QUALITY OF LIFE ANALYSIS IN DIABETES MELLITUS TYPE 2 PATIENTS USING MONOTHERAPY AND COMBINATION TREATMENT OF MEDICINE

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ABSTRACT

Treatment of diabetes mellitus (DM) can be vary, using monotherapy or combination therapy, and it depends on the severity of the disease. That variation will give influences to the patient's clinical condition and also their quality of life (QoL). The objective of this study is to determine the average of QoL's score in DM patients who use monotherapy and combination therapy of antidiabetic oral in Public Health Center of Kotagede 1 Yogyakarta. This study was conducted in a cross sectional study. Subjects were people who had an age above 18, got the diagnose of DM type 2, and also consumed of oral antidiabetic monotherapy or combination. The measurement of QoL is using a DQLCTQ questionnaire in Bahasa Indonesia. Analysis statistic with independent sample T-test was used to determine the differences between QoL in patients who use monotherapy and combination. Subjects who met the inclusion criteria are 52 patients. About 82.70% (43 patients) of the patients used combination and the other (9 patients) used monotherapy. The average of QoL in monotherapy patients (78.95 ± 11.36) was higher than in combination therapy's (75.18 ± 10.57). Result of the analysis statistic showed that there is no significant differences ($p > 0.05$) of QoL between monotherapy and combination therapy patients.

Keywords: Diabetes mellitus, DQLCTQ, monotherapy, combination

INTRODUCTION

Quality of life (QoL) is measured by individual perceptions on various aspects such as physical, emotional, and social aspect. The differences on each particular aspects influenced by ethnic, culture, education, and also income (Myers *et al.*, 2013; Nagpal *et al.*, 2010). Other than that, quality of life also affected by chronic disease. Some studies showed that patients with chronic disease have an average of quality of life lower than healthy patients (Bonomi *et al.*, 2000).

Diabetes mellitus is a chronic disease that increase significantly year by year. Data from *International Diabetes Federation* in 2013 showed that Indonesia was a country which have amount of people with diabetes (20-79 years old) for about 8.5 millions (International Diabetes Federation, 2013). Different with that, according to *International Diabetes Federation* in 2015, total cases of adults (20-79 years old) with diabetes is about 10 million cases (International

Diabetes Federation, 2015). The increasing of amount of diabetes patients needs an attention from many people and adequate of management therapy, which are including self-monitoring blood glucose, exercise, dietary modifications, and also adherence of the medications (Sharma *et al.*, 2014). In order to get a better glycemic index, it requires appropriate therapeutic management, and also it can be a preventive from the complications and with the hope of increasing patient's quality of life.

Treatment of diabetes mellitus patients can be vary using monotherapy or combination therapy, and it depends on the severity of the disease from each person. The treatment that used by the patients will give influences to the patient's clinical condition and also their quality of life. Previous study showed that the increase of complexity regimen in diabetes patients was needed to get a better glycemic control, however the measurement of QoL showed that

patients felt physical inconvenience caused by the increasing of complexity regimen (Lau *et al.*, 2004).

There are many kinds of available instruments for assessing quality of life, including generic and disease-specific which in this study is diabetes-specific. Generic instruments are designed to assess aspects on health that universal, and different with that, disease-specific instrument more detailed and accurate to measure specific impacts of health. The Diabetes Quality of Life Clinical Trial Questionnaire (DQLCTQ) is one of disease-specific instrument that has been validated, reliable and comprehensive to measure quality of life (Shen *et al.*, 1999; Garratt *et al.*, 2002).

The objective of this study is to determine the average of quality of life's score in diabetes mellitus patients who use monotherapy and combination therapy of antidiabetic oral in Public Health Center of Kotagede 1 Yogyakarta.

MATERIAL AND METHODS

Ethics Clearance was granted by the Ethics Committee of Ahmad Dahlan University with approval No.011601013. Informed consent paper was obtained from all participants.

Study design

This study was a cross sectional study which was conducted between February and March 2016 in Public Health Center of Kotagede 1 Yogyakarta, Indonesia.

Participants

The subjects on this study were diabetes mellitus patients' who came to Public Health Center of Kotagede 1 between February – March 2016. The inclusion criterias of this study were patients who had an age above 18 years old, got the diagnose of diabetes mellitus type 2 and attended to the public health center of Kotagede 1 Yogyakarta, consumed of oral antidiabetic monotherapy or combination, and also willing to be a participants. The exclusion criteria in this study was people who did not filled the questionnaire completely. The amount of patients that met the inclusion criterias was 52 patients.

