

Effect of Ginkgo biloba as Add-on Therapy on Serum Uric Acid in Hypertensive Patients on Valsartan Mono-therapy

*Luma M. Saadallah ; **Imad A-J Thanoon

M.B.Ch.,B; M.Sc; Ph.D (Pharmacology)

*Department of clinical pharmacy, College of Pharmacy, University of Mosul.

**Prof. Dr, Department of pharmacology, College of Medicine, University of Mosul.

Corresponding author Mobile: 07702059103, Email:
Lumaalobaidy@yahoo.com

ABSTRACT:

Aim: The study was conducted to evaluate the effect of Ginkgo biloba on serum uric acid level when used as add-on therapy to valsartan in hypertensive patients.

Patients and Methods:

The study was conducted in Private Clinics in Mosul City-Iraq, 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 mono-therapy of both sexes. The patients were administered Ginkgo biloba 80 mg twice daily and followed for 2 months duration. Their serum uric acid level was determined at baseline level and after 2 months from administration of Ginkgo biloba.

Results: There was a significant reduction on serum uric acid level after two months from addition of Ginkgo biloba.

Conclusions: This study revealed that Ginkgo biloba could be regarded as natural and relatively safe drug in reducing serum uric acid level.

Key words: Ginkgo biloba, add-on therapy, valsartan monotherapy, hypertensive patients, serum uric acid.

Introduction:

Ginkgo biloba is one of the most ancient living tree species often referred as a living fossil ⁽¹⁾. It has been cultivated in China for several thousand years, then transported to many countries around the world⁽²⁾. A German surgeon, Engelbert Kaempfer, was the first who used the term “Ginkgo” in 1712, but it was Linnaeus who termed it Ginkgo biloba in 1771 ⁽³⁾. Ginkgo was derived from the Chinese word Yinkus, which means “Silver apricot”, biloba referring to its two lobed, fan shaped leaves⁽⁴⁾.

The Ginkgo leaf contains many active ingredients including polyphenolic flavonoids and terpenoids⁽⁵⁾

Ginkgo leaves extract has shown beneficial effect in treating impairments in memory, Alzheimer's, dementia, edema, inflammation, and vaso-occlusive disorders⁽⁶⁾.

Ginkgo leaf extract appears to be safe to use. It can cause some minor side effects such as, stomach upset, headache, dizziness, constipation, palpitation and allergic skin reactions⁽⁷⁾.

Uric acid is the end product of exogenous and endogenous purine metabolism⁽⁸⁾. The exogenous source of purines varies significantly with diet, while the main sources of endogenous uric acid are the liver, intestine, muscles, kidneys and the vascular endothelium⁽⁹⁾. Hyperuricemia contributes significantly to the development of hypertension and coronary heart disease⁽¹⁰⁾. High uric acid levels have been associated with decreased renal perfusion and decreased tubular secretion of uric acid, which may lead to activation of the intrarenal renin–angiotensin system, and then to subsequent elevation of blood pressure⁽¹¹⁾.

At present, non-steroidal anti-inflammatory drugs, corticosteroids, and urate-lowering drugs are often used for treatment of hyperuricemia⁽¹²⁾. However these drugs have toxic effect to renal and gastrointestinal systems⁽¹³⁾. Thus in the recent years, the need for new and natural sources for treatment of hyperuricemia is increased⁽¹²⁾, therefore and on this base, this study has been conducted.

Subjects, Materials and Method:

This study had been conducted over a period of 6 months from 15 October, 2017 to 15 April, 2018 in Private Clinics in Mosul City. 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.

Descriptive, A prospective case series study design was used in this six months study. Single group of 58 hypertensive patients on valsartan mono-therapy were participated in the study, only fifty patients completed this study, 8 patients refused to complete this study due to different causes. The dose range of valsartan was between 80mg and 160 mg once daily. Serum uric acid was obtained initially at baseline level and after two months from addition of Ginkgo biloba (provided by Adrein Gagnon, Canada) in a dose of 80 mg twice daily as add-on therapy to valsartan. Inclusion criteria include: Hypertensive patients with duration of the disease for at least 1 year, the patients use only valsartan 80mg or 160 mg for at least 6 months for treatment of hypertension, patients are ≥ 18 years old. 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 drugs other than Valsartan for hypertension were excluded from the study.

