

EFFECT OF LATIHAN PASRAH DIRI (LPD) PLUS FLUOXETIN COMPARED WITH FLUOXETIN ALONE TO IMPROVE FRUCTOSAMINE LEVEL IN TIPE 2 DIABETES MELLITUS PATIENTS WITH DEPRESSION SYMPTOMS

Natsir Muin¹, Agus Siswanto², Ahmad Husain Asdie³

¹Specialty Training Program of Internal Medicine, Faculty of Medicine, Universitas Gadjah Mada-Dr. Sardjito General Hospital

²Psychosomatic Division, Department of Internal Medicine, Faculty of Medicine, Universitas Gadjah Mada-Dr. Sardjito General Hospital

³Endocrinology and Metabolism Division, Department of Internal Medicine, Faculty of Medicine, Universitas Gadjah Mada-Dr. Sardjito General Hospital

ABSTRACT

Background. Depression is a risk factor for diabetes and diabetes increase the risk for depression. Depression contributes to progression of diabetes mellitus. Examination of fructosamine is used to monitor blood sugar control for 2-3 weeks (according to age albumin). LPD evoke the relaxation response, which expected to improve symptoms of stress or depression.

Objective. To determine the decrease in fructosamine levels in the group of patients with diabetes mellitus with depression symptoms after administration of fluoxetine alone compared with a combination of fluoxetine and LPD.

Methods. This research conducted in Dr. Soeradji Tirtonegoro General Hospital, in May to August 2014. Distribution of data tested using the Shapiro-Wilk test. The differences between fructosamine and BDI (Beck Depression Inventory) before and after treatment tested with a pair t-test if normally distributed or Wilcoxon test if it was not normally distributed. The decrease in fructosamine and BDI both groups compared by independent t-test if normally distributed or Mann Whitney U test if not normally distributed. Differences were considered significant if $p < 0.05$ with a confidence interval of 95%.

Result. There was a significant decrease in fructosamine levels in treatment group from 293.90 ± 140.042 to 239.01 ± 133.13 after treatment with p value 0.017 ($p < 0.05$). Control group from 263.13 ± 163.65 to 219.01 ± 149.33 with p value 0.001 ($p < 0.05$). The decrease of fructosamine levels not differ in the treatment group 67.24 ± 102.71 than the control group 71.14 ± 72.77 with p value = 0.902 ($p > 0.05$).

Conclusion. LPD had no effect on fructosamine levels of type 2 diabetes mellitus patients with depression symptoms.

Keywords: LPD, symptoms of depression, fructosamine, BDI (Beck Depression Inventory)

ABSTRAK

Latar Belakang. Depresi merupakan faktor risiko terjadinya diabetes dan diabetes meningkatkan risiko untuk terjadinya depresi. Depresi memberikan kontribusi terhadap perjalanan penyakit diabetes melitus. Pemeriksaan fruktosamin digunakan untuk memantau kontrol kadar gula darah selama 2 – 3 minggu (sesuai usia albumin).

LPD menimbulkan respon relaksasi yang diharapkan mampu memperbaiki gejala stres atau gejala depresi.

Tujuan penelitian. Untuk mengetahui penurunan kadar fruktosamin pada kelompok pasien diabetes melitus dengan gejala depresi setelah pemberian fluoxetin saja dibandingkan dengan kombinasi fluoxetin dan LPD.

Metode. Penelitian ini dilakukan di RSUD Dr. Soeradji Tirtonegoro, Klaten pada bulan Mei-Agustus 2014. Distribusi atau sebaran data diuji menggunakan uji statistik Shapiro-Wilk. Perbedaan fruktosamin dan BDI (Beck Depression Inventory) sebelum dan sesudah perlakuan diuji dengan *pair t-test* jika terdistribusi normal atau *Wilcoxon test* jika tidak terdistribusi normal. Perbedaan penurunan fruktosamin dan BDI kedua kelompok dibandingkan dengan *independent t-test* jika terdistribusi normal atau *Mann Whitney U test* jika tidak terdistribusi normal. Perbedaan dianggap bermakna bila $p < 0,05$ dengan interval kepercayaan 95 %.

Hasil Penelitian. Penurunan kadar fruktosamin secara bermakna pada kelompok perlakuan dari 293.90 ± 140.042 menjadi 259.02 ± 116.08 dengan $p=0.017$ juga dialami kelompok kontrol dengan penurunan fruktosamin dari 263.13 ± 163.65 menjadi 219.01 ± 149.33 dengan $p=0.001$. Penurunan kadar fruktosamin pada kelompok perlakuan 67.24 ± 102.71 tidak lebih baik daripada kelompok kontrol 71.14 ± 72.77 dengan nilai $p=0.902$ ($p > 0.05$).

