

The DIAB.&TE.S Project: How patients perceive diabetes and diabetes therapy

**Investigators involved in the study are listed in the appendix*

Abstract. Assessment of quality of life (QoL) in diabetic patients is increasingly retained as a crucial parameter to take into account before concluding on the efficacy of new therapies. Indeed, the trend is to adopt treatments providing a genuine clinical benefit associated with a positive impact on QoL. In this context, DIAB.&TE.S Project aimed at analyzing patient's perception of psychological well-being, quality of treatment and their correlation with glyco-metabolic values control. A total of 1918 diabetic patients, mostly from southern Italy, were enrolled in this observational study. DIAB.&TE.S included a wide range of patients taking insulin monotherapy, OHA (oral hypoglycemic agents) monotherapy or combined therapy (insulin + OHA). Internationally recognized instruments such as the Well-Being Questionnaire (WBQ) and Diabetes Treatment Satisfaction Questionnaire (DTSQ) were used to assess general well-being and diabetes treatment satisfaction. Combined therapy was not highly efficient in achieving both glycemic and quality of life goals when compared to insulin or OHA monotherapies. Oral monotherapy produced better results if compared to insulin treatment, as demonstrated by DTSQ and WBQ scores. However, among the insulin treated subjects, higher scores were reached in patients using advanced devices to administrate insulin. Finally, a correlation between questionnaires outcomes and metabolic control in patients could be established. Our findings support the idea that in diabetes therapy, integration of clinical and psychosocial cares could be helpful in both identifying subjects that need a treatment re-examination and improving patient's quality of life. In addition, this survey by its magnitude provides an overview of diabetes management in Italy and contributes to set up an accurate profile of diabetic people in this part of Europe.

Key words: Diabetes, insulin therapy, insulin devices, DTSQ, WBQ, quality of life

Introduction

Diabetes mellitus is one of the worldwide most common chronic diseases, with a prevalence that approaches 8% of the adult occidental population (1). Disease-associated complications, including retinopathy, nephropathy and neuropathy, increase with the degree of hyperglycemia (2), with a more rapid progression when blood glucose is poorly controlled (3). Thus, numerous efforts have been produced in order

to define new strategies enabling a better control of metabolic patterns and to reduce diabetes-related complications. Besides, beyond physical ill-health related problems, diabetes is endowed of profound effects on the quality of life (QoL) in terms of psychosocial difficulties, which in turn could lead to a deep worsening of the pathology (4). Treatment itself can even exert a strong influence on patients' quality of life. As a matter of fact, quality of life is nowadays considered a key variable of the outcome of therapy, and

has to be taken into account when evaluating the efficacy of new treatments and devices in the management of diabetes (5). In keeping with this line of thinking, a successful treatment approach would include, as major objectives, the restraint of disease-associated complications together with the understanding of the social and psychological ramifications of diabetes (6).

Among the numerous instruments aimed at evaluating patients' perception of their quality of life, the Well-Being Questionnaire (WBQ) and the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (7) have been recommended by St. Vincent Declaration in order to monitor psychological well-being and treatment satisfaction (8,9). Such questionnaires are at the present time internationally recognized as valuable tools, and consequently have been widely used in numerous clinical trials (10), including the *multicentre Diabcare initiative* (11).

The DIAB.&TE.S project, which stands for Diabetes and Territory Survey, sought to give an overview of the well-being status as well as quality of treatment as directly perceived by the patient.

Three were the core objectives of the DIAB.&TE.S project: to collect epidemiological data about diabetes treatment and insulin device use; to get reliable results throughout the use of standard evaluation instruments, and to obtain *real life* data by means of collaboration with the patients.

Materials and Methods

The DIAB.&TE.S project's uniqueness consisted in involving diabetes centers mostly spread peripherally, all over 3 southern Italian regions and partially in 1 Italian northern region, where the physicians would have been the predominantly figure in contact with the patient. In this sense, DIAB&TES gave access to a sample population not easily reachable for big cities structures.

