ORIGINAL ARTICLE

Effects of Frequency of Follow-Up on Quality of Life of Type 2 Diabetes Patients on Oral Hypoglycemics

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Abstract

Background: Poor quality of life (QoL) in diabetes patients is reportedly associated with adverse outcomes. In the present study, we assessed the effects of frequency of follow-up on clinical indicators as well as QoL of type 2 diabetes patients taking hypoglycemic agents.

Subjects and Methods: In total, 155 type 2 diabetes patients were randomly assigned to two groups, which only differed in the frequency of follow-up visits. In both therapy groups, the patients were taking oral hypoglycemic agents. QoL was measured with a QoL Scale for Diabetes Mellitus (DMQLS) at study entry and months 3, 6, 9, and 12. Based on the drugs used, the patients were divided in three medication groups: glimepiride group, metformin group, and glimepiride + metformin group.

Results: Repeated-measures analysis of variance revealed that compared with the conventional therapy group, the intensive therapy group showed significant improvement in the Disease, Psychology, and Satisfaction domain scores of the DMQLS, the overall DMQLS score, and clinical indicator values (fasting blood glucose, 2-h postprandial blood glucose, and glycosylated hemoglobin). Correlation analyses showed that the changes in Disease, Physiology, Psychology, and Satisfaction domain scores of the DMQLS and in the overall DMQLS score were negatively correlated with changes in clinical indicator values.

Conclusions: Intensive frequency of follow-up is associated with improved QoL and clinical indicators and thus may be a preferred approach for type 2 diabetes patients on oral hypoglycemic agents. As QoL is negatively correlated with clinical indicators, it could be used as a comprehensive indicator of therapeutic effects on type 2 diabetes patients.

Introduction

DIABETES MELLITUS IS A GROUP of metabolic diseases whose common feature is an elevated blood glucose (BG) level resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus accounts for 90–95% of all diabetes cases, and it develops when the production of insulin is insufficient to overcome the underlying abnormality of increased resistance to its action.¹ The incidence of type 2 diabetes has increased rapidly during the past few decades worldwide, from approximately 35 million people affected in 1985 to about 171 million in 2000.¹

Many recent studies have reported that health-related quality of life (QoL) is poorer in diabetes patients than in the general population.^{2,3} A recent multinational study showed that diabetes has a notable impact on general health,⁴ and poor QoL in diabetes patients is associated with adverse outcomes, including increased mortality.⁵ The World Health Organization defines health as not only the absence of disease and infirmity, but also the presence of physical, mental, and social well-being.⁶ If the purpose of medicine is to make pa-

tients healthy, the aim of diabetes treatment should be controlling glycemia as well as improving the physical, mental, and social well-being of diabetes patients. Thus, improving the QoL of diabetes patients should also be a focus of diabetes treatment.

In the present study, we for the first time assessed the effects of frequency of follow-up on clinical indicators as well as QoL of type 2 diabetes patients taking hypoglycemic agents and explored the relationship between the changes in QoL and clinical indicators over time.

Subjects and Methods

Subjects

From December 2009 to December 2010, 155 consecutive patients with type 2 diabetes mellitus were recruited to the present study. According to the 1999 World Health Organization diagnostic criteria for type 2 diabetes mellitus,⁷ all patients showed the following: (1) clinical symptoms plus fasting BG (FBG) ≥ 7.0 mmol/L; (2) clinical symptoms plus

