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Article

Quality of life perception of type 1 diabetic patients treated with insulin analogs and receiving medication review with follow-up in a public health care service from Ponta Grossa-PR, Brazil

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Glycemic control in patients with diabetes mellitus type 1 (DM1) reduces the risk of complications but requires a rigorous health care routine. Thus, diabetes education is central to increasing treatment compliance and self-care practices. This study aimed to evaluate the quality of life (QoL) and glycemic control of DM1 patients being treated with insulin analogs and receiving medication review with follow-up. This was a transversal study that included 110 patients registered at the 3rd Health Regional of Ponta Grossa-PR, aged ≥ 18 years, and receiving pharmaceutical care for at least 1 year. The Diabetes Quality of Life Measure (DQOL)-Brazil was used to evaluate QoL. The data were statistically analyzed using SPSS version 17.0 with 95% confidence levels. Of the 110 patients, 58.2% were women. The average age was 33.7 years (±10.5), and the average glycated hemoglobin (HbA1c) value was 8% (±1.4). The mean total DQOL-Brazil score was 2.11 (95% confidence interval, 2.02 – 2.21). All DQOL-Brazil scores were lower in patients with HbA1c ≤ 8%, indicating a better QoL. Good glycemic control, thus, appears to have a positive influence on the QoL, and pharmaceutical interventions are able to contribute to the achievement of therapeutic targets.

Uniterms: Diabetes mellitus type 1/treatment. Diabetes mellitus type 1/treatment/quality of life. Pharmaceutical care. Insulin analogs. Pharmacotherapy follow-up.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders primarily characterized by chronic hyperglycemia. High glycemic levels are associated with micro- and macrovascular complications leading to damage to, and failure of organs such as the eyes (retinopathy), kidneys (nephropathy), nerves (neuropathy), heart, and blood vessels (ADA, 2016; Braga de Souza *et al*., 2015; Gross *et al.*, 2002).

According to the Diabetes Control and Complications Trial (DCCT), the risk of developing chronic complications is higher in patients with chronically high glycated hemoglobin (HbA1c) levels, and the risk gradually increases with HbA1c levels greater than 7% (Pimazoni Netto *et al.*, 2009). The American Diabetes Association (ADA) defines an HbA1c value < 7% as the acceptable limit for diabetes control. With good glycemic control, patients can be symptom-free, and prevent acute and chronic complications (ADA, 2016; UKPDS, 1999; DCCT, 1988).

DM is a chronic condition that requires daily self-care throughout life and has a negative impact on the subjective perception of the quality of life (QoL). However, daily treatment is fundamental to DM control and decreases the risk of complications (Debaty *et al.*, 2008; Wood-Dauphinee, 1999). DM1 therapy includes intensive care demands such as daily blood glucose monitoring, multiple insulin injections, and specific dietary and physical activity recommendations (ADA, 2016). Not understanding all these recommendations and a lack of compliance to treatment leads to a poor glycemic control that can cause severe hyper- or hypoglycemia episodes and chronic complications, affecting QoL.

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Furthermore, a constant fear of these acute and chronic complications can also decrease QoL perception (Braga de Souza *et al.*, 2015; Trento *et al*., 2013).

Understanding every stage of insulin treatment and non-pharmacological therapy besides the risk of developing complications is essential to achieve therapeutic targets. However, some patients have social, cultural, and educational limitations that may decrease compliance to treatment (Kahlili *et al*., 2016; Braga de Souza, *et al*., 2015; Jimmy, Jose, 2011). Thus, diabetes education and continued patient follow-up are central to increasing knowledge of the disease and treatment, developing self-care skills, and reducing and maintaining glycemic levels as established by the ADA, all of which have a positive effect on QoL perception (Brasil, 2013; Falconier *et al.*, 2009; Debaty *et al.*, 2008).

