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Research Article

Health-Related Quality of Life of Type 2 Diabetes Mellitus Outpatients at Dr. Sardjito Hospital, Yogyakarta, Indonesia: An Insulin-Based Therapy Approach

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Abstract
Diabetes mellitus type 2 is a lifelong disease which needs an intensive therapy to maintain stable blood sugar levels. Insulin has been proven as an effective treatment modality for type 2 diabetes mellitus patient. The main aim of this research was to evaluate the effect of insulin based therapy (insulin monotherapy-combination therapy of insulin with oral hypoglycemic agents) towards the health related quality of life in type 2 diabetes mellitus outpatient at Dr. Sardjito Hospital, Yogyakarta. This study is a descriptive cross-sectional study design without control. The methods of collecting data includes conducting questionnaires, interviews and examining medical records of patient. Data were taken concurrently from patients who visited Endocrinology Clinic of Dr. Sardjito Hospital from July 2012 until April 2013. Inclusion criteria for the participant were as follows: participant was a type 2 diabetes mellitus outpatient with insulin based therapy, had no languange barrier and was able to participate the study. Participants were excluded in this study if they had a mental and language retardation, uncomplete medical records, and was a pregnant woman. The quality of life was measured by Diabetes Quality of Life Clinical Trial Quessionnaire (DQLCTQ). The statistical analysis used in this study was Mann-Whitney for QoL analysis based on the type of therapy (insulin monotherapy and combination therapy of insulin-oral hypoglycemic agents). The results from 137 patients shown that patients who received combination therapy had the largest percentage (73%) while the smallest percentage (27%) were single therapy. Whereas, the type of therapy (insulin monotherapy-combination therapy of insulin with oral hypoglycemic agent) significantly influenced the energy domain (p=0,027).

Keywords: Health related quality of life, insulin based therapy, type 2 diabetes mellitus

Kualitas Hidup Terkait Kesehatan dari Pasien Diabetes Melitus Tipe 2 di Rumah Sakit Umum Pusat Dr. Sardjito, Yogyakarta, Indonesia: Suatu Pendekatan Terapi Berbasis Insulin

Abstrak
Diabetes melitus tipe 2 adalah penyakit yang membutuhkan terapi intensif seumur hidup untuk menjaga kestabilan kadar gula darah. Insulin terbukti menjadi salah satu modalitas pengobatan yang efektif bagi pasien diabetes melitus tipe 2. Tujuan utama penelitian ini adalah mengevaluasi perbedaan terapi berbasis insulin (terapi insulin dengan atau tanpa agen hipoglikemik oral) terhadap domain kualitas hidup terkait kesehatan pada pasien rawat jalan diabetes melitus tipe 2 di RSUP Dr. Sardjito, Yogyakarta. Penelitian ini merupakan penelitian deskriptif *cross-sectional* tanpa kontrol. Metode pengumpulan data meliputi wawancara, pengambilan kuesioner dan pemeriksaan rekam medis pasien. Data diambil secara konkuren terhadap pasien yang berkunjung ke Polikinik Endokrinologi RSUP Dr. Sardjito mulai bulan Juli 2012 sampai April 2013. Kriteria inklusi antara lain penderita rawat jalan tipe 2 dengan terapi berbasis insulin, tidak memiliki keterbatasan bahasa dan bersedia berpartisipasi dalam penelitian. Kriteria eksklusi meliputi pasien yang mengalami keterbelakangan mental dan bahasa, catatan medis yang tidak lengkap dan wanita hamil. Pengukuran kualitas hidup menggunakan kuesioner dari *Diabetes Quality of Life Clinical Trial Quessionnaire* (DQLCTQ). Analisis statistik perbedaan jenis terapi berbasis insulin terhadap domain kualitas hidup pasien menggunakan uji statistik *Mann-Whitney*. Diperoleh responden sebanyak 137 orang dimana 73% pasien memperoleh terapi kombinasi sedangkan sisanya 27% mendapatkan terapi tunggal yang berbasis insulin. Kesimpulan penelitian ini yaitu perbedaan jenis terapi (monoterapi insulin versus kombinasi insulin dengan agen hipoglikemik oral) secara signifikan memengaruhi domain energi pada kualitas hidup (p=0,027).

