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THE IMPACT OF STRUCTURED DIABETES EDUCATION ON GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES AT INITIATION OF BASAL INSULIN – THE BASAL-EDUC-RO STUDY: A RANDOMIZED PROSPECTIVE STUDY

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Abstract

Background: *Basal-EDUC-RO Study evaluated the impact of structured education provided at the initiation of basal insulin therapy on glycaemic control in patients with uncontrolled type 2 diabetes mellitus (T2D).* ***Methods:*** *This was a prospective, multicenter, randomized, parallel group study (ACTRN12616001273471) which enrolled 711 patients initiated on insulin therapy with a basal insulin analogue. The subjects were randomized (1:1) to either structured education (structured education group; 353 patients) or standard education (control group; 358 patients) and followed for 6 months.* ***Results:*** *The median HbA1c levels at 6 months after start of basal insulin were significantly lower in the structured education group than in the control group (7.2% vs. 7.4%, p <0.001). In the structured education group, 49.4% of subjects achieved HbA1c targets vs. 34.4% in the control group, p <0.001. Number of documented symptomatic hypoglycemic episodes (all and nocturnal) was lower in the intervention group (139 vs. 217 for all episodes and 13 vs. 26 for nocturnal hypoglycemia) but with no statistical significance. No effect of intervention was seen on body weight, but there was no weight gain in any of the groups at 6 months.* ***Conclusions:*** *A structured diabetes education program delivered to patients with T2D started on a basal insulin analogue significantly improved glucose control at 6 months compared to a less intense education strategy. The positive effect was mainly seen on the percentage of patients who achieved individualized HbA1c pre-set targets, with a non-significant reduction in episodes of overall and nocturnal documented symptomatic hypoglycemia.*

key words: *type 2 diabetes; basal insulin analogue; diabetes self-management education*

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Background and aims

Since the publication of the United Kingdom Prospective Diabetes Study (UKPDS), chronic hyperglycemia has been recognized as an important determinant for the development and progression of chronic complications in type 2 diabetes mellitus (T2D) [1]. A reduction in glycated hemoglobin (HbA1c) remains the cornerstone of diabetes management [2] and until recently the HbA1c goal in most T2D patients was <7% [3]. However, observational studies in various groups of patients with T2D reported that attaining the HbA1c target remained unsatisfactory [4-7], although an improvement in the percentage of patients at target from 1999 through 2010 was shown in one study [8]. One of the main barriers in maintaining long-term glycemic control in T2D is the progressive nature of the disease attributed to a continuous decline in beta-cell function [9] and many patients require insulin after a number of years since diagnosis [10]. As initial insulin therapy, current guidelines recommend a basal insulin regimen, using either intermediate-acting insulin or long-acting insulin analogues [3].

More recently, guidelines also recommend the individualization of HbA1c target according to patient's clinical characteristics (such as age, duration of the disease, life expectancy, established cardiovascular complications, important comorbidities, or patient attitude) and risk of adverse effects associated with use of glucose-lowering medications, among other concerns [2]. No data on how many patients with diabetes attain individualized targets is available.

In addition to pharmacological treatment, diabetes self-management is considered a key element in the care of patients with diabetes. Diabetes self-management education (DSME) should be offered to all patients, either as individual or group sessions, preferably using structured approaches [3,11,12]. DMSE was proven to decrease long-term health care costs by reducing the risk for chronic complications [13], to reduce the number of hospital admissions [14] and rate of readmission [15] and to significantly decrease HbA1c and blood glucose levels (some, but not all studies), as well as to improve diabetes knowledge, self-management skills and psychosocial outcomes [16].

Health care providers have widely recognized the reluctance of patients with T2D to accept and to persist on insulin therapy [17] and this phenomenon was called "psychological insulin resistance" [18]. Later, reluctance to adhere to insulin titration was also included in the concept of psychological insulin resistance [19]. Education and psychological strategies (exposure, desensitization, relaxation and counseling) were proposed as effective approaches in reducing psychological insulin resistance [20].