Ninety diabetes centers, spread in those regions, were asked to participate in the project. Seventy-nine centers have accepted to participate, collecting data from 1,918 diabetic patients. Each physician, who was also responsible for diabetes treatment of his/her

group of patients, collected a minimum set of information (anonymous) for each patient enrolled, including socio-demographic and clinical characteristics.

Subjects were enrolled by using random sampling lists, stratified by diabetes therapy (OHA only, OHA plus insulin, only insulin therapy). Each centre was asked to recruit 36 patients (12 per stratum). Patients were considered not eligible if they were illiterate or unable to fill in the questionnaire for mental problems, if they had type 2 diabetes controlled with diet only or if they suffered from serious co-morbidities.

Patients, on the occasion of the encounter, were asked to fill up three anonymous self-evaluation questionnaires regarding their quality of life and their satisfaction with the treatment they were subjected to. A specific code center and patient gave the possibility to link the physician's anamnesis report with the patient's questionnaires. Self-administered instruments were chosen among those internationally recognized and were: WBQ and DTSQ

The WBQ provides a measure of depressed mood, anxiety, and various aspects of positive well-being and has been primarily used in studies evaluating the effects of new treatments on cognitive symptoms (8). The questionnaire includes four subscales labelled depression (6 items), anxiety (6 items), energy (4 items) and positive well-being (6 items). Each item is scored on a 0 to 3 Likert scale, indicating how frequent the situation applied to the patient in the past few weeks (from "not at all" to "all the time"). A higher score on each subscale indicates a higher level of the mood being measured. A General Well-Being total score can also be obtained by summing up all the 22 items, after reversing the scores of the Depression and Anxiety subscales.

The DTSQ has been specifically designed to measure satisfaction with diabetes treatment regimens and is appropriate for patients with Type 1 and Type 2 diabetes (9). The instrument was originally developed to detect changes in satisfaction related to changes in treatment modalities but it is also appropriate for comparing levels of satisfaction in subjects using different treatment regimens. It is composed of 8 items, 6 of which are summed in a single score ranging from 0 (very dissatisfied) to 36 (very satisfied). The remaining 2 items are individually treated and explore

the perceived frequency of hyperglycemic and hypoglycemic episodes.

Statistical Analysis

Demographic variables of the sample were summarized by using descriptive statistics, such as mean, standard deviation and proportion. For the comparison of the scores in different patient subgroups, Kruskal Wallis 1-way ANOVA was used. A $P < 0.05$ value was considered as statistically significant.

Results

Among the total number of patients, 44.7% were men (mean age was 61 years), 53.3% were women (mean age was 62 years). Analysis of the composition by decade of age showed that the majority of patients aged between 60 and 70 years, whereas one fifth of them were less than 50 years of age. There was a prevalence of women in the > 60 yrs old classes; such a fact could be attributed to longer life span in women rather than some bias in recruitment processes or epidemiological reasons.

The subjects had, in general, a low level of scholarship, in fact two third (66%) stopped school after junior high. Patients retired from work represented 42% of the total; housewives were 31.6%, whereas working subjects were only 22.9% of the total, approximately three quarters of those being men.

Diabetes duration in patients enrolled in the survey was also assessed; 52.8% of the total suffered from diabetes for a minimum of 11 years. Among the patients enrolled, the majority was type II diabetics and only 9.7% suffered from type I diabetes. Obesity affected more than half of the population of the study, mostly women and patients Type II. More than 50% of the subjects developed one or more complications related to the disease, with retinopathy being the most represented. Among the concomitant pathologies, hypertension (70%) and hypercholesterolemia (45%) were the most frequent ones, whereas only 23.9% of the patients were not affected by any other disease.

Indeed, 41.7% of the patients used oral hypoglycemic agents (OHA), 27.1% used a combination of OHA and insulin and 31.2% used insulin alone (Figure 1A).

Among the insulin users, 52.2 % of the subjects used pre-mixed insulin and only a small fraction ($< 3\%$) used instant preparation of insulin.