Questionnaire

Patients who met the inclusion criteria and willing to be a participant will get a questionnaire. Measurement of quality of life in this study using a Diabetes Quality of Life Clinical Trial Questionnaire (DQLCTQ) in Bahasa Indonesia version. DQLCTQ has 8 aspects included physical, energy, health distress, mental health, satisfaction, treatment satisfaction, treatment flexibility, and frequency of symptoms. The measurement of quality of life in DQLCTQ questionnaire using a scale from 0 to 100, which are higher score indicates better quality of life. DQLCTQ questionnaire has been validated in previous study (Shen *et al.*, 1999).

Statistical Analysis

Analysis statistic with independent sample T-test was used to determine the differences between quality of life in patients who use oral antidiabetic monotherapy and combination therapy.

RESULT AND DISCUSSION

A number of 52 patients who met the inclusion criteria have characteristics (Table I). Table I showed that 75% of patients (39) was female, and 50% (26 patients) had ages over 60 years old. Data on this study was different with data from IDF in 2013 which are about 14 million more men than women with diabetes, and the ages of almost half of all adults with diabetes are between 40-59 years old (International Diabetes Federation, 2013). These differences can be occurred due to the insufficient number of participants in this study.

The types of medicine divided into 2 groups which were monotherapy in 9 patients (17.3%) and combination therapy in 43 patients (82.7%). In diabetes mellitus, metformin is an optimal drug for monotherapy, however, if the monotherapy cannot reach the glycemic target, initial combination between metformin plus a second agent can be used to achieve the HbA1C target more quickly (Inzucchi *et al.*, 2015). These data also can be linked with the duration of the disease since diagnosis, which were 65.4% (34 patients) had disease duration since more than 3 years ago. Besides that, the impact of diabetes mellitus is comorbidities, and 69.2% (36 patients) in this study have comorbidities.

Table I. Patient's characteristic

Patient's Characteristic	Number of Patients n=52 (%)
Sex	
Male	13 (25%)
Female	39 (75%)
Age	
< 40	4 (7.70%)
41-60	22 (42.3%)
> 60	26 (50.0%)
Educational Level	
No education	9 (17.3%)
< Senior High School	26 (50.0%)
≥ Senior High School	17 (32.7%)
Marital status	
Not married	1 (1.9%)
Married	37 (71.2%)
Divorce/Widow(ed)	14 (26.9%)
Duration since diagnosis	
< 1 year	1 (1.9%)
1-3 years	17 (32.7%)
> 3 years	34 (65.4%)
Type of Medicine	
Monotherapy	9 (17.3%)
Combination therapy	43 (82.7%)
Comorbidities	
Yes	36 (69.2%)
No	16 (30.8%)

Table II showed about the use of antidiabetic oral in this study. A number of 43 patients (82.70%) use combination therapy, which were all of them use metformin as a first therapy and use sulphonylurea as an additional therapy. Metformin, a biguanides which can reduce the hepatic glucose, is the optimal drug for monotherapy. Its advantages were low cost, minimal side effect of hypoglycemia, and can reduce the CVD events (Inzucchi *et al.*, 2015). The additional therapy were sulphonylurea including glimepiride and glibenclamid. The patients who use glimepiride was higher than glibenclamid. A randomized controlled trial study which compared the effect of glimepiride and glibenclamid on blood glucose in normal man showed that in fasting state there were similar effect on blood glucose level after IV administration of glibenclamid and glimepiride, and different with that, in post-prandial state (3-5h) blood glucose was significantly higher after glibenclamide than after glimepiride administration (Raptis *et al.*, 1999).

Table II. The use of antidiabetic oral in diabetes type 2 patients

Medicines	Sum	%
Monotherapy		
Metformin	8	15,38 %
Glimepiride	1	1,92%
Glibenclamid	0	0
Total	9	17,30%
Combination therapy		
Metformin + Glimepiride	41	78,85%
Metformin + Glibenclamid	2	3,85%
Total	43	82,70%

Quality of life analysis (Table III) showed that the average of quality of life in monotherapy patients was higher than in patients who use combination therapy, although that was not significantly different ($p=0.095$). The result of this study was similar with previous study in hospital of Yogyakarta in 2011, which the average of quality of life in monotherapy patients was higher than in combination therapy, and it was significantly different ($p=0.002$) (Sari *et al.*, 2011).