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TABLE 1. SOCIODEMOGRAPHIC AND MEDICATION DATA OF SUBJECTS

Variable	Conventional therapy		Intensive therapy		Total		χ^2	P
	n	%	n	%	n	%		
Sex								
Male	43	54.2	31	41.3	74	47.7		
Female	37	45.8	44	58.7	81	52.3		
Total	80	100.0	75	100.0	155	100.0	2.924	0.087
Education level								
Illiterate	2	2.5	2	2.7	4	2.6		
Elementary school	11	13.8	20	26.7	30	19.5		
Middle school	24	30.0	23	30.7	47	30.5		
High school	26	32.4	14	18.7	40	26.0		
College and above	17	21.3	16	21.3	33	21.4		
Total	80	100.0	75	100.0	154	100.0	8.337	0.080
Marital status								
With spouse	77	96.2	68	90.7	145	93.5		
Without spouse	3	3.8	7	9.3	10	6.5		
Total	80	100.0	75	100.0	155	100.0	3.031	0.387
Age (years)								
50–59	3	3.8	4	5.3	5	3.3		
60–69	17	21.3	9	12.0	26	17.0		
70–79	33	41.2	27	36.0	60	39.2		
≥80	27	33.7	35	46.7	62	40.5		
Total	80	100.0	75	100.0	153	100.0	5.197	0.158
Medication								
Glimepiride	19	24.3	14	18.7	33	21.6		
Metformin	19	24.3	15	20.0	34	22.2		
Both	41	51.4	46	61.3	87	56.2		
Total	80	100.0	75	100	155	100.0	1.782	0.410

TABLE 2. CLINICAL INDICATOR VALUES OF TYPE 2 DIABETES PATIENTS RECEIVING CONVENTIONAL OR INTENSIVE THERAPY

Variable	Conventional therapy (n=80)	Intensive therapy (n=75)
FBG ^{ab}		
Baseline	9.02±2.62	8.40±1.65
3 months ^c	8.04±1.52	6.78±0.87
6 months ^c	7.88±1.61	6.58±0.69
9 months ^c	7.67±1.54	6.32±0.80
12 months ^c	7.45±0.78	6.06±0.94
PBG2h ^{ab}		
Baseline	14.44±3.35	13.49±2.89
3 months ^c	11.61±3.04	10.05±2.94
6 months ^c	11.42±2.65	9.84±3.22
9 months ^c	11.26±2.43	9.46±3.30
12 months ^c	9.86±1.23	7.76±1.35
HbA1c ^{ab}		
Baseline	8.65±2.25	8.10±1.61
3 months ^c	7.13±0.73	6.54±0.42
6 months ^c	6.86±1.18	6.22±0.41
9 months ^c	6.41±0.79	5.75±0.41
12 months ^c	6.25±0.58	5.04±1.15

By repeated-measures analysis of variance: ^a $P < 0.05$ among time points in each group; ^b $P < 0.05$ for overall between-group difference; ^c $P < 0.05$ between therapy groups at the time point.

FBG, fasting blood glucose; PBG2h, 2-h postprandial blood glucose; HbA1c, glycosylated hemoglobin.

TABLE 3. OVERALL/DOMAIN QUALITY OF LIFE SCORES OF TYPE 2 DIABETES PATIENTS RECEIVING CONVENTIONAL OR INTENSIVE THERAPY

Variable	Experimental group	
	Conventional therapy (n=80)	Intensive therapy (n=75)
Disease ^{abc}		
Baseline	48.80±7.94	48.83±6.46
3 months ^d	49.70±8.72	53.81±7.79
6 months ^d	50.23±9.21	55.22±6.63
9 months ^d	50.43±8.43	56.29±5.81
12 months ^d	50.52±5.48	58.94±5.58
Physiology		
Baseline	50.27±7.68	48.69±10.6
3 months	50.31±9.16	49.55±10.29
6 months	50.76±8.18	50.10±9.45
9 months	51.02±7.63	51.01±6.02
12 months	51.09±3.82	51.16±7.87
Society		
Baseline	50.61±7.94	50.14±9.28
3 months	50.76±8.25	50.49±9.79
6 months	50.80±8.05	50.59±7.61
9 months	50.87±6.21	50.72±5.67
12 months	50.99±3.46	51.23±6.56
Psychology ^{ac}		
Baseline	49.03±8.85	49.41±12.01
3 months	49.39±10.31	51.40±8.52
6 months	50.37±10.45	52.41±7.02
9 months ^d	50.67±6.99	52.91±4.91
12 months ^d	50.69±3.69	62.49±4.02
Satisfaction ^{abc}		
Baseline	47.41±8.25	45.92±7.76
3 months	49.18±8.03	50.71±7.79
6 months ^d	49.31±8.27	53.32±7.11
9 months ^d	49.37±8.99	53.91±6.67
12 months ^d	49.43±4.41	56.39±6.82
Overall ^{abc}		
Baseline	246.12±29.97	243.21±36.62
3 months	249.33±34.89	255.96±31.27
6 months ^d	251.46±34.32	261.65±25.93
9 months ^d	252.36±30.71	264.81±16.98
12 months ^d	252.73±15.61	270.73±20.75

