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The Effect of propolis to blood glucose and total cholesterol of prediabetes patients

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Abstract. Prediabetes is considered as the initial phase of macrovaskular disease associated with increase of blood glucose and cholesterol level. The effect of propolis to treat fasting blood glucose, glucose tolerance, total cholesterol was examined. Experimental Research with Randomized Clinical Trial (RCT) design was utilized in the study. Intervention given was propolis at dose 50 mg/kg bwt and health education administered for 20 days. The quality of propolis was 20%extract and quercetin content 25.29 mg/L tested by Biofarmaka Laboratory Test of Hasanuddin University, health education used counseling strategy. The samples were 64 prediabetic patients consist of 32 patients treated with propolis and 32 treated with health education. The result of Wilcoxon with significant level of 0.05 has proved significantly decreased fasting blood glucose, glucose tolerance and total cholesterol respectively 14.28 (p=0.000), 23.16 (p=0.000) and 16.3 (p=0.000) The result of group given propolis as significant as health education group respectively fasting blood glucose 14.9 (p=0.001), glucose tolerance 13.98 (p=0.000) and total cholesterol 9.76 (p=0.021). Giving propolis and health education are effective for the change of fasting blood glucose, glucose tolerance and total cholesterol. Propolis is potential to use as a pharmacology therapy for prediabetes.

Keywords: Propolis, Fasting Blood Glucose, Glucose Tolerance, Total cholesterol

Introduction

Prediabetes defined as blood sugar level higher than normal, but not high enough to be diagnosed as diabetes and Its raises a person's risk of type 2 diabetes, heart disease and stroke. Prediabetes states include impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and the metabolic syndrome (CDC, 2011; Garber et al, 2008). Prediabetes associated with an increase risk of cancer death, particularly death from liver cancer. Mortality from all cancers rose linearly with increasing glucose concentration (Zhou et al. 2010). Prevalence of prediabetes is increasing worldwide and experts have projected that more than 470 million people will have prediabetes by 2030 (Tabak et al, 2012). Report on result of Basic National Health Research (RISKESDAS) 2007 showed IGT in Urban Area was 10.5%, the center of Indonesia, Jakarta was 24.91%, West papua was 21.8%, West Sulawesi 21.8% and South Sulawesi 17.6%. Prevalence of prediabetes in Indonesia is high (10%) so that a good prevention strategy is needed (Basic Health Survey, 2007).

Prediabetes needs proper intervention to reduce diabetes incidence and others complication. The best solution is lifestyle modification but it is so difficult for many people to do, so medicine treatment is needed. Propolis is a resinous substance produced by honeybees. It has been reported to possess various biological activities such as anticancer, antioxidant and hypolipidemic. It was reported that propolis supplementation in STZ-induced diabetes is associated with a significant decrease in the blood glucose (Viuda-martos et al. 2008: Al-Hariri, 2011). New Zealand rabbits were fed during four weeks had significant reduced in total cholesterol, low density lipoprotein, trygliceride and increased high density lipoprotein (Nader Et al, 2010). We need evidence based On clinical trial about potencial hypoglycemic and anticholesterol effect of propolis to prediabetes patient.

Materials and Methods

Design and Subject

Pretest Posttest Experimental Research design was utilized in the study. Sixty four (64) subjects were chosen randomly. The chosen subjects were then divided equally. Thirty two (32) subjects belong to the experimental group who received the Propolis intervention, while the other thirty two (32) subjects belong to the Control group who received the Health education intervention. The laboratory personnel and the subjects were not informed on who will be included in both experimental and control groups to prevent bias. The experiment proper held at Great Hall Health Laboratory of Makasaar (ISO 1705:2008 Certified), lasted for twenty (20) days.