DSME was also recommended as one of the strategies to reduce burden of hypoglycemia in diabetes [21] and it was recently shown to improve glycemic control in patients already treated with insulin after a 6-week program including additional instructions about self-titration of insulin doses as compared to a basic 2-weeks educational program [22]. Less is known, however, about the potential benefits of concomitant initiation of basal insulin and participation to a structured diabetes education in patients with uncontrolled T2D.

The objectives of the study presented here, Basal-EDUC-RO Study, were to assess the impact of structured education on glycemic control evaluated with HbA1c and on the achievement of individualized targets of HbA1c when provided to patients with T2D at the initiation of basal insulin therapy.

Material and methods

Study design and study population

This was a prospective, multicenter, randomized, parallel group study (ACTRN12616001273471) conducted between 22nd of October 2014 and 17th of August 2015 in 65 outpatient diabetes clinics and independent medical practices in Romania. Eligible patients with T2D for which there was an intention to initiate insulin therapy with basal insulin analogues (glargine or levemir) were randomly assigned (1:1) to receive either a structured education (structured education group) or standard education according to investigator's practice (control group) and followed for up to 6 months. Three study visits were scheduled for all patients in both groups: at baseline (Visit 1), at 3 (Visit 2) and 6 months (Visit 3) after enrollment. The indication to initiate insulin and choice of insulin analogue was solely at the investigator's decision, according to local practice. At first study visit the investigators were asked to provide an HbA1c target value for each patient.

Each site was to enroll a maximum of 12 consecutive patients who fulfilled the inclusion criteria and without any exclusion criteria. Patients' randomization was performed using sealed opaque envelopes numbered with consecutive numbers, corresponding to patients' numbers; for each eligible patient who signed the informed consent form, the investigator had to open the sealed envelope which contained the preprinted study group to which the study participant was assigned.

Patients were enrolled if they were aged >18 and <75 years, had a previous diagnosis of T2D treated with oral antidiabetics on stable doses during the previous 3 months before enrollment, the diabetes was considered as inadequately controlled and the investigators decided to initiate therapy with basal insulin analogues. Patients were included only if they had an HbA1c value measured or available at the time of enrollment, but not older than 1 month prior. The exclusion criteria were therapy with systemic corticosteroids, pregnant or breastfeeding women or the intention to become pregnant during the next 6 months after the study inclusion, or participation in another clinical study. Patients who in the investigator's opinion were unable to comply with visit schedule were also excluded.

The study was approved by the Romanian National Bioethics Committee for Medicine and Medical Devices. The study was conducted in full accordance with the International Conference on Harmonization Good Clinical Practice guidelines and the Declaration of Helsinki. All patients provided written informed consent before any study procedure.

Study interventions

The only intervention in this study was the type of education provided to the patients at insulin initiation. The investigators were free to choose based on their usual practice the insulin starting dose, insulin titration algorithm, the continuation and/or dose of the oral antidiabetic agents after insulin initiation and the recommendations on frequency of self-monitoring of blood glucose (SMBG) provided to the patients in both groups. Patients were asked to bring with them the glucose meter at each study visit.

Structured education consisted of a predefined, standardized education program with two face-to-face individual sessions of 1-hour duration each, performed by trained study nurses at Baseline and Visit 2. During the first education session (Baseline) patients from structured education group received information on the importance of glycemic control, diabetes complications, lifestyle changes, insulin mechanism of action, training on the device and

injection technique for insulin administration, glucose meters and SMBG, hypoglycemia and insulin doses titration. A brochure with this information was also provided to the patients. The second education session performed during Visit 2 consisted of a short interview with the patients to check their knowledge on diabetes management and discuss changes done in the past 3 months. Based on this interview the information provided during the first session was reinforced as needed. The SMBG values and the insulin titration algorithm used by the patient were reviewed and discussed and education on complications of insulin treatment and the possibility of further need for insulin therapy intensification (postprandial glycemia term introduced to the patient) was provided.

The control group was trained according to daily practice routine at the insulin therapy initiation at each investigational site – each patient was trained during Visit 1 on the use of the device and injection technique for insulin administration, glucose meter use and hypoglycemia and was provided an insulin titration algorithm. No re-training was performed to this group during the study duration.