Kata kunci: Kualitas hidup terkait kesehatan, terapi berbasis insulin, diabetes melitus tipe 2

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Introduction

Diabetes mellitus (DM) is a group of metabolic diseases with hyperglycemia characteristic that occurring due to abnormalities in insulin secretion, insulin action or both. The longterm chronic hyperglycemia of diabetes may result in vital organs damage such as eyes, kidneys, nerves, heart and blood vessels.[1,2]

According to major studies by the World Health Organization (WHO), the number of patients with diabetes mellitus in Indonesia in 2010 was 8.4 million people, becoming the 7th largest country with most diabetic patients. Prevalence of people with diabetes mellitus in Indonesia has projected to rise between 1.2% and 2.3% in 15 years.[3,4]

Diabetes mellitus can cause problem to the quality of life through an increased risk of developing various acute and chronic complications. Type 2 diabetes mellitus can lead several classic signs such as polyuria, polydipsia, polyphagia and weight loss. Another patients may suffer from weaknesses, tingling, itching, blurring eyes, erectile dysfunction in men, and pruritus vulva in women.[5] Patients who have been diagnosed with diabetes must receive appropriate therapy associated with the disease management. Such therapies are expected to improve the signs of the patient's clinical problems so as to provide a clinical benefit. Besides that, the given therapy can also prompt early and late side effects. These side effects have become an undesirable experience for the individual diabetic patient.[6]

The metabolic side effects of insulin and oral antidiabetic therapy are strikingly uncomfortable and can cause poor glycemic control that affect the quality of life diabetic patients. One of the obstacles in the use of insulin among patients is hypoglycaemia. These side effects occur due to late meal, inadequate carbohydrate, excessive physical activity or high insulin dose. Moreover, it can happen also due to allergic reaction or insulin resistance in form of immunological reactions to insulin. Sometimes insulin injections may also cause atrophy of subcutaneous fat tissue at the site of injection.[7]

Poor quality of life will lead to a reduction in patients' self-care, and consequently the risk of complications is increasing. Improving patients' quality of life mainly refers to health issues, including the disease impact, treatment function, confidence and well-being of the diabetic patient care.[8] Type 2 diabetes is a chronic disease which affected the physical, psychological and social behavioral aspects. Social support is one of form of interactions between individuals who provide physical and psychological comfort through the needs for affection and security. Social support can play a role to improve the quality of life in patients with type 2 diabetes by regulating the psychological and facilitating a change in behavior. DM symptoms significantly interfere with the physical, psychological and quality of life that contribute to functional incapacity and psychological distress.[9]

This study was carried out in patients with type 2 diabetes mellitus outpatients who visited Endocrinology Division of Dr. Sardjito General State Hospital Yogyakarta. Further consideration in selecting Dr. Sardjito hospital as a research area was based upon epidemiological data. According to the latest 2013 data from Basic Health Research, the rates of diabetes among people of Yogyakarta was higher than that of another provinces. The prevalence rates of diabetes mellitus patients in Yogyakarta reached nearly 2.6%, DKI Jakarta at 2.5% and North Sulawesi at 2.4%.[10] This study aimed to determine some factors that influence the quality of life in term of insulin-based therapy among type 2 diabetes mellitus patients. Currently, quality of life becomes a major health outcome, which describes the ultimate goal of health interventions. Measuring the quality of life

on diabetic patients will play an important role in assessing and evaluating the clinical outcomes of chronic disease. The role of quality of life is so valuable to synergize both clinical outcome and physiological parameters. The information of this study can be used as a strategy for quality improvement effort in diabetes health care.

Methods

The research methodology was an analytic cross-sectional study that carried out at one time point between variables. The target population of this study was patients with type 2 diabetes mellitus who required insulin-based therapy. Sampling was conducted using non-probability sampling technique with a purposive sampling approach based on the accordance with the inclusion and exclusion criteria. Data were taken concurrently from July 2012 until April 2013 by giving the questionnaire to patients with type 2 diabetes which was treated with insulin based therapy, either monotherapy insulin or in combination with oral antidiabetic. The completeness of the data is also checked with patients medical records.

The study began with completing stages of ethical approval from the Institutional Review Board (IRB) Faculty of Medicine, University of Gadjah Mada with number of ethics committee approval Ref: KE/FK/97/EC. The patient recruitment process began by selecting patients with type 2 diabetes mellitus who meet the inclusion and exclusion criteria. The inclusion criteria were as follows: (1) Patients with type 2 diabetes mellitus treated with insulin based therapy either monotherapy or in combination with antidiabetic oral; (2) Patients agreed to enroll the study by assigning the written informed consent and filled out the questionnaires; (3) Patients with age range 22–85 years old; (4) Type 2 diabetes mellitus patients had microvasular and macrovascular complications; (5) Type 2 diabetes mellitus patients had illness duration of 0.33–40 years. The exclusion criteria were as follows: (1) Patients with mental disorder established by written medical records from mental health provider or language barriers that can disrupt the research process; (2) Incomplete patient medical records regarding the therapy and the patient's personal data; (3) Pregnant and lactating women.

