Effect of Ginkgo biloba on lipid profile in hypertensive patients on Valsartan monotherapy

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ABSTRACT

Aim: The study was conducted to evaluate the effects of Ginkgo biloba as an add on therapy to Valsartan monotherapy in hypertensive patients on lipid profile.

Patients and methods: The study was done in private clinics in Mosul City, during a period of sixth months from 15 October 2017 to 15 April 2018. The total number of patients enrolled in the study was 50 hypertensive patients using Valsartan monotherapy of both sexes. The patients were administered Ginkgo biloba 80 mg twice daily and followed for 2 months duration. Their lipid profile was determined at baseline level and after 2 months from administration of Ginkgo biloba.

Results: Treatment with Ginkgo biloba showed a significant reduction in serum total cholesterol and triglycerides, while LDL, VLDL, HDL, and AI showed no significant changes.

Conclusion: This study revealed that Ginkgo biloba could be regarded as a natural and relatively safe drug in reducing total cholesterol and triglycerides in hypertensive patients.

Keywords: Hypertensive patients, Valsartan monotherapy, Ginkgo biloba, lipid profile.

تاثير عقار الجنكوبايلوبا على مستوى الدهون بالدم لمرضى فرط ضغط الدم الذين يستعملون دواء الفالزارتان

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الخلاصة

الهدف من الدراسة: دراسة تاثير الجنكوبايلوبا على مستوى الدهنيات بالدم عندما يستعمل كدواء إضافي الي دواء الفالزارتان لمرضى فرط الضغط الذين يستعملون الفالزارتان لوحده لعلاج إرتفاع ضغط الدم.

المرضى وطرق الدراسة: هذه الدراسة أجريت في العيادات الخاصة في مدينة الموصل. وقد إستغرق إنجازها ستة أشهر للفترة ما بين ١٥ تشرين الاول ٢٠١٧م الى ١٥ نيسان ٢٠١٨م، العدد الكلي للمرضى الذين إشتركوا في الدراسة كان ٥٠ مريضاً من كلا الجنسين ممن يعانون من إرتفاع ضغط الدم ويستخدمون دواء الفالزارتان لوحدة لعلاج إرتفاع ضغط الدم، جميع المرضى تم إعطائهم عقار الجنكوبايلوبا لمدة شهرين متتاليين، وتم قياس مستوى الدهنيات لديهم قبل وبعد إعطاء عقار الجنكوبايلوبا.

النتائج: عقار الجنكوبايلوبا قلل كلاً من الكوليستيرول الكلي والشحوم الثلاثية الكلية الموجودين في مصل الدم بشكل ملحوظ، بينما كل من LDL و VLDLو HDL و AI لم يتغيروا بشكل ملحوظ.

الاستنتاج: هذه الدراسة أكدت أن عقار الجنكوبايلوبا من الممكن أن يكون عامل طبيعي وآمن نسبيا لتخفيض مستوى الكوليسترول والشحوم الثلاثية للمرضى الذين يعانون من إرتفاع ضغط الدم.

الكلمات المفتاحية: مرضى فرط ضغط الدم، فالزارتان علاج أحادي، جنكوبايلوبا، مستوى الدهنيات بالدم.

INTRODUCTION

Ginkgo biloba is one of the most ancient's world living tree species[1]. The extract of Ginkgo biloba leaves has a long history of uses in medicine[2], it is effective for treatment of wide ranges of diseases like Alzheimer's, dementia, traumatic brain injury, stroke, cerebral insufficiency, tinnitus, sexual dysfunction, and macular degeneration[3].

Ginkgo biloba is relatively safe drug and few adverse effects are associated with it[4]. Occasionally it may cause stomach upset, headache, dizziness, constipation, palpitation, allergic skin reactions, in addition it might increase the risk of bruising and bleeding[5].

Hyperlipidemia is defined as elevated blood lipids levels, which include cholesterol and triglycerides[6]. It has an important role in the development and progression of atherosclerosis and coronary heart diseases[7]. Reducing lipid concentration by drugs is highly effective in reducing the risk of cardiovascular disease[8]. There are various synthetic lipid-lowering agents employed in current treatment of hyperlipidemia, including statins, fibrates, niacin, and ezetimibe[9], in spite of their beneficial effects, they are associated with some side effects such as rhabdomyolysis and myopathy. Therefore, there is an increased need for new lipid-lowering agents with high therapeutic value and minimum side effects[10].