Study assessments

HbA1c, fasting plasma glucose levels, weight, height, waist circumference, number of hypoglycemic episodes, insulin dose, oral antidiabetic agents (type and dose) and frequency of SMBG were collected at each study visit. HbA1c and fasting plasma glucose levels were assessed in local laboratories accredited by Romanian Accreditation Association and thus ensuring the standardization of the methods used. Height, weight and waist circumference were measured according to local procedures. Medical history – diabetes duration, cardiovascular and smoking history, diabetes complications, comorbidities – was collected from medical documents and patient interview at baseline.

Information on documented episodes of symptomatic hypoglycemic episodes which occurred between study visits was collected at Visits 2 and 3. Symptomatic hypoglycemic episodes were defined as the presence of symptoms suggestive of hypoglycemia and a glucose value on glucose meter below 70 mg/dl. If the episode of hypoglycemia, as defined above, occurred between 00:00 and 06:00 hours, it was classified as nocturnal. Hypoglycemia episodes requiring assistance from another person were classified as severe.

Outcomes

The primary outcomes were: 1) the HbA1c levels attained at Visit 3 - 6 months following study enrollment – in the structured education and the control groups; and 2) the percentage of patients who achieved pre-set individualized HbA1c target in the two study groups. The secondary outcomes were the frequency of documented symptomatic hypoglycemic events (all and nocturnal) and of severe hypoglycemic events, change in weight, fasting glucose values and insulin doses from study enrollment until the end of study.

Statistical analysis

The evaluation of the first primary endpoint was based on a superiority test. Assuming that a 0.3%-point lower HbA1c in the structured education group at the end of the 6 months' follow-up period would show the superiority over the control group, at the level of two-side α=0.05 and with a 1:1 randomization, the estimated sample size to ensure a 90% power to reject the null hypothesis was 337 patients per study group. Considering a drop-out rate of around 10%, a total sample size of 750 patients (375 per study group) was calculated.

No interim analyses comparing the study groups were planned. All statistical analyses were performed in the intention-to-treat population (ITT) which comprised all randomized patient fulfilling the eligibility criteria.

Data was summarized using descriptive statistics: mean (standard deviation) or median (quartile 1; quartile 3) for continuous variables and proportions for qualitative variables. The comparison of HbA1c and fasting plasma levels between the two study groups was performed by independent samples t-tests, Mann-Whitney U test or median test according to the variables distribution; the comparison of % of patients achieving the target HbA1c levels and the frequency of hypoglycemia was performed by between-groups Chi-square tests.

A two-sided 0.05 significance level was applied to all tests.

Statistical analysis was carried out with IBM® SPSS® Statistics version 24 (SPSS Inc., Chicago, IL, USA).

Results

Study population

Between October 2014 and August 2015, 746 patients with T2D (371 in the structured education group and 375 in the control group) were enrolled at study participating centers. Of these, 35 did not fulfill the inclusion criteria (33 were aged 75 years or older, 2 had no age provided and 1 had no HbA1c measurement available at baseline) and were not included in the ITT population (Figure 1).