Kesimpulan. Penambahan LPD pada terapi fluoxetin tidak berpengaruh pada kadar fruktosamin penderita diabetes melitus tipe 2 dengan simtom depresi.

Kata Kunci: LPD, simtom depresi, fruktosamin, BDI (Beck Depression Inventory)

Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia due to relative or absolute insulin deficiency. The diagnosis of diabetes is made based on the criteria of American Diabetes Association (ADA) that is the fasting blood glucose levels ≥ 126 mg/dL, blood glucose levels 2 hours after loading ≥ 200 mg / dL, HbA1c levels $\geq 6.5\%$, the classic symptoms of hyperglycemia or

hyperglycemic crisis with random blood glucose levels ≥ 200 mg / dL.¹

Latihan pasrah diri is a method that combines relaxation and remembrance with a focus on breathing exercises and words contained in the *dhikir* (Relaxation and meditation prayer). *Latihan pasrah diri* induce the relaxation response, which expected to improve the symptoms of stress or depressive symptoms. These conditions affect directly or indirectly on the inflammatory response and

outcomes improve blood sugar control. Induce the relaxation response that expected to improve the symptoms of stress or depressive symptoms. These conditions affect directly or indirectly on the inflammatory response and outcomes improve blood sugar control. *Latihan pasrah diri* should be done for 21 days so that the body becomes accustomed to it.²

Examination of fructosamine or glycated albumin used to indicate a protein that has been glycated with glucose (the bond between glucose and albumin) via a non-enzymatic reaction. In general, the fructosamine value correlates well with HbA1c. Examination of fructosamine used to monitor blood sugar control for 2-3 weeks (according to age albumin). Examination of fructosamine particularly useful in the condition of pregnancy or the hemoglobin disorders.³

Depression is a risk factor for diabetes and diabetes increase the risk for depression. Depression contributes to the disease course of diabetes mellitus in terms of reduced adherence to treatment and diet, reduced physical activity, reduced glycemic control, reduces quality of life, cause disability, and rising health care costs.⁴ SSRIs such as fluoxetine, fluvoxamin, paroxetin, sertraline, and citalopram are the result of studies to obtain drugs as effective as tricyclic antidepressants with better security.⁵

Research Methods

This study is a retrospective cohort clinical trial to determine the effect of fluoxetine compared to fluoxetine and exercise resigned themselves to the fructosamine levels in patients type 2 diabetes mellitus with symptoms of depression, by taking secondary data. The study conducted at the clinic of Internal Medicine RSUD Dr. Soeradji Tirtonegoro, Klaten. When the study in May 2014 until August 2014.

Patients were included in this study were patients with type 2 diabetes who underwent routine therapy in the clinic accompanied by symptoms of depression, and are willing to participate in the study by signing a letter of consent (informed consent), aged less than 65 years. Patients were excluded if they meet the inclusion criteria like the antidepressant drug therapy, psychotherapy, infections, rheumatoid arthritis disease history, creatinine levels > 3 mg/dL, and patients who cannot read or write, or suffering from heart failure.

The data presented in the form of mean and standard deviations. To measure the distribution of the data used statistical tests Shapiro Wilk. Differences fructosamine and BDI (Beck Depression Inventory) before and after treatment tested with the pair t-test if normally distributed or Wilcoxon test if it is not normally distributed. Differences decrease in fructosamine and BDI both groups compared by independent t-test if normally distributed or Mann Whitney U test if not normally distributed.

Differences were considered significant if $p < 0.05$ with a confidence interval of 95%.

Result

The study conducted over three months at RSUD Klaten. 257 people with type 2 diabetes do charging BDI questionnaire to seek the presence or absence of symptoms of depression. 79 people with type 2 diabetes who had symptoms of depression. 38 people who met the inclusion and exclusion criteria were divided into 2 groups of randomized trials.

The treatment group Latihan Pasrah Diri (LPD) consisting of 19 people and a control group that did not get special treatment 19 people. There are three people in the treatment group who did not continue

research, and 3 people in the control group who did not continue the study, so the LPD group and the control group each attended by 16 people.