The aim of present study is to investigate the effect of ginkgo biloba on lipid profile in hypertensive patients taking valsartan as monotherapy for hypertension.

PATIENTS AND METHOD

Descriptive, a prospective case series study design was used in this study which was conducted in private clinics in Mosul City. Out of 58 patients with hypertension only 50 patients completed this 2 months study in the period from October 2017 to April 2018. Eight patients refused to complete the study due to different causes (three of them because of side effects especially gastric upset and palpitations, while the other five found it is difficult to adhere with Ginkgo biloba twice daily dosage regimens).

The ethical requirement for the study was obtained from the college of pharmacy in Mosul University and a consent form was obtained from each patient. Patients having hypertension for at least one year, and on valsartan monotherapy (Valsartan was chosen because it is one of the most commonly prescribed antihypertensive drugs) for at least 6 months in a dose range of 80 mg to 160 mg daily were included in this study. Patients who have diabetes mellitus, epilepsy, renal or liver diseases, pregnant or breast feeding mothers, or patients who used any drug that might affect the coagulation system or used drugs other than Valsartan for hypertension were excluded from the study.

All patients received Ginkgo biloba 80 mg capsule (provided by Adrein Gagnon, Canada) twice daily for 2 months. The patients continued on their initial antihypertensive drug (Valsartan).

The analysis of biochemical parameters were done at Al-Ehsan laboratories in Mosul city. At the start 5 ml of venous blood sample was taken from each patient after 13 hours from fasting before administration of Ginkgo biloba, the serum was obtained by centrifugation and kept frozen at -20 C° to be used for the spectrophotometric measurement of total cholesterol[11,12], triglycerides [13,12], and HDL-c[14] .

VLDL was calculated by the equation[15]:

VLDL=Total triglycerides/5.

Serum LDL concentration was calculated by the Friedwald equation[15]:

LDL (mg/dl)= total cholesterol-HDL cholesterol-triglycerides/5.

Atherogenic index (AI) was calculated by the equation[16]:

AI=Total cholesterol/HDL.

Anthropometric measurement were recorded including height (cm) and weight (kg) and body mass index (BMI) was calculated as:

BMI(kg/m^2)=Weight (kg)/ Height(m^2)[17].

After 2 months of administration of Ginkgo biloba another blood sample was taken from each patient and, the above biochemical measurements and calculations were repeated again.

Statistical Analysis

Paired student t-test was used to compare results before and after Ginkgo biloba treatment.

RESULTS

1. Patients characteristics':

Fifty patients (23 male 46%) and (27 female 54%) were included in the study, as shown in **Table 1**.

Table 1. Baseline characteristics of the study sample (n = 50).

	Mean	SD	Minimum	Maximum
Age (years)	48.20	10.73	24.0	72.0
Height (Cm)	165.31	8.79	150.0	187.0
Weight (kg)	78.20	12.48	50.0	110.0
BMI (kg/m^2)	28.88	5.87	19.03	44.44

2. Changes in serum lipid profile after 2 months of treatment with Ginkgo biloba:

The mean values of serum lipids before and after treatment with Ginkgo biloba along with their percentage of changes are shown in **Table 2**.

Table 2. Rate of changes in serum lipid profile parameters after 2 months of "ginkgo biloba usage" in the study sample (n = 50).

	Base line (Mean ± SD)	After 2 months (Mean ± SD)	Changes (Mean ± SD)	Change Rate (%)	p-value*
S. cholesterol (mg/dl)	187.20 ± 49.88	173.46 ± 39.49	-13.74 ± 36.32	7.34	0.010
HDL (mg/dl)	43.72 ± 10.00	42.18 ± 8.55	-1.54 ± 10.17	3.52	0.290
LDL (mg/dl)	116.48 ± 44.36	107.88 ± 34.06	-8.60 ± 35.41	7.38	0.092
VLDL (mg/dl)	26.94 ± 15.76	23.78 ± 13.95	-3.16 ± 10.00	11.73	0.030
TG (mg/dl)	135.40 ± 78.60	119.10 ± 69.90	-16.28 ± 49.78	12.02	0.025
Atherogenic index	4.38 ± 1.33	4.28 ± 1.16	-0.10 ± 1.22	2.28	0.574

* Paired Student T-test of two means was used, p-value < 0.05 was significant .