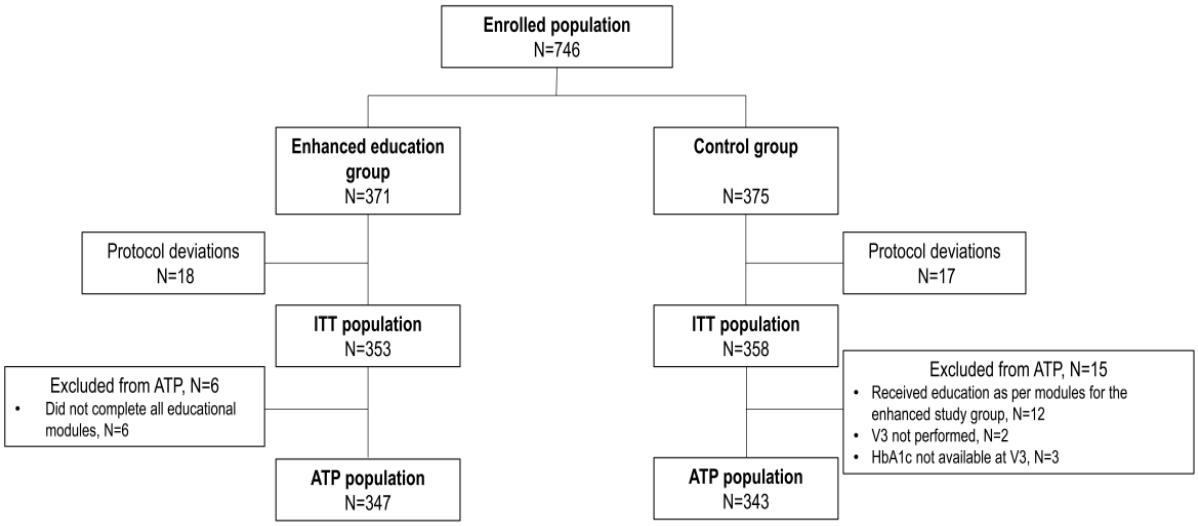

Figure 1. *Patient disposition.*
ITT = intention-to-treat; ATP = according-to-protocol; N = number of patients.

Table 1. Baseline characteristics of study population (ITT population).

	Control Group N=358	Enhanced education group N=353	p-value
Gender, n (%) Women	185 (52.1%)	188 (53.7%)	0.670
Age, years	59.6±8.1	59.2±9.0	0.513
Weight, kg	86.1±15.9	85.2±13.8	0.418
Waist circumference, cm	102.8±13.8	102.8±11.9	0.971
BMI, kg/m^{2*}	30.5 (27.6; 33.7)	30.5 (27.4; 33.6)	0.663
Diabetes duration, years	7.6±5.0	7.4±4.6	0.667

Table 1. *Continued*.

	Control Group N=358	Enhanced education group N=353	p-value
Antidiabetic treatment at baseline, n (%)			0.895
Monotherapy	84 (23.5%)	85 (24.1%)	
2 OADs	217 (60.6%)	219 (62.2%)	
3 OADs	55 (15.4%)	47 (13.3%)	
4 OADs	2 (0.6%)	2 (0.6%)	
Diabetic retinopathy, n (%)	62 (17.3%)	58 (16.4%)	0.752
Diabetic neuropathy, n (%)	198 (55.3%)	202 (57.2%)	0.607
Chronic renal disease, n (%)	38 (10.6%)	28 (8.0%)	0.222
Arterial hypertension, n (%)	273 (76.3%)	262 (74.2%)	0.529
Dyslipidemia, n (%)	259 (72.3%)	278 (78.8%)	0.047
Stroke, n (%)	24 (6.7%)	18 (5.1%)	0.364
Myocardial infarction, n (%)	24 (6.7%)	14 (4.0%)	0.105
Coronary heart disease, n (%)	143 (39.9%)	128 (36.3%)	0.312
Heart failure, n (%)	29 (8.1%)	36 (10.2%)	0.332
Smoker, n (%)	72 (20.2%)	67 (19.0%)	0.704

*Results are displayed as median (quartile 1; quartile 2)
For the other continuous variables results are displayed as mean±standard deviation
N = number of patients in each study group; n (%) = number (%) percentage of patients with a given characteristic; OAD = oral antidiabetics; BMI = body mass index;
ITT = intention-to-treat

