolus injection of insulin glulisine.

RESEARCH DESIGN AND METHODS—Functional health status and treatment satisfaction were investigated using the 36-Item Short-Form (SF-36) Health Survey, the World Health Organization Well-Being Questionnaire (WBQ), and the Diabetes Treatment Satisfaction Questionnaire.

RESULTS—Of 291 randomized patients, 238 completed the study (telecare: 114; self-monitoring blood glucose: 124). Significant improvements were detected in most SF-36 domains, in WBQ depression and anxiety scores, and in treatment satisfaction, without differences between study groups.

CONCLUSIONS—An insulin regimen that substantially improves metabolic control, while minimizing the risk of hypoglycemia, can positively affect physical and psychologic well-being and treatment satisfaction irrespective of the educational support system used.

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Among the barriers to initiation of insulin treatment are concerns about the negative effect of therapy on the quality-of-life (QoL) of patients (1,2). Use of basal and rapid-acting insulin analogs may help overcome those barriers (3). However, initiation and intensification of insulin therapy can be demanding for patients and health care practitioners because daily blood glucose monitoring is required.

Telemonitoring and self-management have a positive effect on patients' lives (4,5), allowing frequent assessment of the patient's condition while maintaining the patient's independence. The Evaluation of Lantus Effect ON Optimization of use of single dose Rapid insulin (ELEONOR) study investigated whether a telecare program helps optimization of basal insulin glargine with the addition of one bolus injection of insulin glulisine at the main meal in patients with type 2 diabetes whose hyperglycemia is uncontrolled with oral hypoglycemic agents (6). This article focuses on the effect on QoL and treatment satisfaction among patients.

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*A complete list of the ELEONOR Study Group can be found in the Supplementary Data online.

RESEARCH DESIGN AND METHODS

—The study was an open-label, multicenter, randomized (1:1), controlled, parallel-group trial conducted in Italy in individuals with type 2 diabetes. Inclusion and exclusion criteria have been described (6). After screening, patients entered a 2- to 4-week qualification phase where oral hypoglycemic agents other than metformin were discontinued, and metformin was uptitrated to 2 g/day (1 g twice daily) until study completion. At the end of this phase (visit 2 [V2], week 4), patients started insulin glargine, once daily at dinner, and were randomized to telecare or self-monitoring of blood glucose (SMBG), but used SMBG throughout this phase. Glargine was titrated to achieve a fasting plasma glucose of 100 mg/dL, with a starting dose of 10 units/day, using a predefined titration algorithm. Patients with a fasting plasma glucose ≤126 mg/dL at weeks 8, 12, or 16 entered the treatment phase, where they performed six-point blood glucose profiles every week to identify the meal with the highest postprandial glucose excursion. At the end of this phase (visit 4 [V4], week 20), eligible patients added one dose of glulisine at the identified meal and optimized their glulisine doses via the telecare or SMBG programs, with the goal of reducing 2-h postprandial plasma glucose to <140 mg/dL.

Functional health status and treatment satisfaction were investigated using the 36-Item Short-Form (SF-36) Health Survey (7,8), the World Health Organization Well-Being Questionnaire (WBQ) (9), and the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (10). All have been translated and validated in Italian (11,12). Patients were requested to fill in a questionnaire that included the three instruments during V2, V4, and V5 (study end). Statistical methods are described in the Supplementary Data.

RESULTS

—A total of 238 patients completed the study (telecare: 114; SMBG: 124). In the telecare group, 76 patients

received full use of the telecare system, transmitting data and receiving an answer from an investigator. Those who did not fully use the telecare system perceived progressively good glycemic control or experienced transmission problems. Baseline characteristics were similar for both groups (9).