Procedure

Prior to the procedure, this paper was submitted to the Ethical Commission of Hasanuddin University, and it was approved by the said Committee with the recommendation number 0260/H4.8.4.5.31/PP36-KOMETIK 2012 and registration number UH12010025. The first step was screening 120 subjects and out of these subjects only 64 subjects were diagnosed to have prediabetes. These subjects then were given informed consent for their approval and participation in the study. Consequently, these subjects were randomly grouped into Experimental and Control Groups. Both Experimental and Control groups were pretested with Glucose Tolerance (mg/dl), Fasting Blood Glucose (mg/dl) and Total Cholesterol. It was then followed by the Intervention phase, in which the Experimental group received the propolis intervention, specifically propolis extract 20% containing quercetin content 25.29 mg/L. A total of 6 drops were given to the subjects, 2 drops in the morning, another 2 drops in the afternoon and the last 2 drops was given during night. On the other hand, the control group received the Health education intervention regarding information about prediabetes, prevention of complication, diet and physical activity. Twenty (20) days, after the Intervention phase, posttest with Glucose Tolerance (mg/dl), Fasting Blood Glucose (mg/dl) and Total Cholesterol were taken and consequently compared with pretest results.

Results and Discussion

Data were analyzed and interpreted utilizing statistical tools such as mean, standard deviation, mean difference and characteristic of subjects. Statistic test used was Wilcoxon text ($\alpha = 0.05$).

Tabel 1 Characteristic of Subjects

Characteristics		Treatment Mean (%) n=32	Control Mean (SD) n=32
Sex	Male	3 (9.4)	3 (9.4)
	Female	29 (90.6)	29 (90.6)
Ethnic	Buginese	25 (78.1)	18 (56.3)
	Javanese	2 (6.3)	2 (6.3)
	Makassar	5 (15.6)	11 (34.4)
	Toraja	-	1 (3.1)
Education	Academy/University	13 (40.6)	9 (28.1)
	High School	9 (28.1)	11 (34.3)
	Under High school	10 (31.2)	12 (37.5)
Age		45.66(14.86)	44.88(14.16)
Family History	Yes	28(87.5)	25 (78.1)
	No	4(12.5)	7(21.9)

Table 1 showed that majority of subjects both in experimental and control groups were female and both got the rate of 29 (90.6%). Buginese ethnic got the highest score among the ethnic groups. For the Educational attainment, 13 subjects (40.6 %) of the treatment group reached Academy/University or College level, while 12 subjects (37.5%) of the Control group reached under high school level. Majority of the subjects both in treatment and control groups had a family history of prediabetes.

Some studies about prediabetes have explain Characteristics of Prediabetes prevalence in Indonesia. The majority of prediabetes in Indonesia are females (61.6%), Seen on age bases, most of the pre-diabetes subjects are in an age range between 38 – 47.

If we account 66.4% under high school (Soewondo 2011). Having a family history of diabetes and being older are major risk factors of developing prediabetes (Kumar et al, 2008: Soegondo, 2011). Prediabetes Epidemiological study in Depok has result that Isolated Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are more frequently found in female subjects (66.2 and 69%) (Yunir et al, 2009).

Studies that Ethnicity plays a role in the different prevalences of diabetes and prediabetes are in Amsterdan and among the three ethnic groups in Chinese, it is showed significantly different. (Ujcic-Voortman et al, 2009 ;Yang Feng et al, 2012).

Table 2. Effect of Propolis to Prediabetes after 20 Days Treatment

Variabel	Perlakuan Mean (SD)				Kontrol Mean (SD)			
	Pre	Post	Δ Mean	P	Pre	Post	P	Δ Mean
Glucose Tolerance (mg/dl)	148.19±14.056	125.03±19.30	-23.16	0.000	143.28±17.81	129.03±27.09	0.000	-13.98
Fasting Blood Glucose(mg/dl)	103.31±14.92	89.03±12.79	-14.28	0.000	102.84±19.672	88.75±14.54	0.001	-14.9
Total Cholesterol	195.16±23.49	178.63±16.99	-16.3	0.000	198.6±21.13	188.84±14.82	0.021	-9.76