Quality of life data was obtained by distributing Diabetes Quality of Life Clinical Trial Quessionnaire (DQLCTQ) to respondents who had signed the informed consent. Questionnaire can be filled by the patients, or under certain circumstances may be accompanied by the investigators based on answers chosen by the patients on interview. DQLCTQ questionnaire is adopted from journal publications research conducted by Shen *et al.* (1999) and has been validated by Hartati at Dr. Sardjito Hospital Yogyakarta. For a thorough analysis of the internal consistency value of all items was valid and reliable results with α=0.82 (>0.5).[11,12]

Descriptive statistics were performed to analyze the distribution of variables and only represented the percentage of each variable category. Distribution of variants were also used to determine the variables distribution. Kolmogorov-Smirnov statistical test was used to determine the normality of the data distribution. Comparative statistics test was used to determine the differences between one or more categories. Mann-Whitney test was used to compare differences between two independent categories which is not normally distributed, while Kruskal-Wallis for variables with more than two categories with 0,05 significance levels.

Results

The study was carried out from July 2012 until April 2013 at Dr. Sardjito Hospital

Yogyakarta on patients with type 2 diabetes mellitus treated with insulin based therapy. The survey response rate of this study achieved 90% from the total of 152 patient who entered the study. It means there were 137 patients who were asked to complete the questionnaire and gave feedback. This study was observational research with cross-sectional design. Researcher employed the cross-sectional approach typically intended to analyze the influence of the dependent variable to the independent variables in one measurement using a questionnaire. Data on demographic characteristic of the study population are described in Table 1.

Data of therapy characteristic in patients with type 2 diabetes mellitus treated with insulin-based therapy were presented in Table 2. It can be seen that there were 100 patients who got combination therapy and 37 patients got monotherapy with most commonly used monotherapy was premixed acting insulin (19%).

Normality test results with Kolmogorov-Smirnov test indicated that each variable data on the type of therapy, disease duration and complication was not normally distributed. Therefore, the two variables was compared with Mann-Whitney analysis, and Kruskall Wallis for more than two variables. The average value of type 2 diabetes patient's quality of life treated with insulin-based therapy were described in Table 3. As shown in Table 3, the average value of patient's quality of life on physical, energy, health distress, mental health, and treatment effect domain with combination therapy was higher than with monotherapy or insulin alone.

Table 4 shows type of complication related to the value of quality of life. It described that patients without complication had higher value of quality of life than others associated with symptoms frequency (p=0.016). Chyun *et al.* (2006) found that the complications experienced by patients with type 2 diabetes was become one of factors causing decrease the quality of life's value.[13]

Duration of diabetes mellitus is one of factors affecting quality of life. The effect of duration of diabetes mellitus on patients'

Table 1 Demographic Characteristics of Study Population (n=137)

Variables	Number of Patients (n)	Percentage (%)
Sex		
Male	76	55.5
Female	61	44.5
Age		
<50 years old	11	8.0
50–59 years old	50	36.5
60–69 years old	46	33.6
≥70 years old	30	21.9
Education		
≤ high school	86	62.8
> high school	51	37.2
Type of Therapy		
Monotherapy	37	27.0
Combination therapy	100	73.0
Disease Duration		
≤5 years	30	21.9
>5 years	107	78.1
Complication		
Macrovascular	17	12.40
Microvascular	40	29.20
Macro and microvascular	6	4.40
No complication	74	54.0

Table 3 Type of Therapy on Health Quality of Life (Average Value)

Domain	Monotherapy	Combination	p-value
Physical	63.08 ± 27.64	71.19 ± 20.96	0.284
Energy	56.74 ± 17.90	73.54 ± 19.38	0.027*
Health distress	68.14 ± 13.53	69.32 ± 14.22	0.875
Mental health	65.66 ± 13.79	70.24 ± 15.72	0.547
Personal satisfaction	71.53 ± 9.47	68.07 ± 10.75	0.650
Treatment satisfaction	70.01 ± 17.68	68.63 ± 17.16	0.855
Treatment effect	61.99 ± 15.61	71.60 ± 12.38	0.208
Symptoms frequency	70.96 ± 14.22	68.28 ± 18.12	0.725
QoL average	62.84 ± 9.59	71.28 ± 9.71	0.269

*=Mann-Whitney (p≤0,05)

quality of life can be seen in Table 5. It explained that differences in disease duration was statistically significant in affecting on symptom frequency domain (p=0.047).