Overall, 187 patients (77.6%) completed all three SF-36 questionnaires (SMBG: 96; telecare: 91), 175 (72.6%) completed the WBQ questionnaires (SMBG: 87; telecare: 78), and 180 (74.7%) completed the DTSQ questionnaires (SMBG: 92; telecare: 88). Completers did not significantly differ from noncompleters in age, sex, baseline HbA_{1c}, or BMI. In both groups, scores of all SF-36 domains, as well as physical and mental component summary scores, improved after glargine titration (Table 1), and the benefits were maintained thereafter. Significant improvement in WBQ depression and anxiety scores was documented in the SMBG group at V4 and V5 compared with baseline (Table 1). In the telecare group, a significant improvement was detected in the anxiety, energy, and general well-being scores. Treatment satisfaction markedly increased over time in both groups. Improvement was associated with a significant decrease in the frequency of perceived hyperglycemic episodes and a moderate increase in the perceived frequency of hypoglycemic episodes. No difference emerged between the two groups on any of these instruments. Changes in functional health status and satisfaction scores between V5 and V2 were related to the frequency of hypoglycemic episodes (none, 1–3, >3 episodes) that occurred in the previous 30 days (Supplementary Data). Multivariate analyses showed that HbA_{1c} changes (measured by the Exacta Central Laboratory, Verona, Italy) and >3 hypoglycemic episodes in the previous 30 days were the variables more consistently associated with changes in QoL and satisfaction scores (Supplementary Data).

CONCLUSIONS—A number of patient concerns about insulin initiation have been reported (13–15), but our study shows that insulin initiation is not associated with a worsening in physical functioning, social functioning, or psychologic well-being. Indeed, most scores improved after the start of glargine therapy and remained stable or improved further after glulisine addition. The positive effects on HbA_{1c} levels, coupled with a minor effect on body weight and a low

Table 1—*SF-36, WBQ, and DTSQ scores at baseline (V2), after the titration of glargine (V4), and at study end (V5), according to study arms*

	Common SMBG					Telecare					Common SMBG vs. telecare	
				P					*P**		*P***	
Scale	V2	V4	V5	V4 vs. V2	V5 vs. V2	V2	V4	V5	V4 vs. V2	V5 vs. V2	V4–V2	V5–V2
SF-36												
PF	77.8 ± 22.8	82.4 ± 20.8	83.7 ± 18.4	0.02	0.006	79.1 ± 21.4	82.4 ± 20.1	84.2 ± 20.0	0.10	0.004	0.41	0.99
RP	73.9 ± 36.2	82.8 ± 30.6	82.1 ± 31.9	0.03	0.07	71.6 ± 37.1	78.6 ± 35.9	82.2 ± 33.6	0.05	0.007	0.71	0.41
BP	72.0 ± 25.9	79.2 ± 21.0	79.3 ± 21.8	0.007	0.01	74.3 ± 24.9	78.5 ± 23.8	77.0 ± 25.9	0.07	0.37	0.69	0.17
GH	58.0 ± 19.4	62.9 ± 16.5	65.9 ± 16.4	0.008	<0.0001	57.2 ± 19.9	60.7 ± 18.1	63.1 ± 18.2	0.07	0.001	0.54	0.85
VT	61.0 ± 22.2	65.9 ± 18.4	67.5 ± 19.5	0.04	0.005	62.0 ± 19.0	65.6 ± 19.3	68.2 ± 19.1	0.04	0.001	0.92	0.61
SF	77.1 ± 21.5	83.0 ± 16.4	83.2 ± 17.4	0.005	0.01	77.3 ± 22.4	76.6 ± 25.1	80.9 ± 21.7	0.97	0.10	0.06	0.97
RE	75.3 ± 33.1	87.0 ± 27.2	83.0 ± 31.1	0.001	0.02	71.5 ± 37.2	76.0 ± 37.3	81.3 ± 33.4	0.12	0.005	0.18	0.71
MH	67.3 ± 21.7	71.0 ± 19.0	73.7 ± 17.2	0.06	0.004	68.3 ± 19.8	69.5 ± 19.6	75.0 ± 17.0	0.35	<0.0001	0.49	0.46
PCS	47.2 ± 8.1	49.5 ± 7.2	49.8 ± 6.8	0.001	<0.0001	47.8 ± 8.0	49.8 ± 7.7	49.3 ± 7.5	0.006	0.04	0.61	0.17
MCS	47.6 ± 10.7	50.3 ± 9.0	51.2 ± 8.4	0.12	0.04	47.4 ± 10.8	48.1 ± 10.9	50.5 ± 9.3	0.69	<0.0001	0.42	0.28
WBQ												
Depression	4.0 ± 3.1	3.2 ± 3.0	3.0 ± 2.8	0.07	0.03	3.3 ± 2.3	3.5 ± 2.7	3.5 ± 3.1	0.80	0.86	0.21	0.12
Anxiety	6.6 ± 4.3	5.4 ± 3.9	5.5 ± 3.8	0.01	0.01	5.8 ± 3.7	5.1 ± 3.7	4.7 ± 3.7	0.03	0.01	0.65	0.99
Energy	7.8 ± 2.8	7.9 ± 2.9	8.1 ± 2.5	0.86	0.42	7.4 ± 2.7	7.7 ± 2.8	8.2 ± 2.6	0.35	0.008	0.40	0.09
Positive well-being	13.5 ± 4.0	13.6 ± 2.8	13.4 ± 2.3	0.67	0.21	13.7 ± 4.0	13.1 ± 2.7	13.5 ± 2.6	0.13	0.50	0.42	0.76
General well-being	46.7 ± 11.7	48.8 ± 10.1	49.0 ± 9.2	0.39	0.35	47.9 ± 10.2	48.3 ± 10.2	49.4 ± 10.5	0.57	0.05	0.80	0.47
DTSQ												
DTSQ	24.7 ± 7.6	29.1 ± 6.4	30.4 ± 4.7	<0.0001	<0.0001	25.6 ± 7.8	29.4 ± 5.9	30.1 ± 5.2	<0.0001	<0.0001	0.33	0.38
Hyper	4.2 ± 2.0	2.4 ± 1.6	2.4 ± 1.7	<0.0001	<0.0001	4.7 ± 1.6	2.8 ± 1.4	2.4 ± 1.5	<0.0001	<0.0001	0.83	0.10
Hypo	0.6 ± 0.9	1.6 ± 1.4	1.8 ± 1.5	<0.0001	<0.0001	0.8 ± 1.4	1.8 ± 1.4	1.7 ± 1.6	<0.0001	<0.0001	0.97	0.25

