Original Research Article

EFFECTS OF ACE INHIBITOR (LISINOPRIL) WITH FOLIC ACID SUPPLEMENTATION IN THE MANAGEMENT OF HYPERTENSION ASSOCIATED WITH HYPERURICEMIA

ABSTRACT

Background: Hypertension is one of the most common health problems in both developed and developing countries throughout the world. It's linked to diabetes, dyslipidemia, and hyperuricemia, among other things. ACE inhibitors are a kind of antihypertensive drug that is widely used across the world. They not only lower blood pressure, but they also lower uric acid levels.

Aims & Objectives: To evaluate the efficacy of ACE inhibitors alone and along with the folic acid on systolic & diastolic blood pressure & on serum uric acid level.

Methodology: This case-control research was carried out at the Medicine Department with the help of the Department of Biochemistry at LUMHS Jamshoro and the PAQSJ Medical Institute in Gambat. A total of 200 mild to moderate hypertension individuals with hyperuricemia were chosen. They were split into two groups: the control group got 10 mg of lisinopril, while the case study group received 10 mg of lisinopril with 0.8 mg of folic acid for 10 to 12 weeks.

Results: The mean value of systolic B.P in control group after treatment was126 ± 4.9 ($P<0.05$) while in case study group after treatment was 118 ± 6.12 mmHg ($P<0.05$). Diastolic B.P in control group after treatment was 90 ± 4.76 mmHg while in case study group was 82.3 ± 3.66 mmHg ($P<0.05$). The serum uric acid level after treatment in control group was 6.7 ± 4.78 mg/dl while in case study group, it was 5.5 ± 5.11 mg/dl ($P<0.001$). Serum Folic acid levels after the

treatment in control group was 12.31 ± 2.89 while in case study group it was 27.09 ± 3.47 nmol/L (P<0.001).

Conclusion: Folic acid boosts the effectiveness of an ACE inhibitor (lisinopril) and has a substantial influence in the lowering of serum uric acid in the therapy of mild to moderate hypertension associated with hyperuricemia, according to this study.

Key Words: Hyperuricemia, ACE Inhibitors, Hypertension, Folic Acid, Serum Uric Acid.

INTRODUCTION

In humans, uric acid is the last catabolic byproduct of purine metabolism.[1]The incidence of Hyperuricemia (HUA) has been steadily increasing over the last three to four decades.[2] HUA is also the major cause of gout.[3] HUA has also been linked to established systemic clinical illnesses such as hypertension, diabetes, and myocardial infarction, among others.[4] An increase in uric acid levels might lead to a stroke or coronary heart disease.[5]

Hypertension is linked to elevated uric acid levels as well as coronary heart disease.[4,6] Uric acid levels can be raised by diuretics and aspirin, which are commonly used by hypertensive patients.[7] According to several research findings, HUA is an independent risk factor for hypertension.[8] There are a variety of therapeutic treatments for HUA, including allopurinol, which inhibits the enzyme xanthine oxidase, benzene bromide, and probenecid, which increases the renal excretion rate of uric acid.[9] These medications merely lower serum uric acid levels and have no effect on blood pressure. These anti-HUA medications have a variety of adverse effects, including allergic reactions, changes in liver function enzymes, gastrointestinal issues such as vomiting and diarrhoea, decreased renal function, and bone marrow suppression.[10,11] As a result, a treatment regimen that controls blood pressure and lowers uric acid levels is required.

Angiotensin-converting enzyme (ACE) inhibitors are a kind of antihypertensive medication that protects the kidneys while simultaneously lowering uric acid levels.[12] Some experts believe that folic acid is also helpful in the treatment of HUA.[13] One phenomenon is that reduced uric acid excretion in the urine might cause homo cysteine and methylenetetrahydro folate reductase levels to rise.[14] Folic acid lowers the levels of these two compounds, making it useful in the treatment of HUA.

The goal of our study was to see if ACE inhibitors combined with folic acid had a long-term effect on lowering blood uric acid levels, which might be useful in the treatment of hypertension caused by HUA.

METHODOLOGY:

The Civil Hospital Liaquat University of Medical & Health Sciences (LUMHS)Hyderabad/ Jamshoro and the Hospital of Pir Abdul Qadir Shah Jeelani Medical Institute Gambat Sindh participated in this randomised control trial. With their own consent, 200 diagnosed patients of mild to moderate hypertension associated with HUA (serum Uric acid no more than 7.5mg/dl) were recruited from medical and cardiology OPDs of LUMH Hyderabad, Jamshoro, and Gambat Sindh hospitals. Both males & females aged between 31 – 60 years with systolic blood pressure between 130 to 150 mmHg and diastolic blood pressure range from 90-110mmHg taking lisinopril 10mg with no any other vitamin B complex therapy during study period were included in this study. Patients aged 30 to 60 years old with a systolic blood pressure of more than 150mmHg and a diastolic blood pressure of more than 110mmHg who were taking antihypertensive drugs other than ACE inhibitors and had a history of vitamin B therapy and anti HUA agents were excluded from the study. Pregnant women and those with known liver or renal diseases were also excluded..

A total of 5 mL of blood was obtained from each individual at two points: before the commencement of treatment, known as the zero level, and after the experiment was completed, known as level –I. The serum uric acid level was determined using the uricase principle for the calorimeter technique, and the Vitamin B9 level was determined using an auto analyzer for the kit approach.

Total subjects were divided into two groups, each with an equal number of participants: group A received only ACE inhibitors; lisinopril group (Tb. Zestril 10mg) once a day for 10 months was considered the control group, while group B received ACE inhibitors; lisinopril group (Tb.

Zestril 10mg once a day along tablet folic acid 0.4mg twice a day) was considered the case study group.