Fluoxetine treatment group therapy plus LPD

The group was getting a workout technique LPD with subsections psychosomatic supervision by staff, and then performs LPD 2 times daily for 21 days (3 weeks) in a row. The control group did not receive special treatment, just a plain relaxation. The evaluations of the results toke after treatment in the form of fructosamine levels and BDI score.

Table 1 Baseline characteristic

Characteristic	LPD Group	Control Group	P value
Gender			
Male	6 (37.5%)	4 (25%)	$p=0.453$
Female	10 (62.5%)	12 (75%)	
Age (years)	52.38 ± 4.23	54.38 ± 5.63	$p=0.266$
Blood Pressure			
Systolic	128.75 ± 15.86	134.38 ± 18.25	$p=0.377$
Diastolic	86.87 ± 135	86.87 ± 135	$p=0.984^*$
BDI score			
Before treatment	18.31 ± 10.05	17.75 ± 15.46	$p=0.488$
Fructosamine			
Before treatment	293.90 ± 140.04	263.13 ± 163.86	$p=0.572$

Description: LPD=*latihan pasrah diri*; statistical test by unpaired t-test,*= statistical test by Mann-Whitney U test.

Table 2 Mean fructosamine levels of the treatment group and the control group before and after treatment.

Group	Fructosamine Before Treatment Mean±SD	Fructosamine After Treatment Mean±SD	P value
LPD Group	293.90±140.042	259.02±116.08	p=0.017
Control Group	263.13±163.65	219.01±149.33	p=0.001

Description: LPD=*latihan pasrah diri*; statistical test by paired t-test

Table 3 The mean score BDI treatment group and the control group before and after treatment.

Group	Nilai BDI Before treatment		BDI Score After treatment		P score
	Mean±SD	Min-Max	Mean±SD	Min-Max	
LPD Group	18.31±10.05		16.50±12.69		p=0.041
Control Group	17.75±15.46	2-61	14.62±12.5	2-41	p=0.001*

Description : LPD=*latihan pasrah diri*; statistical test by paired t test, * = statistical test by Wilcoxon test

Table 4 The mean BDI and fructosamine impairment treatment group and the control group after treatment.

Impairment BDI score and Fructosamine	LPD Group		Control Group		p value
	Mean±SD	Min-Max	Mean±SD	Min-Max	
Impairment BDI score	7.94±3.18	1-25	6.12±6.33	0-20	p=0.437*
(Δ BDI score)					
Impairment Fruktosamin (ΔFruktosamin)	67.24±102.71		71.14±72.77		p=0.902

Description: LPD=*latihan pasrah diri*; statistical test by unpaired t-test, *= statistical test by Mann-Whitney U test.

Fructosamine levels and the BDI score showed a normal distribution so the analysis by paired t-test before and after treatment. Fructosamine levels decrease significantly in the treatment group from 293.90±140.042 to 259.02±116.08 with p-value = 0.017

also in the control group from 263.13±163.65 to 219.01±149.33 with p value = 0.001. Decreased levels of fructosamine in the treatment group was no better than the control group, with p value = 0.902 (p > 0.05). BDI scores decrease significantly in the treatment group from 18.31±10.05 to

16.50±12.69 with p value= 0.041 and also in control group also decrease from 17.75±15.46 to 14.62±12.5 with p value = 0.001. Impairment of BDI in the treatment group and the control group was not normally distributed so tested by Mann Whitney U test with a result that no significant difference with p value = 0.437 (p> 0.05). The result was not reported any complaints of side effects of drugs.

Discussion

This study conducted to determine the effects of *Latihan Pasrah Diri* (LPD) to decrease the levels of fructosamine in patients with type 2 diabetes mellitus with symptoms of depression that treated with fluoxetine at RSUD Klaten. There are 257 patients with type 2 diabetes and inspection score BDI (Beck Depression Inventory) and we find 79 people (30.1%) with a score ≥ 10 or with symptoms of depression. This result is similar to that reported by Anderson et al., 2001 that found symptoms of depression by 31% in patients with type 2 diabetes who control routine and higher than reported by Roy and Lloyd in 2012 amounted to 19.1%. BDI with a cut-off score ≥ 10 had a sensitivity of 84.6% and a specificity of 86.4%.⁶

The treatment group who received LPD consisted of six men (37.5%) and ten women (62.5%), whereas in the control group consisted of 4 men (25%) and 12 women (75%). Statistical test in both groups showed no significant difference (p = 0.453). This

means sex differences between the treatment group and the control group is not a confounding factor. Age in the treatment group (52.38 ± 4.23) years and the control group (54.38 ± 5.63) years. Statistical test of mean age in the treatment group and control groups did not differ significantly (p = 0.266). The mean systolic blood pressure in the treatment group (128.75 ± 15.86) mmHg, and the control group (134.38 ± 18.25) mmHg (p = 0.377).