Discussion

This study included 76 (55,5%) male patients and 61 (44,5%) female patients. In relation to the ages percentage, there were 8% of patients aged <50 years old, 36.50% of patients aged 50–59 years old, 33.60% of patients aged between 60–69 years old, and 21.90% of patients aged ≥70 years old. According to Abioda *et al.* (2013), the illness duration was categorized with more or less than 5 years.[14] Most patients had disease duration more than 5 years (78.1%) and without complication (54%). Patients were divided into two groups according to the type of therapy. The first group included patients with a monotherapy (27%) while the second group included patients with combination therapy (73%).

According to Mooridian *et al.* (2006) the use of premixed insulin acting regimen can simplify and reduce the number of daily insulin injections. In this study, the data demonstrated that premixed insulin used is a mixture of rapid and intermediate-acting insulin.[15] Clinical trials have shown that these agents

Table 2 Therapy Characteristic in Patients with Type 2 Diabetes Mellitus Treated with Insulin-based Therapy (n=137)

Therapy Characteristic	Number of Patients (n)	Percentage (%)
Monotherapy	37	27.1
Rapid acting	2	1.5
Long acting	9	6.6
Premixed acting	26	19.0
Combination	100	72.9
Rapid acting, metformin, acarbose	1	0.7
Long acting, acarbose	5	3.6
Long acting, glimepiride	1	0.7
Long acting, metformin	7	5.1
Long acting, pioglitazone	1	0.7
Long acting, metformin, acarbose	10	7.3
Long acting, metformin, acarbose, pioglitazone	1	0.7
Premixed acting, acarbose	12	8.8
Premixed acting, metformin	24	17.5
Premixed acting, glikuidon	1	0.7
Premixed acting, metformin, acarbose	29	2.2
Premixed acting, acarbose, pioglitazone	5	3.6
Premixed acting, metformin, pioglitazone	3	2.2

Table 4 Complication on Health Quality of Life (Average Value)

Domain	Macrovascular	Microvascular	Macro and Microvascular	No Complication	p-value
Physical	48.74 ± 25.24	67.79 ± 26.42	59.67 ± 20.81	75.07 ± 20.25	0.084
Energy	60.26 ± 16.95	69.36 ± 19.12	59.25 ± 12.38	71.60 ± 20.17	0.679
Health distress	67.41 ± 18.81	62.23 ± 14.70	48.67 ± 15.17	74.68 ± 12.3	0.220
Mental health	76.79 ± 22.08	58.90 ± 14.72	80.42 ± 15.22	71.74 ± 13.82	0.246
Personal satisfaction	65.26 ± 13.87	70.81 ± 10.26	65.50 ± 9.11	69.16 ± 9.88	0.963
Treatment satisfaction	57.47 ± 16.86	69.90 ± 17.21	69.42 ± 6.75	71.13 ± 18.09	0.639
Treatment effect	49.79 ± 15.61	71.29 ± 12.20	55.17 ± 14.86	73.30 ± 13.15	0.126
Symptoms frequency	64.24 ± 16.54	57.33 ± 15.93b**	43.83 ± 19.48	78.45 ± 17.10**	0.016*
QOL average	59.29 ± 14.36	62.23 ± 8.41	53.67 ± 7.27	76.14 ± 9.25	0.141

*=Kruskall-Wallis (p≤0,05), **=Mann-Whitney (p≤0,05)

may improve postprandial glucose control and reduce the risk of hypoglycemia.[16] Table 2 shows that all respondents with combination therapy (n=100) had various distribution. There were two categories of combination therapy namely combination therapy insulin with one type of oral antiglicemic agent and with more than one type of oral antiglicemic agents. Combination drug therapy regimen commonly used in type 2 diabetes mellitus patients included one type of oral antiglicemic agent (metformin) with premixed insulin. The effect of metformin combined with premixed insulin may improve the sensitivity of insulin receptors. In addition, they can decrease fasting blood glucose, HbA1c value and significantly reduce the insulin requirement.[17] These benefits are thought to cause modest weight loss and risk of hypoglycemia.[18]

In this study, combination drug therapy of insulin with acarbose is quite widely used in patients. Combination use of insulin and acarbose might be a benefit to individuals who cannot control their diet.[15] Other combination therapies that were found in this study was a combination of long acting insulin with metformin. Long acting insulin is usually used for type 2 diabetes patients with HbA1c >7.5–10% and post-prandial adequately controlled for patients with eating difficulty.[16] Combination therapy of insulin with two types of antidiabetic oral agents, which widely used was a combination of premixed insulin with acarbose and metformin, was found in this study. Combination of 3 types of oral diabetic agents in patients has increased the risk of adverse drug effects and consequently need of implementing complex dosing formulae.[17]