By repeated-measures analysis of variance: ^a $P < 0.05$ among time points in each group; ^b $P < 0.05$ for interaction between time and therapy in each group; ^c $P < 0.05$ for overall between-group difference; ^d $P < 0.05$ between therapy groups at the time point.

2-h postprandial BG (PBG2h) ≥ 11.1 mmol/L; (3) clinical symptoms plus random BG ≥ 11.1 mmol/L; or (4) for those without clinical symptoms, FBG ≥ 7.0 mmol/L or PBG2h ≥ 11.1 mmol/L at two different times. Patients also fulfilled the following inclusion criteria: (1) definite diagnosis of type 2 diabetes mellitus within the past 5 years; (2) 35–70 years old; (3) BG not satisfactorily controlled after diet and exercise therapy (7.0 mmol/L $\leq$ FBG ≤ 13.9 mmol/L); (4) body mass index of 19 – 31 kg/m²; (5) without ketosis or other severe stresses in the past 6 months; and (6) willing to sign the consent form. The exclusion criteria included the following: (1) chronic complications of diabetes mellitus; (2) ketoacidosis or hyperosmolar coma; (3) heart failure, severe arrhythmia, or cerebrovascular diseases; (4) severe hepatic or renal insufficiency; (5) progressive, systemic diseases; (6) mental illnesses;

FIG. 1. Profile charts for clinical indicators over time in the conventional therapy and the intensive therapy groups: fasting blood glucose (FBG), 2-h postprandial blood glucose (PBG2h), and glycosylated hemoglobin (HbA1c). * $P < 0.05$ compared with the conventional therapy group at that time point. Color graphs available online at www.liebertonline.com/dia

(7) pregnant or lactating women; (8) allergic to hypoglycemic agents or sulfa drugs; or (9) a history of alcoholism or drug abuse. The study was approved by the Ethics Committee of Central South University. Written informed consent was obtained from all participating patients before the start of the study.

Experimental group assignment

In total, 155 consecutive patients were randomly assigned to an intensive therapy group ($n = 75$) and a conventional therapy group ($n = 80$), which only differed in the frequency of follow-up visits. According to previous reports,⁸ conventional therapy and intensive therapy can decrease PBG2h by 6 mmol/L and 8 mmol/L, respectively, with an SD of 3.6 mmol/L. Based on the reported data and a two-tailed $\alpha = 0.05$ and power = 0.90, a sample size of 68 for each group was originally calculated for comparison of means between two groups.^{9,10} Taking into account of an anticipated 10% dropout rate, $n = 75$ was determined as a minimum sample size for each group. All patients completed the study.