Mean diastolic blood pressure in the treatment group (85.29 ± 6.29) mmHg, and the control group (86.87 ± 13.5) mmHg (p = 0.984). BDI before the carrying score in the treatment group (18.31 ± 10.05) and control group (17.75 ± 15.46) (p = 0.488). Fructosamine levels before treatment group (293.90 ± 140.04) and the control group (263.13 ± 163.86) (p = 0.572). These data showed that the treatment group and the control group had baseline data were not significantly different.

Fructosamine levels decrease significantly in the treatment group from 293.90±140.042 to 259.02±116.08 with p value= 0.017 also in the control group from 263.13±163.65 to 219.01±149.33 with p value = 0.001. BDI scores decrease significantly in the treatment group from 18.31±10.05 to 16.50±12.69 with p value= 0.041 and also in control group also decrease from 17.75±15.46 to 14.62±12.5 with p value = 0.001. It is equal with that reported by Lustman et al. 2000, which showed an

improvement in the value of BDI significantly after treatment with fluoxetine for 8 months, but blood sugar levels are not significantly affected.

Decreased levels of fructosamine in the treatment group 67.24 ± 102.71 not better than the control group 71.14 ± 72.77 with p value = 0.902 ($p > 0.05$). Decreased levels of fructosamine in both groups, but the addition of *latihan pasrah diri* themselves to the treatment group did not provide an improvement in the decrease of fructosamine. Impairment of BDI in the treatment group and the control

Conclusion

Latihan Pasrah Diri (LPD) as non-drug intervention therapeutic does not significant affect the decrease in fructosamine levels in patients with type 2 diabetes mellitus with symptoms of depression who gained fluoxetine therapy. Further research is needed to compare the effect of LPD and fluoxetin to frukosamin level in patients with type 2 diabetes mellitus

References

1. American Diabetes Association. 2013. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. Vol 36 Supplement 1, S67.
2. Asdie A.H. 2000. Patogenesis dan Terapi Diabetes Melitus Tipe 2.
3. Medika. Fakultas Kedokteran Universitas Gadjah Mada, Yogyakarta.
4. Khan H.A., Sobki S.H., Alhomida A.S., Khan S.A. 2007. Paired

group was not normally distributed so as tested by Mann Whitney U test with a result that no significant difference with $p = 0.437$. McGinnis et al., 2005 showed that the relaxation for 3 months could lower the value of BDI, blood pressure and A1C. McGinnis researches unfinished in combination with fluoxetine administration. So our results may affect by the administration of fluoxetine as a standard therapy for depression. Fructosamine complaints from the use of fluoxetine and practice surrender.

with symptoms of depression. Necessary to check the levels of albumin, new stressors, monitoring medicines consumed by patients in the form of continuity of treatment during the study, recording the rest of the drug and supervisors to take medication, and most importantly, a strict monitoring in doing LPD and relaxation with a decrease in pulse 2-4 beats / min.

5. Values of Serum Fructosamine and Blood Glucose for the Screening of Gestational Diabetes Mellitus. Indian Jo of Clinical Biochemistry; 22 (1) 65-70.
5. Bogner H.R., Morales K.H., de Vries H.F., Cappola A.R. 2012. Integrated Management of Type 2 Diabetes Melitus and Depression Treatment to Improve Medication Adherence: A Randomized

- Controlled Trial. *Ann Fam Med*;10:15-22.
6. Cuevas C.D. & Sanz E.J. 2006. Safety of Selective Serotonin Reuptake Inhibitors in Pregnancy. *Curr Drug Safety*;1;17-24.
 7. McDowell I. dan Newell C. 1996. *Measuring Health: A Guide to Rating Scales and Questionnaires* 2nd ed. New York: Oxford University Press.
 8. Anderson JR, Freedland KE, Clouse RE, Lustman PJ. 2001. The Prevalence of Comorbid Depression in Adults with Diabetes. *Diabetes Care*. vol. 24 no. 6 1069-1078
 9. Roy T., dan Lloyd C.E. 2012. Epidemiology of depression and diabetes: A systematic review. *Journal of affective disorder*. Supplement, Pages S8–S21