The mean SD and statistical analysis was done by SPSS version 21 by applying the independent Student *t* test to know the significance value (P.value).

RESULTS:

For this study, 200 hypertension individuals were selected and divided into two groups. The control group included 59 males and 41 females, whereas the case study group included 64 males and 36 females. The comparison of all variables in the control group before and after treatment associated with folic acid is provided in Table No.01. Only a significant drop in systolic and diastolic blood pressure levels was detected in this group, whereas there was no significant reduction in serum uric acid levels or an increase in folic acid levels.

The comparison of variables in the case study group before and after the treatment period is given in table no. 2. After therapy with lisinopril and folic acid, substantial reductions in systolic and diastolic blood pressure, serum uric acid level, and increased folic acid level were found in his group. After the therapy phase, the blood uric acid levels in the control and case study groups were compared graphically. In compared to the control group that did not get folic acid with the lisinopril medicine, there is a substantial decrease in blood uric acid levels in the case study group.

Table No: 01. Variables of Control Group (Group A) Before & After Treatment

Variable	At Zero Level	At Level-I	P. Value
Age	45 ± 6.1	45 ± 6.2	Not Significant
BMI (kg/m^2)	22 ± 2.2	22 ± 2.0	Not Significant
Systolic B.P (mmHg)	142 ± 5.76	126 ± 4.9*	**<0.05**
Diastolic B.P (mmHg)	105 ± 5.23	90 ± 4.76*	**<0.05**
Serum Uric Acid (mg/dl)	6.9 ± 5.1	6.7 ± 4.78	0.12
Serum Folic Acid (nmol/L)	10.31 ± 4.67	12.31 ± 2.89	0.223

Table No: 02. Variables of Case Study Group (Group B) Before & After Treatment

Variable	At Zero Level	At Level-I	P. Value
Age	44 ± 7.13	44.12 ± 7.11	Not Significant
BMI (kg/m^2)	22.4 ± 3.10	22.56 ± 2.87	Not Significant
Systolic B.P (mmHg)	145 ± 4.76	118 ± 6..12*	**<0.05**
Diastolic B.P (mmHg)	103 ± 3.88	82.3 ± 3.66**	**<0.001**
Serum Uric Acid (mg/dl)	7.1 ± 3.89	5.5 ± 5.11*	**<0.05**
Serum Folic Acid (nmol/L)	12.31 ± 2.88	27.09 ± 3.47**	**<0.001**

Table No: 03. Variables after Study period in Control & Case Study Groups

Variable	Control Group	Case Study Group	P. Value
Systolic B.P (mmHg)	126 ± 4.9	118 ± 6..12*	**<0.05**
Diastolic B.P (mmHg)	90 ± 4.76	82.3 ± 3.66*	**<0.05**
Serum Uric Acid (mg/dl)	6.7 ± 4.78	5.5 ± 5.11**	**<0.001**
Serum Folic Acid (nmol/L)	12.31 ± 2.89	27.09 ± 3.47**	**<0.001**

DISCUSSION:

According to our knowledge, this is the first blinded randomised control study on the effects of folic acid in combination with lisinopril (ACE inhibitor) on blood uric acid levels in patients with HUA who had hypertension. Haibo Li et al (2015)[15] conducted a study in China on the effects of Enalapril and folic acid on the same criteria and found substantial findings similar to ours. All across the globe, ACE inhibitors are often used to treat hypertension. Because ACE inhibitors limit uric acid reabsorption in the proximal tubules and increase the rate of urate and uric acid excretion via the kidney, they have an influence on blood pressure and serum uric acid levels.[16,17] As a result, ACE inhibitors may be beneficial in lowering uric acid levels in hypertensive individuals with HUA. There are other ideas on how folic acid affects uric acid in HUA, but two processes support our findings. Folic acid and its metabolites may inhibit xanthene oxide (XO), which reduces the breakdown of purines and so reduces the generation of uric acid. Folic acid may also enhance the breakdown of uric acid, increasing the rate of excretion and lowering serum uric acid.[18] The second crucial factor that supports our results is that folic acid lowers homocysteine levels, which reduces the development of HUA.[19]

Folic acid is particularly beneficial in painful gout since one of the functions of folic acid and its metabolite is to break down proteins, which increases the breakdown of uric acid and lowers the blood uric acid level.[20] Several investigations on the effects of folic acid HUA in gout patients have been conducted. Lyu LC et al (2003)[21] in Taiwan conducted a case control research to examine the effects of vitamin B supplementation, folic acid, and ascorbic acid in gout patients and found that they were effective in reducing HUA. Zhang Y et al (2018)[22] investigated the effects of folic acid, vitamin B6, and vitamin 12 on HUA and found that folic acid has a beneficial impact on blood uric acid. Although no studies on the combined effects of folic acid and antihypertensive medicines have been identified in the past, Forman JP et al (2005)[23] claimed that folic acid may lower the incidence of hypertension. The use of folic acid can improve the efficiency of antihypertensive medications, according to Van Dijk RA et al (2001)[24]. However, some further investigations, such as Boss Gr et al (1980)[25], do not confirm our findings. They claimed that more than 1,000 mg of folic acid was administered but no favorable results were found.

Thus, the idea that this study subject is fresh necessitates several studies with different groups of ACE inhibitors, experiments on different races, different locations of the nation, correct dietary history, and maybe a proper dietary pattern throughout the experiment or research time.

CONCLUSION

It was concluded as per findings of this study that folic acid boosts the effectiveness of an ACE inhibitor (lisinopril) and has a substantial influence in the lowering of serum uric acid in the therapy of mild to moderate hypertension associated with hyperuricemia

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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