The majority of the patients (60%) performed a minimum of 3 insulin injections a day, 19% performed 2 insulin injections a day and 20.2% only one injection a day. In these patients, the daily insulin dose ranged from 16 units (for those performing 1 injection) to 52 units (for those performing more than 4 injections). The mean insulin dose was 36 units/day. Among the devices used to deliver insulin, the durable pen was the most widely used (in 51.6% of the cases). The remaining number of patients could be divided into two groups, the syringe users (26.7%) and the pre-filled pen users (24.5%) (Figure 1B).

Figure 2 shows the results obtained by analyzing the outcomes of the patients' replies, clustered by dif-

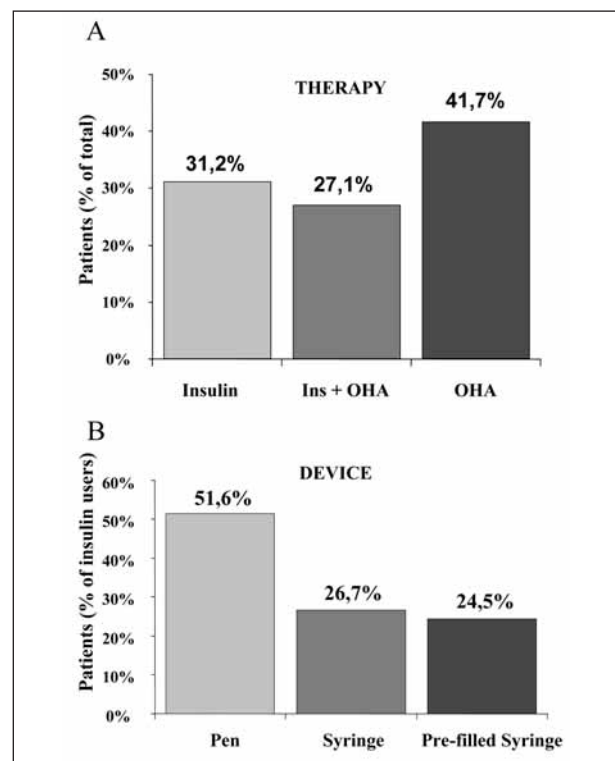


Figure 1. Patients distribution by type of treatment (A) and by device used (B; insulin treated subjects only)

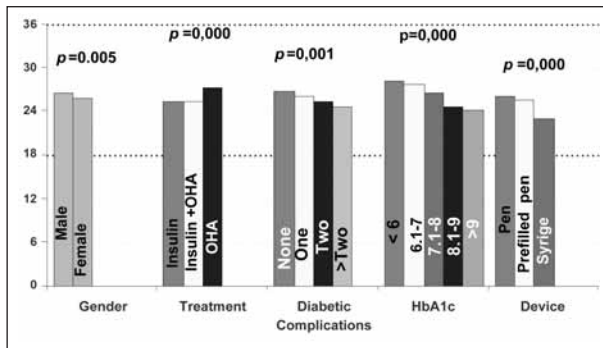


Figure 2. Outcome of the replies (mean score) to DTSQ analyzed by patients sub-targets

ferent sub-targets. Men were in general more satisfied than women about their treatment. Better results were achieved in patients treated with OHA monotherapy if compared to those treated with insulin or combined therapy. As expected, a less treatment satisfaction could be observed in correlation with exacerbated disease-related complications.

Interestingly, within insulin treated patients, a significant difference in DTSQ scores was reported by subjects using advanced devices (pre-filled and durable pen) compared to those using the syringe. Finally, there was an inverse correlation between treatment satisfaction and HbA1c levels, indicating that the questionnaire could be informative to some extent regarding glyco-metabolic parameters.