Data are presented as mean ± SD. BP, bodily pain; GH, general health; Hyper, perceived frequency of hyperglycemic episodes; Hypo, perceived frequency of hypoglycemic episodes; MCS, mental component score; MH, mental health; PCS, physical component score; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality. *Wilcoxon signed rank test. **Mann-Whitney *U* test.

incidence of hypoglycemic episodes, as well as the ease of glargine titration and flexibility in the basal-plus regimen, may have all contributed to attenuating the effect of insulin initiation. Injection-related anxiety (15) was also not documented, given that the WBQ anxiety score significantly decreased in both study arms. Acceptance of insulin treatment was also documented by the significant increase in treatment satisfaction.

The lack of difference in functional health status between common SMBG and telecare is probably attributable to comparable reductions in HbA_{1c} and similar rates of hypoglycemia. In addition, the ease of insulin regimen titration may have made telecare less useful. However, only two-thirds of the telecare group actually used the system, which may also have contributed to the lack of difference.

Our study has limitations. First, the use of diabetes-specific instruments investigating aspects more strictly related to diabetes self-management would have been helpful in exploring the differential effect of SMBG versus telecare. Second, part of the improvements might be related to a "trial effect."

In conclusion, the results of the ELEONOR study show that an insulin regimen that substantially improves metabolic control, while minimizing the risk of hypoglycemia, can positively affect physical and psychologic well-being and treatment satisfaction in patients with type 2 diabetes. Insulin-based therapy can improve patient-reported outcomes, including well-being and treatment satisfaction, irrespective of the educational support used by individuals.

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A.N. researched data and wrote the manuscript. S.D.P. researched data and contributed to discussion. G.V. researched data and reviewed the manuscript.

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