DISCUSSION

Hypertension and hyperlipidemia are considered to be important risk factors for cardiovascular diseases. [18] Several epidemiological studies have reported that gradual increases in blood pressure or prevalence of hypertension are associated with hyperlipidemia.[19]

Ginkgo biloba extract (GBE) is widely used as a dietary supplement for the treatment of cardiovascular disorders particularly ischemic cardiac syndrome[20]. The mixture of biologically active ingredients present in GBE has a number of physiological effects, including antioxidant[21], vasodilation[22] and inhibition of platelet aggregation [23]. In addition to these actions, GBE reduces the formation and size of atherosclerotic plaques in high-risk cardiovascular patients, minimizes lipid peroxidation, and decreases the level of lipoprotein (a)[24]. These observations reveal the modulating effect of GBE on cholesterol metabolism. In this study the use of Ginkgo biloba resulted in significant reduction in cholesterol and triglycerides levels, non-significant reduction in LDL-cholesterol. The rate of improvement for total cholesterol, triglycerides and LDL were 7.34%, 12.02%, and 7.38% respectively. However, there is a slight reduction in HDL-chlolesterol which is not significant. The level of VLDL which is proportional to triglycerides was also reduced significantly. Atherogenic index was reduced although the reduction was not significant since it is affected by both cholesterol and HDL. The effect of Ginkgo biloba on lipid metabolism was studied more in animals than in human.

In a study done by Yao *et al*[25] in rats, Ginkgo biloba was found to lower circulating free cholesterol and inhibit production of brain β -amyloid precursor protein and amyloid β-peptide. These findings indicate that free circulating and intracellular cholesterol levels affect the processing of β-amyloid precursor protein and amyloidogenesis, and both of them were reduced by Ginkgo biloba. In another study done on rats also, Dubey *et al*[26] reported that treatment with

GBE produced a significant reduction in serum cholesterol, no effect on triglyceride which is in contrast with our results, and almost no effect on HDL-c which is in agreement with our findings.

Studies have referred that GB had an effect on the absorption of triglyceride and cholesterol, metabolism of cholesterol and this might explain the lipid lowering effects of ginkgo biloba[27-29].

Pancreatic lipase (triacylglycerol acyl hydrolase, PL), is an enzyme secreted by pancreas and catalyzed the hydrolysis of triacylglycerides in the gastrointestinal tract, is the key enzyme for lipid absorption[30]. Bustanji *et al*[27] proved that the trilactone terpenes (ginkgolides A, B, and bilobalide) which are important bioactive constituents in G. biloba leaves extract[31], are considered as potential PL inhibiter [27]. This might explain the action of ginkgo biloba on triglyceride.
The hydrolysis of cholesterol esters in the lumen of the small intestine is catalyzed by pancreatic cholesterol esterase, which liberates free cholesterol[32]. Adisakwattana *et al*[28] reported that polyphenols rich plants like Ginkgo biloba inhibited the intestinal digestion and absorption of dietary lipids by inhibition of pancreatic cholesterol esterase activity.

In another study by Xie *et al*[29] studied the enzyme activity, cholesterol flux, and changes in gene expression levels in cultured hepatocytes treated with Ginkgo biloba or Lovastatin. They found that GB decreased the total cholesterol content in cultured hepatocyte, inhibited the activity of 3-Hydroxymethylglutaryl-CoA reductase, which is the rate limiting step in endogenous cholesterol biosynthesis. In addition Ginkgo biloba decreased cholesterol influx, and induced significant increases in the expression of cholesterogenic genes and genes involved in cholesterol metabolism.

In conclusion: Ginkgo biloba has a natural and relatively safe effects in reducing total cholesterol and triglycerides levels in hypertensive patients when added to other antihypertensive drugs.

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