Original Article

Effect of Green Tea Polyphenols on HbA1C in Type 2 Diabetic Patients

1. Farah Deeba Khan 2. Ghazala Irshad 3. Samra Hafiz 4. Mehboob Bari

1. Asstt. Prof. of Biochemistry, UCMD, TUOL 2. Asstt. Prof. of Biochemistry, UCMD, TUOL 3. Asstt. Prof. of Biochemistry, FMHMC 4. Prof. of Biochemistry, UCMD, TUOL

ABSTRACT

Objectives: In many previous studies, green tea has been shown to prevent and treat type 2 diabetes16-18.. Some controversial results have also been noticed in few studies. Primary objective of the present study was to determine the effect of green tea polyphenols on glycaemic control among the patient with type 2 diabetes.

Background: Conflicting data exists according to previous studies about green tea that it might have a positive effect on the glycaemic control in patients with diabetes mellitus type 2. The aim of the present study was to give evidence whether a crude extract of green tea improves glycated haemoglobin A1C (HbA1C) and fasting plasma glucose in patients with type 2 diabetes.

Study Design: Study was prospective, interventional and randomized.

Place and Duration of Study: This study was conducted at the Department of IMBB (Molecular Biology), University of Lahore from April 2007 to June 2007.

Materials and Methods: A total of 60 patients, 20 with diagnosed diabetes mellitus type 2 taking oral anti-diabetics and 20 diabetic individuals who were not taking any hypoglycemic drug, of either sex were randomly assigned to take green tea extract twice a day, at the dose of 15 gram, for 3 months. A group of 20 healthy subjects was also enrolled in the study.

Results: A very significant difference between the pre- and post-intervention fasting plasma glucose level was observed in both the groups of diabetic patients while no significant difference was seen regarding HbA1C level. Significant changes were not observed in either of the parameters in healthy individuals, as was expected throughout the study. No adverse effects were observed in any of the three groups.

Conclusions: The green tea extract seems to have a moderate effect in reducing fasting plasma glucose concentrations in diabetic patients with poor glycaemic control.

Key Words: Green tea polyphenols, diabetes mellitus type 2, fasting plasma glucose, HbA1C.

INTRODUCTION

One of the deadliest diseases ever known, Diabetes Mellitus, has also been one of the most silent.

The subcontinent currently has 47 million people with diabetes that will grow to 80 million by the year 2025[1]. Despite the advances in the treatment, incidence of diabetes is not falling down. Herbs have been used for food and medicinal purposes for centuries[2]. Increasing dissatisfaction over undesirable side effects and the cost of conventional medicines, has led people choose some alternative mode of treatment. Amongst these, tea is the most commonly used beverage, second after water, first cultivated by China and India, with a lot of health benefits[3]. Green tea has been shown to lower high serum cholesterol level[4-6], treating periodontal diseases[7], improving osteoporosis[8], and as a strong anti-oxidative, anti-mutagenic and anti-carcinogenic agent in many types of cancers [9-12].

All tea plants belong to same species, *sinensis* and all teas, black, green, oolong belong to same plant, camellia sinensis[13]. The difference between the teas is in their processing. Green tea is prepared in such a way as to preclude the oxidation of green leaf polyphenols. The unfermented GT leaves contain the highest concentration of powerful antioxidants called polyphenols and the healthful properties of GT are largely attributed to these compounds[14]. It contains a variety of polyphenols, including flavanols, flavandiols, flavanoids and phenolic acids. Polyphenols may account for up to 30% of the dry weight and they give GT a somewhat bitter flavour. Most of the GT polyphenols are flavonols, commonly known as catechins. Some major GT catechins are, Epigallacatechin Gallate (EGCG) 60%, Epigallocatechin (EGC) 20%, Epicatechin Gallate (ECG) 13%, Epicatechin (EC) 6% and Gallocatechin (GC) 2%[15]. Green tea is commonly sold as rolled dried leaves usually taken as brewed in hot water.

MATERIALS AND METHODS

Study was prospective, interventional and randomized. Seventy subjects were approached from friends, immediate families and private clinics. Sixty out of them were enrolled and placed in three groups A, B and C; each containing 20 individuals each.

Group A: Healthy individuals.

Group B: Diabetic patients who were on oral hypoglycemic drugs.

Group C: Diabetics who were not taking any medication.

Inclusion Criteria: Healthy volunteers and non-complicated diabetic patients of either sex were included.

Exclusion Criteria: Women with menorrhagia and individuals taking anticoagulant therapy were not included[19].

Study was planned to be done primarily in TUOL. All the individuals were explained about the study and written consent was taken. A clinical questionnaire was filled for each subject to get a full account of present and past illness, family and drug history, their dietary habits and physical activity (Table 1).