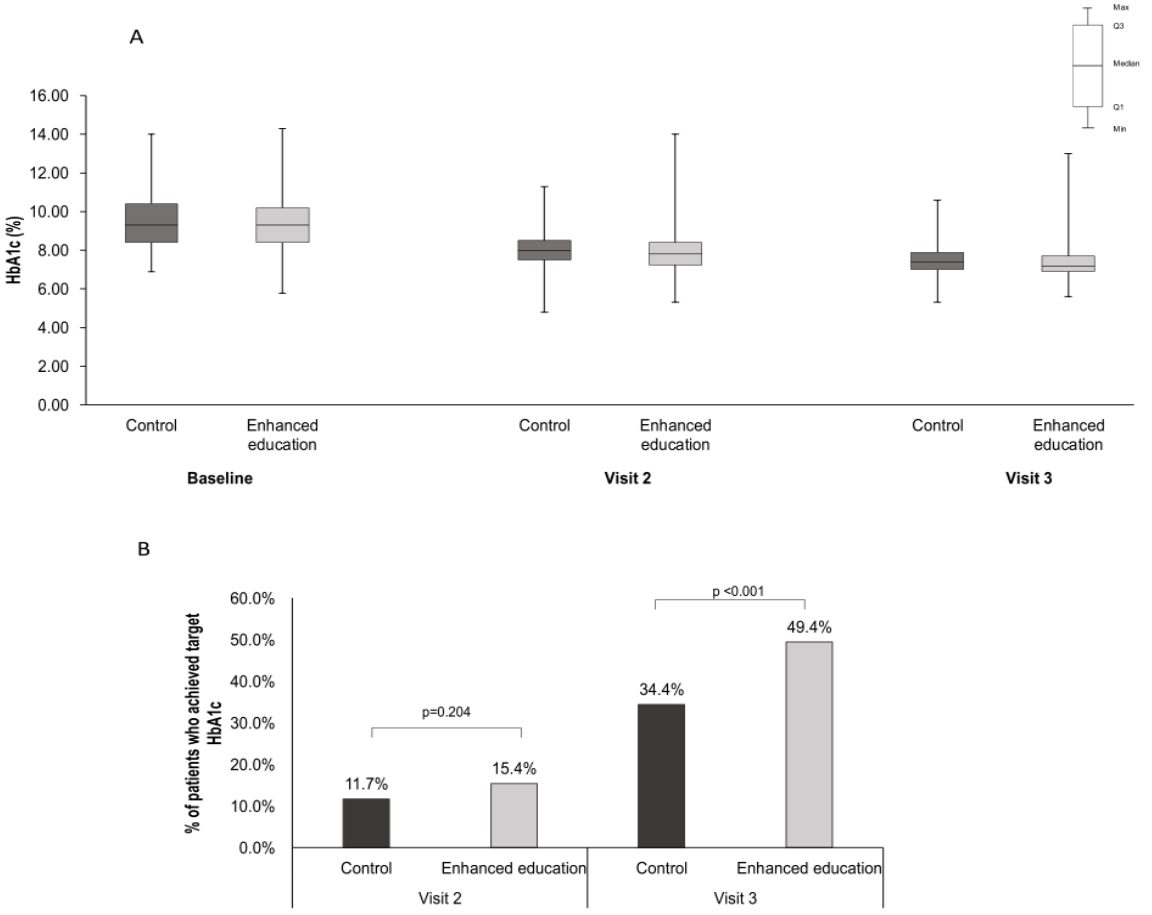

Figure 2. *HbA1c median levels (panel A) and frequency of patients achieving HbA1c individual targets (panel B; ITT population).* ITT = intention-to-treat; Min/Max, minimum/maximum; Q1 and Q3, first and third quartiles.

Except for the frequency of dyslipidemia, baseline characteristics were similar in the two study groups (Table 1). In both study groups mean age was 59 years and mean diabetes duration was 7 years. Median levels of the preset HbA1c targets established at baseline were similar between groups: 7.0% in the intervention group vs. 7.0% in the control group (p=0.905).

Glycemic control

At Visit 3, median HbA1c values were significantly lower in the structured education group compared to the control one: 7.2% vs. 7.4%, p <0.001 (Figure 2A). The percentage of patients who achieved individual treatment targets at Visit 3 was 49.4% in the structured education group, significantly higher compared to the control one (34.4%, p <0.001; Figure 2B). The decrease of median HbA1c from baseline to Visit 2 and Visit 3 was statistically significant in both study groups (p for trend <0.001). The median HbA1c decreased from 9.3% at baseline to 7.8% at Visit 2 and 7.2% at Visit 3 in the structured education group and from 9.3% at baseline to 7.8% at Visit 2 and 7.4% at Visit 3 in the control group.

The median HbA1c change at Visit 2 compared to baseline was -1.3% (-2.2%; -0.8%) in the enhanced education group and -1.2% (-2.1%; -0.6%) in the control group (p between groups=0.274). The median HbA1c change at Visit 3 compared to baseline was -2.0% (-2.9%; -1.3%) in the structured education group and -1.9% (-2.9%; -1.1%) in the control group (p between groups=0.274).