WBQ was used as an instrument to assess psychological well-being in patients, taking into account the type of treatment followed (insulin, insulin +OHA, OHA) or the device used to implement insulin injections (durable pen, syringe, pre-filled pen). Four items were considered: energy, well-being, anxiety and depression. Scores obtained for each item of the questionnaire are reported. As shown in figure 3A, the use of insulin reduced WBQ mean scores for energy and well-being items and increased mean scores for anxiety and depression items. The outcomes obtained in patients using the syringe were similar (Figure 3B), compared to those using the pen or the pre-filled pen. On the contrary, relatively high WBQ mean scores for energy and well being items (and relatively low for anxiety and depression) were reported in patients subjected to OHA monotherapy.

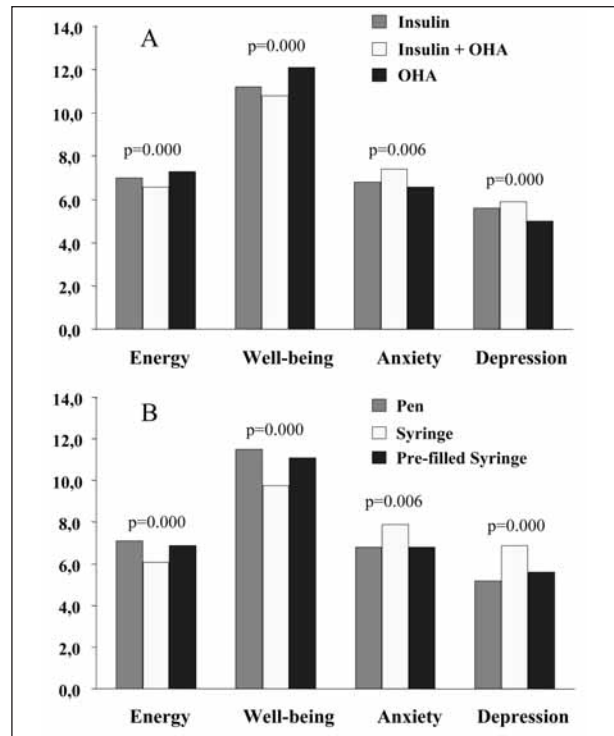


Figure 3. Outcome of the replies (mean score) to WBQ assessed by type of treatment (A) and by device used (B; insulin treated subjects only)

Taken together the results illustrated in Figure 3A and 3B indicate that when insulin therapy is adopted, the use of advanced devices to administrate insulin would contribute to improve in a significant way the psychological well-being in patients. Besides, patients using the traditional syringe have overall a worse health status and present some socio-demographic characteristics summarized in Table 1. They are mostly men with a low educational level, a mean age of 66 years and a long history of type II diabetes with a relatively high blood pressure. In addition, analysis of WBQ mean scores clustered by genders showed that anxiety and depression scales are significantly higher in women (data not shown).

Parameters of metabolic control were also measured and analyzed according to the type of treatment followed by the patients. Statistically significant values are reported in Table 2. In the group of patients undergoing combination therapy (insulin +OHA), almost all metabolic values were slightly more elevated when compared to insulin or OHA mono-therapies.

Table 1. Comparison of main characteristics of syringe user vs other devices users

Patient's characteristics and parameters	Syringe users	Other devices users
Male (%)	37.0	43.4
Degree (%)	12.3	25.2
Age (years)	66.0 ± 10.8	59.0 ± 14.5
Type II (% of patients)	90.2	81.6
Time since diabetes onset (years)	17.3 ± 9.7	15.6 ± 9.8
Time since treatment beginning (years)	6.0 ± 7.0	6.2 ± 7.4
HbA1c (%)	8.3 ± 1.8	8.0 ± 1.6
Systolic/diastolic pressure (mm Hg)	78/138	77/134
Total cholesterol (mg/dL)	195.6 ± 36.3	196.7 ± 37
Triglyceridemia (mg/dL)	150.6 ± 78	144.5 ± 93.8
Creatinemia (mg/dL)	0.99 ± 0.58	1.05 ± 0.94

Table 2. Main clinical parameters values (breakdown by type of treatment)