Dosage: Crude extract of two tea bags, twice a day (150mg/kg body wt) was planned to give for three months. Brewing method was explained to the participants.

RESULTS

Twelve hour fasting blood sugar levels and HbA1C were estimated at day one. Then fortnightly their blood sugar levels were taken and physical condition was assessed to see any adverse effect. At the end of study again sugar levels and the level of HbA1C were repeated.

Blood sugar estimations were carried out by enzyme oxidase method (GOD-PAP method) [20] using Apel PD-303 (Japan) UV spectrophotometer. A1C levels were done from a private lab.

Statistical data thus collected was subjected to paired student t-test analysis. The difference was considered significant when P<0.01(Table 2).

Table No.1: Basic Characteristics of Study Population

Groups of Subjects:		A	B	C
N		18	16	17
Gender	Male	5	4	3
	Female	13	12	14
Family history of diabetes	Yes	6	10	11
	No	12	6	6
Family history of hypertension	Yes	7	6	8
	No	11	10	9
Hypertension	Yes	0	13	12
	No	18	3	5
Diabetes (year)		nil	8.8+/-5.2	4.3+/-2.6
Age (year)		20.5+/-3.5	54.76+/-7.6	53.1+/-11.9

Data are means+/-SD or *n* (%)
Group A: Healthy Individuals
Group B: Diabetics without any medication
Group C: Diabetics on medication

Relative to initial concentrations, modest effects on blood sugar levels were seen in diabetic individuals (from 142+/- 20 to 126+/-16 P<0.01) in group of diabetic who were already on hypoglycaemic drugs. A very significant reduction in FBS observed in patients who were not taking any medication (from 181+/- 51 to 131 +/-34 P<0.01). Results in healthy individuals were not significant (from 89+/-7 to 84+/- 8 with P<0.01).

Final levels of A1C were not significant in any of the three i.e., from 7.8 +/- 0.9 to 7.6 +/- 1.2 in group C; 8.4+/1.6 to 8.3+/-1.5 (P=0.34) in group B while 6.1+/-0.6 from 6.0+/-1.2, (P=0.00) in group A.

Table No.2: Study Variables

	A	B	C
Fasting Blood Sugar at baseline (mg/dl)	89+/-7	181+/-51	142+/-16
Fasting Blood Sugar post intervention	84+/-8	131+/-34**	126+/-16*
HbA1C baseline (%)	6.1+/0.6	8.2+/-1.6	7.8+/-0.9
HbA1C post intervention	6.0+/-1.2	8.3+/-1.5	7.6+/1.2

Data are means +/- SD
Values of blood sugar levels have been rounded up.
** significant from baseline P<0.001
* significant from baseline P<0.01

DISCUSSION

Green tea has been used in Asian countries since ages for the treatment of various ailments. Its inverse relationship with blood glucose levels has been studied extensively in animals and in humans. To our knowledge this was the first study to evaluate the effect of green tea on glycemic control in type 2 diabetes in Pakistan. Similar study has been done to show the effect of green tea on fasting glucose level but not on A1C by the writer herself[21]. Our recent results are in consistence with the results of Todd A MacKenzie, who showed a significant reduction of fasting blood glucose but no effect on the HbA1C in 3 months period after the treatment with green tea polyphenols on the diabetic patient who were already taking hypoglycaemic drugs[22].

Hiroshi et al, also have shown the effect of green tea extract in diabetic mice after administering various doses (30, 150, 300mg/kg) [23]. There was mild lowering of FBS at 150mg/ kg, while significant lowering of FBS seen on 300mg/kg. No elevation of serum insulin levels was observed by them during the decrease in blood sugar level. All the studies done previously, have shown reduction in FBG while poor control on glycaemia with HbA1C which means maintaining only FBS does not rule out the possibility of developing diabetic complications. Hosoda et al. gave similar results on FBS level in diabetics with oolong tea but they did not measure A1C[24]. The reported benefits of green tea on FBS but negligible effect on HbA1C can

best be explained by the relatively small contribution of green tea on random glucose levels.

This study had several limitations. It is possible, but unlikely, that subjects might be taking inadequate dose of GTP, as they were not on strict observation. The dose given twice a day perhaps was not sufficient to maintain the therapeutic level throughout 24 hours period, to achieve good glycaemic control. The dose could have been made more frequent to achieve a good therapeutic level

It is also possible that 90 days duration is not enough periods to maintain 120-day lifespan of red blood cells showing false-negative results. Although, we believe those 90 days is a sufficient time to show a positive effect. However Todd A MacKenzie recommended the regular intake of green tea on an account of its other health benefits, but evidence that it improves glycemic control, is limited and conflicting.