FPG had similar values at Visit 2 in the two study groups (median FPG was 140 mg/dl in the structured education group and 142 mg/dl in the control group); at Visit 3 the values were significantly lower in the structured education group compared to the control one (120.5 mg/dl vs. 128.0 mg/dl, p=0.005) (Table 2).

Table 2. Weight, fasting plasma glucose and basal insulin dose according to study group (ITT population)

	Control Group N=358	Enhanced education group N=353	p-value
Weight, kg			
Baseline	86.1±15.9	85.2±13.8	0.418
Visit 2	86.5±15.7	85.4±13.4	0.316
Visit 3	86.5±15.5	85.1±13.3	0.186
Fasting plasma glucose, mg/dl			
Baseline	120.0 (110.0; 130.0)	120.0 (110.0; 130.0)	0.548
Visit 2	142.0 (127.0; 161.0)	140.0 (123.0; 156.0)	0.071
Visit 3	128.0 (111.0; 143.0)	120.5 (108.0; 138.5)	0.005
Insulin dose, IU			
Baseline (recommended)	16.0 (12.0; 22.0)	16.0 (12.0; 20.0)	0.593
Visit 2 (last dose actually administered after titration)	24.0 (16.0; 30.0)	24.0 (18.0; 30.0)	0.958
Visit 3 (last dose actually administered after titration)	28.0 (18.0; 36.0)	28.0 (20.0; 36.0)	0.947

Results are displayed as mean±standard deviation for weight and as median (quartile 1; quartile 2) for fasting plasma glucose and insulin dose
ITT = intention-to-treat; N=number of patients

Insulin dose and oral antidiabetic agents

The median values of insulin dose were similar in the two study groups at all visits (Table 2). The median dose recommended at Baseline was 16.0 IU in both study groups. The median insulin dose reported by patients at Visit 2 was 24 IU in both study groups (ranging from 8 IU to 68 IU in the structured education group and from 4 IU to 80 IU in the control group) and at Visit 3 was 28 IU in both study groups (ranging from 8 IU to 72 IU in the structured education group and from 2 IU to 84 IU in the control group).

No statistically significant difference between the percentage of patients using a given antidiabetic class was observed at Baseline (Table 3). Except for α-glucosidase inhibitors which were more frequently prescribed in the structured education group, the use of oral antidiabetics classes was similar between groups also at Visit 3.

Table 3. Oral antidiabetic agents according to study group (ITT population).

	Control Group N=358	Enhanced education group N=353	p-value
Baseline			
Metformin, n (%)	317 (88.5%)	316 (89.5%)	0.679
Sulfonylurea, n (%)	288 (80.4%)	284 (80.5%)	0.998
Thiazolidinedione, n (%)	11 (3.1%)	6 (1.7%)	0.231
DPP-4 inhibitors, n (%)	29 (8.1%)	24 (6.8%)	0.509
Meglitinides, n (%)	13 (3.6%)	8 (2.3%)	0.282
α-glucosidase inhibitors, n (%)	33 (9.2%)	34 (9.6%)	0.850
Visit 3			
Metformin, n (%)	291 (81.3%)	301 (85.3%)	0.155
Sulfonylurea, n (%)	192 (53.6%)	188 (53.3%)	0.920
Thiazolidinedione, n (%)	3 (0.8%)	1 (0.3%)	0.323
DPP-4 inhibitors, n (%)	7 (2.0%)	7 (2.0%)	0.979
Meglitinides, n (%)	14 (3.9%)	9 (2.5%)	0.305
α-glucosidase inhibitors, n (%)	10 (2.8%)	21 (5.9%)	0.039

N = number of patients in each study group; n (%) = number (%) percentage of patients with a given characteristic; DPP-4 = dipeptidyl peptidase 4; ITT = intention-to-treat

Body weight

No difference in the body weight between the two study groups was observed during the study (Table 2). In the structured education group, the mean body weight was 85.2 kg at Baseline, 85.4 kg at Visit 2 (p=0.167 for Visit 1 vs. Visit 2) and 85.1 kg at Visit 3 (p-value for difference between Visits 2 and 3=0.013, p-value for difference from baseline=0.670). In the control group mean body weight increased from 86.1 kg at Baseline to 86.5 kg at Visit 2 (p=0.012) and maintained the same value at Visit 3 (p=0.519). Patients from the structured education group had a mean weight change from Baseline to Visit 3 of -0.09 kg and those in the control group of 0.29 kg (p=0.197 between groups).