In this context, diabetic patients' QoL is influenced by factors such as age, sex, obesity, comorbidities, complications, knowledge regarding DM, type of treatment, and glycemic control. The Health-Related Quality of Life (HRQoL) has been used to evaluate the impact of diabetes and its treatment on patient humanistic outcomes as it relates health, not to the absence of disease, but as complete physical; mental; and social well-being (Braga de Souza *et al*., 2015; Trento *et al*., 2013; Falconier *et al.*, 2009; Debaty *et al.*, 2008; Cases *et al.*, 2003; HSGCD, 2001; Testa, Simonson, 1996).

The Diabetes Quality of Life Measure (DQOL), which measures the disease impact and the restrictions imposed on different areas of daily life, is the most commonly used instrument to evaluate QoL in patients with diabetes (Brasil *et al.*, 2015; Brasil, 2013; Falconier *et al.*, 2009; Debaty *et al.*, 2008; Cases *et al.*, 2003; Redekop *et al.*, 2002; HSGCD, 2001; Testa, Simonson, 1996; Gafni, Birch, 1993). It was originally developed by the DCCT group in English, and the Portuguese version was translated, adapted, and validated in Brazil (Brasil *et al.*, 2015; Correr *et al.*, 2008; Melchiors *et al.*, 2005; Coffey, Brandle, Zhou, 2002; DCCT, 1988).

QoL has been used around the world as a relevant parameter to evaluate the results and quality of health care services; it is particularly useful for patients with chronic diseases in whom the QoL is a critical outcome once the cure of chronic condition is not ensured (Quah *et al.*, 2016; Haines *et al.*, 2016; Trento *et al.*, 2013; Wood-Dauphinee, 1999). Studies suggest that the type of insulin treatment can modify QoL perception. Insulin analogs demonstrate better glycemic control with less severe episodes of hypoglycemia and postprandial hyperglycemia when compared with human insulin, and produce greater satisfaction with treatment, and thus, can have a positive impact on the QoL of DM patients (Wojciechowski *et al*., 2015; Rys *et al*., 2011; Shatlin, Philip, 2008). Therefore, this study evaluated the QoL of DM1 patients being treated with insulin analogs and receiving medication reviews with follow-up.

MATERIAL AND METHODS

Participants

Patients were invited to participate in the study at the time of drug dispensation. The sample size was calculated based on a 5% rate of error and a 95% level of confidence. The sampling process was systematic, based on accessibility sampling (Marotti *et al.*, 2008), and in accordance with the inclusion and exclusion criteria. The inclusion criteria for participation were: age ≥ 18 years, a diagnosis of DM1, treatment with insulin analogs and medication review with follow-up for at least a year, and indication of willingness to participate in this research by signing the Terms of Consent (TCLE). Patients with high understanding- and visual difficulties, hypoglycemia or mental confusion at the time of questionnaire administration, and those that did not fit the inclusion criteria were excluded.

This is a transversal study, performed at the Especial Pharmacy of 3rd Health Regional of Ponta Grossa-PR, where patients are registered to receive free DM1 medication and supplies and are included in the pharmaceutical care program. Medications are dispensed monthly; the patient's health condition is evaluated at the first dispensation, and pharmaceutical care service is offered. Glycemic control is assessed based on HbA1c values, and frequency of hypo- or hyperglycemic events. Poor glycemic control, low understanding, and low treatment compliance result in increased frequency of pharmacist consultations. Medication review with follow-up is offered once a week in the first month, then once every two weeks, and then once a month until the participating patients fully understand the treatment with insulin analogs and non-pharmacological treatment.

The pharmaceutical care service provided information and interventions such as a) insulin analogs therapy: handling automatic insulin delivery pens, injection techniques, frequency and schedule of administration, correct dose calculation of short-acting insulin at every meal, risks of wrong dosage, transportation and home storage, and appropriate discard procedure for contaminated needles and lancets; b) blood glucose self-monitoring: technique, importance of daily monitoring, interpretation of glycemic results,

dealing with hypoglycemic episodes, need to achieve and maintaining HbA1c target, and education regarding the risk of acute and chronic complications; c) non-pharmacological treatment: dietary and physical activity recommendations (patients are referred to a nutritionist or a physical educator, as needed).