Minus (-) in mean difference (Δ Mean) means decrease

SD = Deviation standart

Table 2 clearly showed that there was a significant decrease in all the variables being investigated namely Glucose Tolerance (mg/dl), Fasting Blood Glucose (mg/dl) and Total Cholesterol in both the Treatment/Experimental and Control groups. Therefore, it is suffice to say that both propolis intervention and Health Education on prediabetes, prevention of complication, diet and physical activity can decrease both the blood sugar and cholesterol levels of prediabetes individuals. These findings are correlated with the following explanations; Lifestyle modification is still the best intervention for prediabetes, but many people are undisciplined or not adherent to lifestyle modifications, so it needs alternative

intervention and one of these is the administration of propolis to human subjects which has proven to decrease blood glucose and total cholesterol of prediabetes patients.

Compunds identified in propolis were amino acids, aromatic acids, aromatic esters, flavones and flavonols terpenoid, steroid, etc (Marcucci, 1995). Propolis contains some minerals such as Mg, Ca, I, K,Na, Cu, Zn, Mn and Fe as well as some vitamins like B1,B2, B6, C and E, and a number of fatty acids. In addition, it contains some enzymes as succinic dehydrogenase, glucose-6-phosphatase, adenosine triphosphatase and acid phosphatase (Tikhonov et al, 1987).

Propolis consist of many substances such as amino acids, flavones and flavonoids, terpenoids and other compounds, vitamins and minerals. Some of substances have benefit to prediabetes. Quercetin has proven exist in propolis by testing in Biofarmaka laboratorium of Hasanuddin University, each propolis almost contain quercetin but in defferent level. Based on many evidences or research and theoritically, quercetin can decrease blood glucose and has strong antioxidant effect to oxidative stress. Quercetin, a flavonoid with antioxidant properties brings the regeneration of the pancreatic islets and probably increases insulin release in streptozocin-induced diabetic, thus exerting its beneficial antidiabetic effects (Vessal et al, 2003). It assumes has protective roles against mulltple diseases associated with oxidative stress, quercetin affects adipogenesis and apoptosis in 3T3-L1 cells by activating monophosphate-activated protein kinase (AMPK) signal pathway in 3T3-L1 preadipocytes (Ahn et al, 2008).

One of the propolis composition is chromium, many studies shown chromium have beneficial effects without any documented side effects on glucose tolerance state and type 2 DM. The mechanism of actions of chromium involves increased insulin binding, increased insulin receptor number and increased insulin receptor phosporylation (Anderson, 1998). Propolis has proven effective in control blood glucose, modulate lipid metabolism and improve the insulin sensitivity (Li Yajing et al, 2010; El-Sayed et al, 2009:Zamami et al, 2007). It also has effect to stress oxidative or free radicals in rats with diabetes mellitus (Fuliang et al, 2005: Bhadauria et al, 2007). Propolis as a food supplement modulated antioxidant enzymes (AOE) and significantly decreased lipid peroxidation processes (LPO) in plasma, liver, lungs, and brain of mice (Sobocanec et al, 2006). Free Amino acids exist in propolis are arginine and prolin (Gabrys, 2006). Total cholesterol prediabetes patient treated with propolis also decreased significant, based on research and theoritically arginine contained in propolis has effect as anti atherogenic. Propolis Evidence by research about effect propolis has proven decreased total cholesterol (Abo-salem et al, 2009). Polyphenols from propolis are able to reduce atherosclerotic lesions through mechanisms including the modulation of inflammatory and angiogenic factors (Daleprane et al, 2012).

Conclusions

Health Education has been found out to be effective in decreasing both the blood sugar and cholesterol levels, therefore it is important that the Health care team will carry out their role as adviser, counsellor and educator. Propolis has both antihypoglycemic and anticholesterol effects.Therefore, it is highly recommended that further studies should focus

on the the product development of propolis, specifying the effective and safe dose for all ages, side effects and toxicity level of the said product.

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