Hypoglycemic events

At least one episode of documented symptomatic hypoglycemia was reported for 66 patients, 34 in the structured education group and 32 in the control group. Overall, 356 episodes of documented symptomatic hypoglycemia were reported: 139 in the structured education group and 217 in the control one. The median number of documented symptomatic hypoglycemic episodes per each patient who reported hypoglycemia was 3.0 in

the structured education group and 5.0 in the control group (Table 4; p=0.064). At least one episode of documented nocturnal symptomatic hypoglycemia was reported for 16 patients, 6 in the structured education group and 10 in the control group. Overall, 39 episodes of documented symptomatic nocturnal hypoglycemia were reported: 13 in the structured education group and 26 in the control one. The median number of documented nocturnal hypoglycemic episodes per each patient who reported symptomatic nocturnal hypoglycemia was 1.0 in the structured education group and 2.5 in the control group (Table 4; p=0.119). No episode of severe hypoglycemia was reported during the study.

Table 4. Number of documented symptomatic hypoglycemic episodes according to study group (ITT population)

	Control Group N=358	Enhanced education group N=353	p-value
Number of patients with at least 1 episode of symptomatic hypoglycaemia reported, n (%)	32 (8.9%)	34 (9.6%)	0.750
Number of patients with at least 1 episode of symptomatic hypoglycaemia reported, n (%)	10 (2.8%)	6 (1.7%)	0.326
Number of symptomatic hypoglycemic episodes; median (Q1; Q3)*	5.0 (2.0; 9.0)	3.0 (1.0; 6.0)	0.064
Number of nocturnal symptomatic hypoglycemic episodes; median (Q1; Q3)**	2.5 (1.0; 4.0)	1.0 (1.0; 1.0)	0.119

*Percentage calculated of those who reported at least one episode of documented symptomatic hypoglycemia
**Percentage calculated of those who reported at least one episode of documented nocturnal symptomatic hypoglycemia
N = number of patients in each study group; n (%) = number (%) percentage of patients with at least one hypoglycemic episode; Q1 and Q3 = first and third quartiles; ITT = intention-to-treat

Discussion

The main finding of this study was that a relatively short structured individual education (2 sessions over a 6-month period) was associated with an improved glycemic control in outpatients with T2D started on a basal insulin regimen when compared with basic education at insulin initiation according to local practice. The median HbA1c levels at 6 months after start of basal insulin in the structured education group were statistically significantly lower than in the control group (7.2% vs. 7.4%). From a clinical perspective, the effect of the two educational approaches may be regarded as similar. However, given that in Romania no standardized DSME programs are available to patients with diabetes and that the content, form and duration of diabetes education is highly variable and often limited by the limited access of patients to specialized diabetes educators , here we have shown that a structured educational program of only 2 sessions providing information pertaining more for a good clinical practice and affordable in term of time consumption for healthcare providers can provide additional benefits in term of glycemic control. Furthermore, this limited DSME intervention improved significantly the percentage of patients achieving the individualized glycemic targets set by their treating physician within 6 months from the insulin initiation. Compared to the control group, in our study a significantly higher percentage of patients in the structured education group achieved individualized HbA1c targets preset at study enrollment (50% vs. 34%).