In summary, this study provides evidence that Green Tea is not effective in improving glycaemic control in type 2 diabetes. Consistent with other recent researches, our failure to demonstrate any effect on Hb A1C, introduces significant doubt regarding the efficacy of green tea in diabetic subjects.

CONCLUSION

The green tea extract seems to have a moderate effect in reducing fasting plasma glucose concentrations in diabetic patients with poor glycaemic control.

REFERENCES

1 Claudia B.Diabetes becoming growing threat for affluent Asians. VOA'S Asia New center in Hong Kong 2007.

2 Walter ME, Wang XL. ECGC, a constituent of green tea, represses hepatic glucose production. J Biochem 2002;277(38):34933-40.

3 Jaqualine H. A review on the health effects of green tea. (E PubMed) 2002.

4 Sadia A, Farah D, Mazhar M. Hypocholesterolemic effects of green tea on raised serum cholesterol in Pakistani population. The Professional J 2012;19(3): 84-89.

5 Ikeda I, Tsuda K, Suzuki Y. Tea catechins with agalloyl moety supress post-parandial hypertria-cylglycerolemia by delaying lymphatic transport of dietary fat in rats. J Nutri 2005;135(2): 155-9.

6 Yang YC, Koo CH. Protective effects of habitual tea consumption on hypertension. Arch Inter med 2002;164(14):116-24.

7 Sakanaka S, Okada Y. Inhibitory effects of green tea polyphenols on the production of a virulence factor of the periodontal disease causing anaerobic bacterium porphyromonas gingivitis. J Agric Food Chem 2004;52 (6):1688-92.

8 Yun JH, Pang EK, Kim CS, Yoo YJ..Inhibitory effects of green tea polyphenols, EGCG, on the expression of matrix metalloproteinase 9 and on the formation of osteoclasts. J Periodontal Res 2004; 39 (5); 300-307.

9 Azam S, Hadi N, Khan NU. Pro-oxidant property of green tea polyphenols epicatechins and epigallocatechin-3-gallate: implications for anticancerproperties. Toxicol 2004;18 (8): 555-61.

10 Beek SJ, Kim JS, Jackson FR, Lee SH. Epicatechingallate induced expression of NAG-1 is associated with growth inhibited apoptosis in colon cancer cells. Carcinogenesis 2004. (E Pub ahead of print)

11 Ju J, Liu Y, hong J. Effect of green tea on high fat diet on arachidonic acid metabolism and abberareit crypt foci formation in an azoxymethane-induced colon carcinogenesis in mouse model. Nutr Cancer 2003;46(2): 172-8.

12 Lu QY, Jin YS, Zhang ZF, Herber D. Green tea extract modulates actin remodeling via Rho activity in an in-vitro multi-step carcinogenic model. Clin. Cancer Res 2005;11 (4): 1674-8.

13 http://www.whfoods.com World's Healthiest Food Org. Feeling Great.

14 Robak J, Gryglewski RJ. Flavanoids are scavangers of superoxides anions. Biomedical Pharmacology 1998;37(5).

15 Graham H. Green tea composition, consumption and polyphenol chemistry. Pre Med 1992;21: 334-50.

16 Wu LY, Juan CC, Huang LS, Ho LT. Green tea supplementation ameliorates insulin resistance and increases glucose transporter IV content in a fructose fed model. Eur J Nutr 2004;43(2): 116-124.

17 Kobayashi Y, Suzuki M, Suzuki H, Shimizu M. Green tea polyphenol can inhibit the sodium dependant glucose transporter of intestinal epithelial cells by a competitive mechanism. J Agric Food Chem 2002;48: 5618-5623.

18 Farah DK, Jaffery, Abdussalam. Hypoglycemic effect of camellia sinensis in type 2 Diabetic patients. JFJMC 2008;2(1): 34-38.

19 Kang WS, Chung KH, Zhang YH, Yun YP. Antiplatelet acttivity of green tea catechins is mediated by inhibition of cytoplasmic calcium increase. J Cardiovasc Pharmacology 2001;38(6): 875-884.

20 Trinder P. Glucose Oxidase Method. Sixth Edition. Varley's Clinical Biochemistry 1969;624-6.

21 Mackenzie TA, Leary L, Brooks WB..The effect of an extract of green and black tea on glucose control in adults with type 2 diabetes mellitus: double-blind randomized study. Metaboism-Clinical and Experimental 2007;56(10):1340-4.

22 Hiroshi T, Mitsuyo I, Tirasuana M, Kimura I. Effect of green tea on blood glucose level and serum proteomic patterns in diabetic mice and glucose metabolism in healthy humans. BMC Pharmacology 2004;4(18):1-14.

23 Hosoda K, Wang MF, Liao ML. Antihyper-glycemic effects of oolong tea in type 2 diabetes mellitus. Diabetic care 2003;1714-18.