Sociodemographic data were obtained from questionnaire-based interviews. To evaluate glycemic control, we considered the most recent HbA1c values at the time of questionnaire administration. Questionnaire administration and data collection were conducted from July 2013 to December 2013. HbA1c values were collected from the electronic system of the Management and Follow-up of Medication unit of the Specialized Component of Pharmaceutical Assistance, where the patients are registered in the DM1 Optimization Program of the State of Parana to receive free DM1 treatment.

HbA1c is one of the required parameters from the DM1 Optimization Program to evaluate glycemic control, and some studies have shown its negative influence on the QoL of patient with DM (Tahirovic *et al.*, 2012; Campbell, 2002; HSGCD, 2001). However, the impact of glycemic control on QoL remains controversial, and other variables need to be considered for more reliable results (Braga de Souza *et al*., 2015). Although validated instruments are available to evaluate treatment compliance (Jimmy, Jose, 2011), in the context of the present study, HbA1c values were more appropriate as the focus was to evaluate QoL.

Quality of life

QoL was evaluated using the DQOL-Brazil instrument consisting of 44 multiple-choice questions, divided into four domains: satisfaction (15 questions), impact (18 questions), vocational/social preoccupations (7 questions), and diabetes-related concerns (4 questions). The DQOL-Brazil answers are organized using an inverted 5-point Likert scale, and scores range from 1 to 5. Scores closer to one reflect a better QoL.

The DQOL-Brazil is a self-administered questionnaire, but for patients with visual or motor skill impairments, the instrument was administered via a structured interview; the questions were read out exactly as written, and the answers were marked appropriately. To reduce bias the researchers administering the questionnaire received standard training to ask questions directly and without extra comments.

Statistical analysis

To evaluate the internal consistency and questionnaire reliability, Cronbach's alpha was calculated separately for each individual domain, and for the instrument as a whole. Values greater than 0.7 were considered acceptable (Hair *et al.*, 1998).

The results were tested for normality of distribution using the Kolmogorov-Smirnov test, and other appropriate statistical tests were utilized.

Spearman's correlation coefficient was used to identify associations between the DQOL-Brazil scores and the continuous variables in the sample population. The Mann-Whitney test was used to compare the averages.

Statistical calculations were performed using SPSS version 17.0 with a 95% confidence levels.

Ethics

This research project was approved by the Research Ethic Committee of State University of Ponta Grossa (protocol nº 127.211/2012).

RESULTS

The calculated sample size was 130 patients. However, only 110 patients agreed to participate in the study and signed the TCLE. Of the 110 participants who answered the DQOL-Brazil questionnaire, 58.2% were women. The participants' ages ranged from 19 to 65 years, with an average of 33.7 years (± 10.5). The average HbA1c value was 8.0% (±1.4), with a range of 5.0 to 12.1%. The mean duration of questionnaire administration was 10 minutes.

The average DQOL-Brazil score was 2.11 (95% confidence interval (CI) 2.02 – 2.21). Among the domains, the average scores were 2.17 (95% CI 2.04 – 2.29) for satisfaction, 2.08 (95% CI 1.99 – 2.18) for impact, 1.94 (95% CI 1.77 – 2.10) for vocational/social preoccupations, and 2.37 (95% CI 2.23 – 2.50) for diabetes concern.

The total score and the scores for satisfaction, impact, and diabetes concern exhibited a normal distribution on a Kolmogorov-Smirnov test; the age and HbA1c values were also normally distributed. However, normal distribution was not verified for vocational/social preoccupation domain score.

The reliability analyses (internal consistency) for the total questionnaire and its individual domains are shown in Table I.