Intervention procedures

The only difference between the conventional therapy and the intensive therapy was the frequency of follow-up visits. In both therapy groups, oral hypoglycemic drugs were used based on the patients' disease condition, obesity, physical activity, and BG level. In the conventional therapy group, outpatient follow-up was conducted for each patient every 3 months for 12 months, resulting in a total of four follow-up visits during the study. In the intensive therapy group, outpatient follow-up was conducted for each patient every 1 month for 12 months, resulting in a total of 12 follow-up visits during the study. In both groups, FBG, PBG2h, glycosylated hemoglobin (HbA1c), and QoL were measured at each follow-up, and the treatment plan was adjusted accordingly. QoL was measured at the study entry and months 3, 6, 9, and 12 in both therapy groups. The oral hypoglycemic drugs used included glimepiride and metformin. Glimepiride was taken once daily (1 mg) and adjusted according to the disease condition. Metformin was taken three times daily, 0.5 g each time, and adjusted according to the disease condition. Based on the drugs used, the patients were divided in

FIG. 2. Profile charts for the Disease, Psychology, and Satisfaction domain and total scores for quality of life over time in the conventional therapy and the intensive therapy groups. * $P < 0.05$ compared with the conventional therapy group at that time point. Color graphs available online at www.liebertonline.com/dia

three medication groups: glimepiride group, metformin group, and glimepiride + metformin group.

Instrumentation

A demographics form was used to collect the patients' demographic data. QoL was measured with a QoL Scale for Diabetes Mellitus (DMQLS) we developed.¹¹ The DMQLS is a self-administered questionnaire containing 87 items covering five domains, including Disease (20 items), Physiology (17 items), Society (19 items), Psychology (16 items), and Satisfaction (15 items). Each item is scored on a 5-point scale. For each domain, the score of each item is summed up. Higher scores indicates better QoL. The DMQLS has excellent reliability and validity. Its test-retest reliability is 0.996, Cronbach's α is 0.969, and split-half reliability coefficient is 0.879.¹¹

Statistical analysis

Statistical analyses were performed with SPSS version 13.0 for Windows (SPSS, Inc., Chicago, IL). For continuous variables, all data were expressed as mean $\pm$ SD values and analyzed with Student's t tests, repeated-measures analysis of variance, and correlation analyses. Categorical variables were compared with χ^2 tests. The statistical significance level of this study was set at two-sided $\alpha = 0.05$.

Results

As shown in Table 1, there was no significant difference in sociodemographic variables and medication between the conventional therapy and intensive therapy groups at baseline. No significant differences were found in clinical indicators and overall/domain QoL scores between the two groups

TABLE 4. EFFECTS OF TIME AND MEDICATION ON OVERALL/DOMAIN QUALITY OF LIFE SCORES AND CLINICAL INDICATOR VALUES

	Time		Medication group	
	F	P	F	P
Quality of life domain				
Disease	10.182	0.000	0.439	0.645
Physiology	0.405	0.805	0.149	0.862
Society	0.147	0.964	0.170	0.844
Psychology	2.144	0.077	0.429	0.652
Satisfaction	10.556	0.000	0.163	0.849
Overall	5.040	0.001	0.009	0.991
FBG	39.118	0.000	1.385	0.253
PBG2h	76.204	0.000	3.006	0.052
HbA1c	120.929	0.000	0.742	0.478

Effects of time and medication for the glimepiride group, metformin group, and glimepiride + metformin group were analyzed by repeated-measures analysis of variance.

FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; PBG2h, 2-h postprandial blood glucose.

before intervention (Tables 2 and 3). The results indicate that the two therapy groups were comparable at baseline and that the effect of potential confounders was minimized.

As shown in Table 2, repeated-measures analysis of variance revealed that time had a significant main effect on FBG, PBG2h, and HbA1c, indicating that the clinical indicators improved over time in both therapy groups. Compared with the conventional therapy group, the intensive therapy group showed significant improvement in FBG, PBG2h, and HbA1c, indicating that intensive therapy had a significant main effect in improving the clinical indicators. However, no significant interaction between time and therapy was noted. The data are also illustrated in Figure 1.