Glyco-metabolic parameters	Insulin	Insulin + OHA	OHA
Systolic pressure (mm Hg)	132.5	138.3	136.4
Diastolic pressure (mm Hg)	76.8	78.2	79.3
HbA1c (%)	8.0	8.2	7.3
Total Cholesterol (mg/dL)	193.4	200.7	199.8
Triglyceridemia (mg/dL)	132.4	163.2	151.6
Microalbuminuria (% of patients)	18.2	21.9	14.2
Proteinuria (% of patients)	7.3	5.9	3.9

Finally, considering the principal characteristics of the subjects (age, type of diabetes, educational level and treatment), patients enrolled in the DIAB.&TES project could be clustered into 4 groups. Briefly, group #1 represented 64% of the patients, they were elderly subjects, with a type II diabetes, a low educational level and taking OHA; group #2 represented 12% of the patients, they were mature, well educated subjects, with type II diabetes and under a combined therapy (insulin +OHA); group #3 represented 13% of the patients, these subjects presented the same features as the previous group with the exception of their treatment which entirely relied on OHA; group #4 represented 6% of the sampling, they were relatively young, highly educated subjects, with a type I diabetes and using the highest daily dose of insulin.

Discussion and conclusions

Due to the chronic nature of diabetes and the peculiarities of its treatment-associated complications, it is crucial to consider the disease from clinical as well

as psychosocial points of view (12). DIAB.&TES project represents an observational study in line with the above concept and aimed to find which demographic and treatment issues could be focused in considering the quality of life in the diabetic population studied.

Other investigators have previously assessed, discussed and subsequently validated the efficacy of questionnaires such as the DTSQ and WBQ to evaluate the patients' perception of their quality of life (9, 13). This survey adds to this end by demonstrating a correlation between the outcomes of the replies to the questionnaires, demographic characteristics, the health status and the type of anti-diabetic treatment in these patients. Subjects reported superior treatment satisfaction and well-being when treated with OHA only or insulin monotherapies if compared to the insulin-OHA combination therapy. It could demonstrate that this approach (which, in the history of diabetic patients, generally represents a bridge from OHA period to the full insulin regimen period) is a sub-optimal starting for insulin therapy and is not as efficient as the other therapies to help patients in metabolic pa-

rameters control probably because of a late setting up of insulin therapy in those patients.

One might also speculate that starting insulin therapy (as in the OHA-insulin group) is perceived more as a hassle by patients with respect to the oral medication. Nevertheless, a more accurate analysis of the insulin treated subjects demonstrated that syringe using patients were significantly less satisfied than those using more advanced devices, namely the durable or the pre-filled pen. The heterogeneity in the devices used to deliver insulin might therefore account for the disparity observed in terms of quality of treatment and well-being when comparing insulin and OHA monotherapies. Along with this rationale, despite the fact that switching to injectable insulin is perceived as a major concern among patients taking oral agents, in other investigations DTSQ demonstrated that treatment satisfaction usually increases in patients upon switching to insulin (11, 14). Moreover, it is worth noticing that our study and earlier others performed in over 60 years old patients (15, 16) confirmed that advanced insulin devices, such as pre-filled pen, were highly accepted in this population, and resulted in an improvement of metabolic control, as measured by HbA1c levels.

The fact that the crossover analysis of questionnaires and clinical-metabolic evaluations were mostly in concurrence was also supported by other investigators (15, 17), and provided the possibility to cluster patients in different groups, identifying those with higher risks, that is to say: a) diabetic women; b) subjects treated with combination of insulin plus OHA; c) syringe using subjects. These are the subjects in major need of a targeted therapeutic and educational effort. Although it may appear anomalous, the combination OHA plus insulin therapy not only produced the worst outcomes to the items assessed by the questionnaires but also was poorly effective in glyco-metabolic control, likely because of poor compliance. It could be also hypothesized that in these patients insulin treatment was not prompt and/or inadequate in terms of dosing.

Results from this investigation show how instruments nowadays available for the evaluation of both quality of life and treatment could facilitate the understanding of diabetes studies outcomes. In addition,

such resources allowed us to depict general features of a diabetic population at a territorial level and to identify groups of patients in need of specific therapeutic targeting.

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