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

$$\text{BMI}(\text{kg}/\text{m}^2) = \text{Weight}(\text{kg}) / \text{Height}(\text{m}^2)^{(14)}$$

Uric Acid was determined by enzymatic spectrophotometric method⁽¹⁵⁾ using a kit provided by Biolabo (France).

Serum uric acid concentration was determined according the following equation:

$$\text{Uric acid concentration} = \frac{\text{absorbance of sample}}{\text{absorbance of standard}} \times n \text{ (mg/dl)}$$

$$n = \text{concentration of standard} = 10 \text{ (mg/dl)}$$

The reference ranges of serum uric acid are between 2.6 and 7.2 mg/dl⁽¹⁶⁾.

Results:

3.1 Personal and anthropometric characteristics of the study sampled population:

Fifty patients (23 male and 27 female), were participated in the study figure (3.1), the age range of the selected group were between 24 and 72 years old (mean 48.2 ± 10.73). The BMI of 26% were below 25 and 74% were above 25 (mean 28.88 ± 5.87) table (3.1).

Regarding dose of valsartan, 28 of hypertensive patients in the study sampled taking 80 mg / day (56.0%), and the other 22 patients receiving 160 mg / day (44.0%) as prescribed by their physicians.

Table (3.1): Personal and anthropometric characteristics of the study sampled population at the beginning of the study, (n = 50).

Characteristics	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

3.2 The mean uric acid level of the study sampled population at the baseline level:

The mean value of serum uric acid of patients before receiving Ginkgo biloba is shown in table (3.2).

Table (3.2) : The mean value of serum uric acid of patients at the beginning of study (n=50) .

Parameters	Mean	SD	Minimum	Maximum
Uric acid (mg/dl)	4.65	0.95	2.70	6.50

The results are expressed as mean and SD.

3.3 Effect of GB on serum uric acid:

There was a significant reduction in serum uric acid levels after using Ginkgo biloba as add-on therapy to valsartan table (3.3).

Table (3.3): Changes in serum uric acid after 2 months of "GB usage" in the study sampled patients, (n = 50).

Parameters	Base line Mean \pm SD	After 2 months Mean \pm SD	P-value*
Uric acid (mg/dl)	4.65 \pm 0.95	4.15 \pm 1.30	0.001

* Paired T-test of two means was used.

Discussion:

Several studies suggest multiple mechanisms of the beneficial effects of Ginkgo biloba through its antioxidant, antiplatelet, antithrombotic, and vasodilatory properties⁽¹⁷⁾.

In this study Ginkgo biloba caused a significant reduction in uric acid level after two months from treatment, to our knowledge this was the first study that deals with the effect of GB on serum uric acid level in human.

A study done by Elatrash and Abd El-Haleim ⁽¹⁸⁾ administered monosodium glutamate (MSG) to rats to cause liver and renal toxicity. Significant elevation of serum uric acid level produced by the effect of MSG, then Ginkgo biloba was added and caused a significant reduction in uric acid levels.

Another study which emphasized our results was that done by Chen *et al* ⁽¹²⁾. They used rats with acute gout, the pathogenesis of acute gout and the therapeutic effects of Ginkgo biloba extract were investigated by metabolic approach. Twenty-seven potential biomarkers were identified to be involved in tryptophan metabolism, pyrimidine metabolism, pentose phosphate pathway, Tricarboxylic acid cycle, tyrosine metabolism, lysine degradation and purine metabolism, among these biomarker was uric acid, which was the main product of purine metabolism. The therapeutic effect of Ginkgo biloba extract for acute gout with hyperuricemia model rats was evaluated by detecting the degree of metabolic disorder recovery, after treatment with Ginkgo biloba extract, the levels of uric acid and allantoin (a stable biomarker of urate oxidation) were recovered significantly.

The mechanism that might give us a possible explanation about the effect of Ginkgo biloba on uric acid, was xanthine oxidase inhibition effect by flavonoids ⁽¹⁹⁾, which was the main active ingredient in Ginkgo biloba ⁽⁵⁾. Xanthine oxidase has an important role in the endogenous production of uric acid since it is the key enzyme in the catabolism of purines ⁽⁸⁾. These flavonoids rich compounds are structurally similar to xanthine oxidase substrate and so can inhibit the enzyme activity⁽¹⁹⁾.

In conclusion: Ginkgo biloba has smooth, natural and relatively safe effects in reducing serum uric acid level.

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