As shown in Table 3 and Figure 2, repeated-measures analysis of variance revealed that compared with the conventional therapy group, the intensive therapy group showed significant improvement in the Disease, Psychology, and Satisfaction domain scores of the DMQLS and the overall DMQLS score. There was significant improvement over time in the Disease, Psychology, and Satisfaction domain scores of the DMQLS and the overall DMQLS score in either therapy group. Significant interaction between time and therapy was noted on the Disease and Satisfaction domain scores of the DMQLS and the overall DMQLS score. The data are also illustrated in Figure 2.

As shown in Table 4, repeated-measures analysis of variance revealed no significant difference in clinical indicators

and overall/domain DMQLS scores among the different medication groups (glimepiride group, metformin group, and glimepiride + metformin group).

Correlation analyses were performed for the entire cohort ($n = 155$) of type 2 diabetes patients. The changes in the Disease, Physiology, Psychology, and Satisfaction domain scores of the DMQLS and in the overall DMQLS score showed significant negative correlation with changes in clinical indicator values (Table 5).

Discussion

Treatment of diabetes is no longer simply to control blood glucose levels, but also to prevent complications, relieve symptoms of the disease, and improve the QoL of diabetes patients.^{12,13} The present study compared the clinical indicator values and QoL scores of type 2 diabetes patients taking conventional and intensive oral hypoglycemic therapies and evaluated the trend of changes in clinical indicator values and overall/domain QoL scores of the patients.

The only difference between the conventional therapy and the intensive therapy was the frequency of follow-up visits. Although there was no significant difference in FBG, PBG2h, and HbA1c among the different medication groups (Table 4), the intensive therapy group showed significantly lowered FBG, PBG2h, and HbA1c values compared with the conventional therapy group (Table 2), indicating that the frequency of follow-up visits is key to improving the therapeutic effects of oral hypoglycemic agents for type 2 diabetes patients.

Health-related QoL is a multidimensional concept that includes domains related to physical, mental, emotional, and social functioning. It goes beyond direct measures of population health, life expectancy, and causes of death and focuses on the impact health status has on the subject's physical, mental, and social well-being.¹⁴ Thus, QoL has been widely used for comprehensive evaluation of the impact of disease and treatment on patients' physical and mental health. Thus, the focus of diabetes treatment should be controlling glycemia as well as improving the patient's QoL. In the present study, both the conventional therapy group and the intensive therapy group showed significant improvement in QoL compared with baseline (Table 3). The intensive therapy group showed higher overall QoL score than the conventional therapy, but there was no significant difference among the medication groups (Table 4). This indicates that the intensive therapy can better improve the QoL of type 2 diabetes patients, in agreement with previous reports.¹⁵ In view of the fact that the intensive therapy only had more frequent follow-up visits than the conventional therapy group, our findings also indicate that frequent follow-up visits can improve QoL

TABLE 5. CORRELATION AMONG SCORE CHANGES IN OVERALL/DOMAIN QUALITY OF LIFE SCORES AND CHANGES IN CLINICAL INDICATOR VALUES

Clinical indicator	Quality of life domain					
	Disease	Physiology	Society	Psychology	Satisfaction	Overall
FBG	-0.625 ^b	-0.146	-0.214 ^b	-0.340 ^b	-0.304 ^b	-0.456 ^b
PBG2h	-0.526 ^b	-0.148 ^a	-0.222 ^b	-0.293 ^b	-0.294 ^b	-0.414 ^b
HbA1c	-0.478 ^b	-0.139	-0.295 ^b	-0.228 ^b	-0.211 ^b	-0.373 ^b

^a $P < 0.05$, ^b $P < 0.01$.

FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; PBG2h, 2-h postprandial blood glucose.

of type 2 diabetes patients receiving oral hypoglycemic treatment.

FBG, PBG2h, and HbA1c are widely used clinical indicators for diabetes patients. The higher values of the indicators, the more severe the patient's disease condition. Our results showed that changes in QoL are negatively correlated with changes in clinical indicator values (Table 5). This suggests that QoL could be used as a comprehensive indicator of therapeutic effects on type 2 diabetes patients, for changes in QoL can reflect not only the changes of clinical indicator values, but also the therapeutic effects on the patients' physical, mental, and social well-being.