Although the clinical significance of the difference of 0.2% between groups can be debated and the initial assumption of a 0.3% difference between groups was not reached, the results of our study are in line with previous studies which showed limited impact of DSME on HbA1c in patients with diabetes. The effects

of DSME on glycemic control in T2D was evaluated in a number of studies which were very heterogeneous in terms of demographic characteristics of study participants, antihyperglycemic treatments, type of interventions (individual or group sessions), frequency and duration of sessions, length of follow-up, among many other characteristics. In a meta-analysis published in 2009 [23], nine studies with a total of 1359 participants were included. From the nine studies, six compared individual education to usual care and three compared individual vs. group education. The overall quality of studies was not high and no long-term studies were found among those selected. Individual education did not significantly improve glycemic outcomes, with a weighted mean difference in HbA1c of -0.1% points. A subgroup analysis which included only studies involving participants with a mean baseline HbA1c greater than 8% found a difference of -0.3% points in HbA1c which was statistically significant. Group vs. individual education did not demonstrate different effects on HbA1c. In another meta-analysis including only studies with interventions of at least one session and ≥6-month follow-up group education was proven to have significant positive effects on HbA1c levels when compared to usual care [16], with a difference of 0.44% points at 6 months, 0.46% points at 12 months and 0.87% points at 24 months. Among studies included in the previously mentioned meta-analyses of Duke, Colagiuri & Colagiuri and Steinsbekk et al [16,23] no study specifically examined the effects of education in insulin-treated T2D.

Another important finding of our study was the effect of the structured education on the incidence of hypoglycemic episodes. Number of documented symptomatic hypoglycemic episodes (all and nocturnal) was lower in the intervention group but the difference did not reach statistical significance. The study was not powered to evaluate the effect of the DSME on the frequency of hypoglycemic events and this may explain the lack of statistical significance for the difference observed between groups. Clinically significant iatrogenic hypoglycemia represents an important cause of morbidity and mortality, a limiting factor in achieving glucose control in patients with diabetes [24] and an important driver of the decreased quality of life of patients with diabetes [25]. Intensification of diabetes management to achieve optimal diabetes control is frequently associated with hypoglycemic episodes [26,27] and severe hypoglycemia has been associated with cognitive impairment [28], increased risk of dementia [29], and increased mortality [30,31]. Furthermore, hypoglycemic episodes have been associated with a lower quality of life. Fear of hypoglycemia may determine patients to engage in behaviors aiming at preventing new hypoglycemic episodes, such as omitting insulin doses, administering lower insulin doses than needed or overeating, and thus increasing the risk of poor diabetes control and consequent diabetes associated chronic complications [32]. Previous interventional clinical studies have shown both in patients with type 1 and type 2 diabetes, treated with insulin or oral antidiabetics, that structured educational programs may improve diabetes control while having also a beneficial effect on the frequency of hypoglycemic episodes [33,34].

The positive results of our study could contribute to a better understanding of the benefits of a relative simple, non-time or resource consuming DSME programs in patients with T2D. This is particularly important when insulin treatment becomes necessary and when psychological insulin resistance needs to be overcome not only in terms of accepting the treatment but also because insulin titration is a

well-recognized requirement for optimal glucose control. To the best of our knowledge, Basal-EDUC-RO Study is the largest study examining the effects on glucose control when a structured diabetes education program is applied in patients with insulin-treated T2D, with over 700 patients included. It is also the only study yet performed in the field of diabetes education which included patients newly started on a basal insulin analogue.

Several limitations of the study should be acknowledged. Measurements of HbA1c at baseline and during study were done in local laboratories. However, all local laboratories were accredited by the National Accreditation Authority, which requires use of standardized methods for HbA1c determination. Patients were provided with blood glucose diaries but completion of blood glucose values and of episodes of hypoglycemia were not mandatory because of concerns of limiting patients' compliance to other study procedures. This limitation could have resulted in lower rates of reported hypoglycemic episodes, although the limitation could equally apply to both groups. At site level, the same study nurse delivered the structured diabetes education and the basic diabetes education sessions, which might represent a bias with regards to information provided. This bias was at least in part avoided through organizing a pre-study training for nurses involved in the study; the importance of complying with the two different education strategies as part of study design was clearly explained, as well as the possible impact of non-compliance on study outcomes.

Conclusion

A structured diabetes education program delivered to patients with T2D at initiation of a basal insulin analogue significantly improved glucose control at 6 months compared to a less intense education strategy.

The positive effect was mainly seen in the percentage of patients who achieved individualized HbA1c pre-set targets, with a non-significant reduction in the episodes of overall and nocturnal documented symptomatic hypoglycemia.

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