The quality of life average of combination therapy group was higher than monotherapy group. Patients who received combination therapy had significant higher score of energy domain on quality of life than monotherapy (p=0.027), means that patient on combination

Table 5 Disease Duration on Health Quality of Life (Average Value)

Domain	≤5 Years	>5 Years	p-value
Physical	77.37 ± 16.30	66.65 ± 24.20	0.187
Energy	79.05 ± 19.42	66.18 ± 19.02	0.115
Health distress	70.07 ± 14.40	68.70 ± 13.94	0.866
Mental health	61.68 ± 14.48	71.05 ± 15.37	0.250
Personal satisfaction	73.22 ± 9.55	67.82 ± 10.64	0.509
Treatment satisfaction	71.92 ± 15.72	68.18 ± 17.69	0.647
Treatment effect	81.05 ± 11.59	65.62 ± 13.58	0.059
Symptoms frequency	81.72 ± 14.81	65.43 ± 17.51	0.047*
QoL average	78.23 ± 7.82	66.41 ± 10.07	0.149

therapy reported that they have been feeling more energetic, less exhausted and rarely fatigue than the monotherapy group. Some evidences suggested that several beneficial effect of combination therapy in type 2 diabetes mellitus include it could reduce the required insulin dose and common side effect (such as hypoglicemia and weight gain), and improve glycemic control and compliance, compared with monotherapy insulin.[18]

The use of oral antidiabetic drugs in combination therapy with insulin was more beneficial than insulin monotherapy. Early insulinization with oral antidiabetic agents shown better clinical outcomes by improving pancreatic beta cells, reducing glucotoxicity, preventing endothelial damage, suppressing inflammatory process, reducing the incidence of apoptosis and improving lipid profile.[19] In addition, synergistic effect of the combination of insulin and oral anti-diabetic agents may allow to reduce insulin dosage.[20] Reduced dose of insulin injections will reduce the presence of injection related anxiety to the patient. Ventegod (2003) reported that patients with excessive anxiety experience towards use of drugs will be affected in muscle tension, decrease in immune system, nervousness and sleeplessness. It will indirectly affect the satisfaction of treatment that will also impact on the quality of life of patients.[21]

The systematic review and meta-analysis regarding comparison of insulin monotherapy and combination insulin with oral antidiabetic agents had caused an improvement in the quality of life on combination insulin with oral antidiabetic agents. In addition, combination therapy of insulin-oral anti-diabetic insulin can reduce the total dose of about 46% compared to monotherapy. Judging from the weight loss, combination therapy NPH insulin and metformin or a sulfonylurea significantly reduced weight. Metformin reduces insulin needs and prevents weight gain, both in combination with sulfonylureas or insulin regimen intensified. Thus, anti-diabetic combination therapy of oral insulin may be considered as initial modest therapy in most patients with type 2 diabetes who require insulin-based therapy.[22]

Table 4 shows that patients without complications had higher value of quality of life associated with the physical function, energy, health distress, treatment satisfaction, treatment effect, and symptoms frequency domain. Patients with no complication were affected due to their positive perception to the treatment which given regardless of the presence of disease complications.

The study results showed that patients with disease duration of less than or equal to 5 years had average value of quality of life higher than patients with disease duration of more than 5 years. Reid & Walker (2009) stated that people who suffered from diabetes for a long period of time were significantly related to anxiety levels, which will result in the decrease of quality of life of type 2 diabetes patients.[23] Another study conducted by Redekop *et al.* (2002) reported that longer duration of the patient's illness was defined by lower of quality of life value. The research concluded that patients with diabetes duration of less than 5 years old have the highest quality of life.[24]

There were some limitations in this study, for instance other factors which associated with therapeutic efficacy and quality of life cannot be controlled by investigators, such as treatment adherence, social and economiy aspect, alternative therapies, diet, physical activity and the patient's lifestyle.

Conclusion

The difference between monotherapy insulin and combination insulin therapy with antidiabetic agents is statistically significant in affecting on energy domain. Illness duration and complication difference is

statistically significant in influencing on symptoms frequency domain on quality of life. It is required to do in-depth interview with qualitative analysis design in order to have detailed information about the predictive factors that influence the value of quality of life in type 2 diabetes mellitus patients.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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