In conclusion, intensive frequency of follow-up is associated with improved QoL and clinical indicators and thus may be a preferred approach for type 2 diabetes patients taking oral hypoglycemic agents. In addition, as QoL is negatively correlated with clinical indicators, it could be used as a comprehensive indicator of therapeutic effects on type 2 diabetes patients. This study provides insights into selecting individualized therapy for type 2 diabetes patients based on QoL and clinical indicators and will serve as an important reference for comprehensive evaluation of the effects of clinical therapies on type 2 diabetes patients.

Acknowledgments

This work was supported by the Ministry of Science and Technology of China (grant 2001BA702B05).

Author Disclosure Statement

No competing financial interests exist.

References

- Schulze MB, Hu FB: Primary prevention of diabetes: what can be done and how much can be prevented? *Annu Rev Public Health* 2005;26:445–467.
- Rubin RR, Peyrot M: Quality of life and diabetes. *Diabetes Metab Res Rev* 1999;15:205–218.
- Saito I, Inami F, Ikebe T, Moriwaki C, Tsubakimoto A, Yonemasu K, Ozawa H: Impact of diabetes on health-related quality of life in a population study in Japan. *Diabetes Res Clin Pract* 2006;73:51–57.
- Alonso J, Ferrer M, Gandek B, Ware JE Jr, Aaronson NK, Mosconi P, Rasmussen NK, Bullinger M, Fukuhara S, Kaasa S, Leplege A; IQOLA Project Group: Health-related quality of life associated with chronic conditions in eight countries: results from the International Quality of Life Assessment (IQOLA) Project. *Qual Life Res* 2004;13:283–298.
- Kleefstra N, Landman GW, Houweling ST, Ubink-Veltmaat LJ, Logtenberg SJ, Meyboom-de Jong B, Coyne JC, Groenier KH, Bilo HJ: Prediction of mortality in type 2 diabetes from health-related quality of life (ZODIAC-4). *Diabetes Care* 2008;31:932–933.
- Constitution of the World Health Organization: Handbook of Basic Documents, 5th ed. Geneva: World Health Organization, 1952:3–20.
- World Health Organization: Technical Report Series No. 727: Diabetes Mellitus: Report of a WHO Study Group. Geneva: World Health Organization, 1985.
- Influence of intensive diabetes treatment on quality-of-life outcomes in the diabetes control and complications trial. *Diabetes Care* 1996;19:195–203.
- Polit DF, Sherman RE: Statistical power in nursing research. *Nurs Res* 1990;39:365–369.
- Polit DF, Hungler BP, eds. *Nursing Research: Principles and Methods*, 7th ed. Philadelphia: J.B. Lippincott, 2004:498.
- Jones P: Quality improvement initiative to integrate teaching diabetes standards into home care visits. *Diabetes Care* 2002;28:1009–1019.
- American Diabetes Association: Standards of medical care in diabetes. *Diabetes Care* 2004;27(Suppl 1):S15–S35.
- Wang LS, Sun ZQ, Cai TS, Zhou ZG: [Development and validation of quality of life scale for patients with type 2 diabetes mellitus]. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2005;30:21–27.
- Choi YJ, Lee MS, An SY, Kim TH, Han SJ, Kim HJ, Chung YS, Lee KW, Kim DJ: The relationship between diabetes mellitus and health-related quality of life in Korean adults: the Fourth Korea National Health and Nutrition Examination Survey (2007–2009). *Diabetes Metab J* 2011;35:587–594.
- Ménard J, Payette H, Baillargeon JP: Efficacy of intensive multitherapy for patients with type 2 diabetes mellitus: a randomized controlled trial. *CMAJ* 2005;173:1457–1466.

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