The correlations between the individual domain scores and the total instrument score are presented in Table II. The DQOL-Brazil domains were interrelated and had significant positive correlations with the total questionnaire score ($p < 0.01$).

TABLE I - Internal Consistency analysis of the Satisfaction, Impact, and Preoccupations domains of the DQOL-Brazil for DM1 patients

	Number of items	Cronbach's alpha
Total DQOL-Brazil	44	0.92
Satisfaction	15	0.88
Impact	18	0.85
Vocational/Social preoccupations	7	0.82
Diabetes concern	4	0.78

We observed sex-specific differences in the perception of QoL (Table III). Women showed significantly higher scores in satisfaction, impact, diabetes concern domains, and in the total score than men. The vocational/social preoccupation scores were not significantly different, even though they were higher in women.

Age was negatively correlated ($p < 0.01$) with the vocational/social preoccupations domain score suggesting that lower QoL scores and hence, a better perception of QoL was related to more advanced age.

HbA1c, which is a highly specific marker for DM, showed a significant positive correlation ($p<0.05$) with the scores for satisfaction and impact domains, as well as with the total instrument score.

Using glycemic control results as indicated by the HbA1c levels, the total and individual domain scores were compared to determine whether the questionnaire could distinguish participants with different HbA1c levels. The HbA1c level was chosen as it is the gold standard for diabetes treatment monitoring and as there is a direct relationship between a patient's mean glycemia and the chronic disease complications (SBD, 2003).

As illustrated in Table IV, the average score for the total instrument, and for the satisfaction and impact domains differed based on participants' HbA1c levels (>8% vs. <8%). Despite the lack of significance for the preoccupations domain, participants with HbA1c values ≤ 8% exhibited lower scores for all the domains, indicating a better QoL. Therefore, our data suggests that better glycemic control is associated with a better subjective perception of QoL.

DISCUSSION

The DQOL-Brazil questionnaire is divided into four domains that evaluate the influence of DM1 on several aspects of life: the impact of DM1 and its treatment on the social life, family, and job, and the impact the disease has on patient's health-related concerns. Poor glycemic control greatly increases the likelihood of experiencing hypo- or hyperglycemic events, thereby increasing the risk of developing chronic complications, that can, in turn, affect the QoL perception of patients.

Several studies have reported sex-specific differences in the QoL perception, and women usually score higher;

TABLE II - Correlations between the domain scores and the total score obtained from the DQOL-Brazil administered to DM1 patients

	Satisfaction	Impact	Vocational/Social Preoccupations	Diabetes Concern	Total DQOL-Brazil
Satisfaction	-	0.62	0.28	0.45	0.83
Impact	0.62	-	0.47	0.63	0.89
Vocational/Social Preoccupations	0.28	0.47	-	0.44	0.61
Diabetes Concern	0.45	0.63	0.44	-	0.70

Correlation analyses using Spearman's coefficient. All the "r" values were significant ($p<0.01$).

TABLE III - Scores of DQOL-Brazil according to sex

	Men	Women	p value
Satisfaction	1,99	2,29	0.013
Impact	1,98	2,16	0.033
Vocational/Social Preoccupation	1,85	2,00	0.229
Diabetes Concern	2,25	2,45	0.040
Total DQOL-Brazil	1,99	2,21	0.009

TABLE IV - DQOL-Brazil results for patients with DM1 stratified by HbA1c values greater or less than 8%