The endpoints of diabetes mellitus from the UK Prospective Diabetes Study (UKPDS) are reducing the achieved HbA1C of 7.0% (for intensive treatment group) versus 7.9% (for conventional treatment group), reducing microvascular endpoints (retinopathy, nephropathy, and neuropathy), and decreasing the need of laser treatment and cataract surgery (UK Prospective Diabetes Study, 1998). If the use of monotherapy can reduce the blood glucose and find the target of glycemic index, patients will get the benefit and increase their quality of life.

Furthermore, the result from table III showed that patients who use monotherapy had a good score in physical function, energy, health distress, mental health, satisfaction, treatment flexibility, and frequency of symptoms. It has been known that diabetes has negative impact on physical, psychological, and social functioning (Koopmanschap, 2002). Stress and coping with diabetes can affect the severity of the disease directly, also with pathophysiological processes and patient's perception of illness will affect to the patient's adherence and daily functioning.

Table III. Analysis QoL between monotherapy and combination therapy

Quality of Life Domain	Type of therapy		p value
	Monotherapy (n=9)	Combination therapy (n=43)	
Physical Function	91.11±13.6	73.02±17.3	0.005*
Energy	78.67±12.2	71.72±10.5	0.850
Health Distress	81.78±8.02	78.60±9.9	0.376
Mental Health	82.22±11.2	77.21±9.5	0.170
Satisfaction	76.19±7.6	73.13±6.3	0.207
Treatment Satisfaction	72.84±14.2	83.46±9.5	0.008*
Treatment Flexibility	69.44±10.5	68.37±8.5	0.742
Frequency of Symptoms	79.37±13.6	75.95±13.1	0.484
Total QoL	631.62±90.92	601.46±84.6	0.095
Average of QoL	78.95±11.36	75.18±10.57	0.095

Note *= Significantly differences ($p < 0.05$)

There are 2 domains that different significantly, including physical function and treatment satisfaction domains. Physical function score in monotherapy patients was higher than in combination therapy patients, it can be happened because the monotherapy patients were not feel restricted in their daily activities. This differences were statistically different with the significant value 0.005 ($p < 0.05$).

The use of combination treatment in diabetes mellitus type 2 patients is if non insulin monotherapy at maximal tolerated dose does not achieve or maintain HbA1C target over 3 months. Other than that, increasing the physical activity also important to get the HbA1C target before adding another oral agent (ADA, 2016). Thus, patients who use combination therapy are patients who cannot maintain their glicemic index and needed additional treatment.

Other, in the treatment satisfaction domain, the score of patients who use combination therapy was higher than monotherapy patients, and it was statistically different that proved by the significant value which is 0.008 ($p < 0.05$). This data was different with the previous study, which were score of treatment satisfaction domain in combination therapy patients was lower than in monotherapy patients ($p = 0.645$) (Sari *et al.*, 2011). The meaning of this result was combination therapy patients feel satisfied with their treatment.

Combination therapy is given to patients who cannot adequately decrease the blood glucose with monotherapy. In this study, quality of life higher in combination therapy patients than in monotherapy, which means that patients can feel the positive impact from the combination therapy. Result from different study, in patients with unresectable or metastatic cutaneous *BRAF* Val600-mutation-positive melanoma (COMBI-v) showed the results that treatment with combination of dabrafenib plus trametinib gives a benefit rather than with monotherapy vemurafenib (Grob 2015).

Furthermore, other domains such as energy, health distress, mental health, satisfaction, treatment flexibility, and frequency of symptoms were not different statistically between monotherapy and combination therapy patients. All of their score were higher in monotherapy than in combination therapy.

Finally, limitation of this study was the insufficient number of participants and it made an impact to the quality of life's score. In order to improve this study, the number of participants should be increased and balanced between monotherapy and combination therapy patients. Others, a lot of factors that can affect to the quality of life, such as comorbidity, absence of adverse event, Body Mass Index (BMI), or emotional patients which should be added in the next study.

CONCLUSION

From this study, we found that there is no significant differences ($p = 0.095$) of quality of life between monotherapy patients and combination therapy patients.

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