	HbA1c ≤8% (N = 61)	HbA1c >8% (N = 49)	p value
Total DQOL-Brazil	1.99 (1.87 – 2.11)	2.23 (2.11 – 2.36)	0.002
Satisfaction	1.96 (1.82 – 2.11)	2.38 (2.21 – 2.55)	0.001
Impact	2.00 (1.88 – 2.13)	2.15 (2.02 – 2.28)	0.044
Vocational/Social Preoccupation	1.82 (1.60 – 2.03)	2.03 (1.81 – 2.25)	0.066
Diabetes Concern	2.31 (2.14 – 2.48)	2.45 (2.26 – 2.64)	0.416

indicating poorer QoL perception, when compared to men (Trento *et al*., 2013; Urzúa, Chirino, Valadares, 2011; HSGCD, 2001). Our results are in agreement with these reports. Women demonstrated worse QoL perception than men, and the differences were significant. Our results may be a reflection of the greater care towards health shown by women socially. Women seek health care services more frequently than men, and appear more vulnerable to the pressures imposed by DM1; the disease generates higher social concerns and worries in them, thus negatively affecting their QoL (Urzúa, Chirino, Valadares, 2011).

The age of the participants completing the questionnaire ranged from 19 to 65 years, imparting different perspectives in the "Vocational/Social Preoccupations" domain. This domain evaluates areas related to studies; jobs; and marriage, which, depending on the participant age, may not be a concern if they have already been achieved/overcome. Consequently, the younger the patient, the higher the vocational/social preoccupations score, indicating greater worries that result in a poor QoL perception. Older participants exhibit more adaptations within, and acceptance of the areas within this domain, thereby leading to lower scores and better QoL perceptions.

HbA1c test is currently considered the gold standard to verify metabolic control in DM1 patients, and although many studies have evaluated the influence of psychosocial factors beyond clinical factors on the QoL scores of patients with DM1 (Walker, Bradley, 2002; Trieff *et al.*, 2001), metabolic control plays a significant role in the subjective perception of QoL (Campbell, 2002; HSGCD, 2001). Patients with HbA1c ≤ 8% had lower scores in all the DQOL-Brazil domains compared with patients with higher HbA1c values, suggesting that metabolic control affects the QoL and reduces the risk of acute and chronic complications, thereby also improving the perceived QoL.

A study performed in Bosnia and Herzegovina in 2012 evaluated the relationship between glycemic control and QoL in children and teenagers with DM1 and demonstrated that children and teenagers with better metabolic control (HbA1c values <8%) had a better QoL than those with poor metabolic control (> 8%) (Tahirovic *et al.*, 2012). Similarly, Vanelli *et al.* (2003) studied teenagers with DM1 in Italy and found that teenage patients with lower HbA1c values had fewer worries and a better overall QoL; teenagers with higher HbA1c values exhibited more discontent, a worse perception of their health condition, and the worst QoL scores. Both studies corroborate our results demonstrating a better perception of QoL in patients with HbA1c values ≤8%.

Maintaining HbA1c values within the target limits established by the ADA (ADA, 2016) requires an intense care routine. Compliance with a rigorous scheme of insulin treatments, as well as non-pharmacological treatments, requires effort and persistence by the patient, which itself can cause discomfort and may discourage the patients from comply the treatment, worsening QoL perception (Braga de Souza, *et al.*, 2015). However, patients with lower HbA1c values had a better perception of their QoL indicating that intensive treatment, when it is understood and adopted as part of a routine, can prevent acute complications and positively influence QoL scores.

Participants with high HbA1c values had significantly higher DQOL-Brazil scores, suggesting a worse perception of QoL. Poor glycemic control results in clinical conditions of hypo- or hyper-glycemia, which require frequent hospitalizations, thus increasing the impact of diabetes on the patient's life, thereby reducing general life satisfaction and decreasing the subjective perception of QoL.

Saleh *et al*. (2014) evaluated DM2 patients from Bangladesh and demonstrated a similar relationship between treatment and QoL. Patients who were considered non-adherent to the treatment (diet, physical activity, smoking cessation, and glycemic values) had a lower QoL index (Saleh *et al*., 2014). However, the study by Martínez *et al*. (2008) on DM2 patients from México reported no association between QoL and treatment compliance but observed that the patients' education levels influenced most QoL domains. Patients with higher education

exhibited better QoL perception and higher treatment compliance (Martínez *et al*., 2008).

Fear of chronic complications is common among DM1 patients. Independent of metabolic control and patient's knowledge of the disease, a diagnosis of diabetes presents an uncertain picture of the future that causes much apprehension. The risk of micro- and macrovascular complications decreases when HbA1c values are maintained closer to 7%; however, even among patients with good glycemic control, there remains the fear of diabetes-associated conditions such as kidney damage; blindness; amputation; vessel disease; and heart attack, all of which negatively influence the diabetes concern domain of the DQOL-Brazil.

Glycemic values within the therapeutic targets are achieved by patients who are compliant to the treatment and work in tandem with a health care team. Treatment targets must be individualized according to patient age, the presence of comorbidities, life expectancy, and the patient's perception of his health problems. As part of a health care team, pharmacists, with a more extensive patient contact, can contribute to patient follow-up by providing diabetes education and self-care incentives. Studies have shown significant improvements in HbA1c values, fasting glucose levels, and compliance indicators, when pharmacists are included in the health care team, thereby improving the subjective perception of QoL (Correr, Otuki, 2013; Jennings, Marx, 2012; Collins *et al*., 2011; Armor *et al*., 2010; Campbell, 2002).

Among the participants included in this study, 26.4% had HbA1c values ≤7.0% and 29.1% had values between 7.1 and 8.0%. These results differ from the general Brazilian population where only 10.4% of the DM1 patients exhibit good glycemic control (SBD, 2011). This suggests that pharmacist intervention via continuous medication review with follow-up and non-pharmacological measures can improve compliance to antidiabetic treatment but other methods besides HbA1c are necessary for more reliable results.

Despite this efficacy evidence in Brazil, few health units include pharmaceutical care practice as part of the DM1 treatment routine. Patients treated at the 3rd Health Regional of Ponta Grossa-PR receive this follow-up service, and the results suggest that pharmaceutical intervention can improve health outcomes and help patients in reduction and maintenance of their glycemic values within the therapeutic targets, thus enabling a better QoL.

The number of study participants was not sufficient to be a representative sample and constitutes a limitation in obtaining more consistent results. However, our results indicate that glycemic control is associated with QoL and also that the implementation of pharmaceutical follow-up in health care units can improve treatment compliance, reduce HbA1c values, and consequently enhance diabetic QoL.

We could not identify a sufficient number of DM1 patients treated with NPH (Neutral Protamine de Hagedorn) and regular insulins, or with insulin analogs without continuous pharmacist interventions in the city of Ponta Grossa. As these patients would have served as controls in our study, we could not perform a case-control comparison, which constitutes another study limitation.

Furthermore, a detailed investigation exploring the treatment compliance barriers and glycemic control in DM1 patients must be undertaken. Moreover, future studies are necessary to evaluate the real impact of pharmaceutical interventions on patient's QoL through the triangulation of such methods as questionnaires, interviews, and focus groups, capable of obtaining more reliable results on the relation between treatment compliance and QoL. This study may be replicated in other cities of Brazil to update the epidemiological data on DM1.

CONCLUSIONS

DM1 patients tend to have a lower QoL due to the intensive health care routine they need to follow rigorously. This study analyzed the QoL of DM1 patients being treated with insulin analogs and receiving medication review with follow-up, analyzed the individual domain scores with age, gender, and glycemic control. Women demonstrated poorer QoL perceptions in all domains of the DQOL-Brasil than men, and younger patients demonstrated higher scores, and hence higher concerns and poor QoL, in the social/vocational preoccupations domain. Patients with HbA1c ≤ 8% showed better QoL perception suggesting that glycemic control can impact on QoL. Helping patients to achieve glycemic targets is central to reducing the risk of complications and improving the QoL perceptions in DM1 patients. The inclusion of trained pharmacists in the health care team can be a strategy to improve diabetes treatment outcomes and reduce hospitalization rates in DM1 patients.

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