

Comparison between the effects of the losartan and enalapril on uric acid concentration in hypertensive patients

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Abstract

A total of 80 patients with mild to moderate hypertension were divided into two groups, the 1st group treated by losartan 50mg/day, 2nd group on enalapril 20mg/day, for 4 weeks duration, along with 41 apparently healthy persons (control group) were included in this study. The aim of this study comparison between losartan and enalapril effects on serum uric acid level. For each patient (before and after therapy)and control, blood pressure and serum uric acid level were measured. Results of this study were shown both losartan and enalapril are effective in reducing blood pressure when compared before and after treatment, (however, enalapril is more effective), only losartan is significantly reducing serum uric level.

المقارنة بين تأثير عقار اللوسارتان مع الانلابريل على تركيز الحامض البولي في المرضى الذين يعانون من فرط ضغط الدم الشرياني

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الملخص

اجريت هذه الدراسة على ثمانين مريضاً يعانون من فرط ضغط الدم الشرياني من النوع الخفيف والمتوسط (شخصوا حديثاً) قسموا الى مجموعتين متساويتين، الاولى اعطيت عقار اللوسارتان 50ملغم يومياً لمدة اربعة اسابيع واعطيت المجموعة الثانية عقار الانلابريل 20 ملغم يومياً يومياً لنفس المدة. اضافة الى ذلك كان هناك 41 من المتطوعين (يبدون اصحاء) تم اعتبارهم لمجموعة ضبط والغرض من الدراسة هو المقارنة بين تأثيرات اللوسارتان بالانلابريل على تركيز حامض البولي ومستوى فرط ضغط الدم الشرياني لكلا مجموعتي المرضى، الاضافة الى مجموعة الضبط، تم قياس ضغط الدم الشرياني ومستوى حامض البولي في الدم لكلا المجموعتين المرضى قبل وبعد فترة العلاج ومجموعة الضبط لمدة واحدة فقط. وقد بينت نتائج هذه الدراسة بان مجموعة المرضى الذين كانوا يتعاطون عقار اللوسارتان انخفض لديهم مع دلالات ضغط الدم الشرياني وكذلك مستوى حامض البولي في الدم انخفاضاً معنوياً ومن ناحية اخرى فان مجموعة المرضى الذين تعاطى عقار الانلابريل ايضاً انخفضت لديهم معدلات ضغط الدم الشرياني ولكن دون تأثير على مستوى حامض البولي في الدم. بالمقارنة تبين ان معدلات ضغط الدم الشرياني قد انخفضت في مجموعة اللوسارتان ولكن الانخفاض في مجموعة الانلابريل كانت هي الاكبر بالاضافة كان اللوسارتان تأثير اكبر على خفض مستوى حامض البولي. بناء على ما سبق اثبتت هذه الدراسة ان كلا العقارين فعال في خفض ضغط الدم الشرياني ولكن الانلابريل اكثر فعالية وان تأثير اللوسارتان على خفض مستوى حامض البولي كان اكبر من الانلابريل.

Introduction

Several epidemiological studies have identified an association between increased serum uric acid (SUA) level and cardiovascular risk in the general population, ^(1, 2) and among patients with hypertension. ⁽³⁾ Raised SUA level is found in approximately 25% of untreated hypertensive patients, ⁽⁴⁾ Some study concluded that there is merely an association of SUA with other risk factors, including hypertension, renal disease, elevated lipoprotein levels, and use of diuretics agents. ⁽⁵⁾ Moreover, the development of hypertension was prevented by concurrent treatment with Xanthine Oxidase inhibitor (allopurinol) or a uricosuric agent (benzbromarone), both of which lowered the SUA level. ⁽⁶⁾ It was reported that the angiotensin II receptor blockers (ARB), Losartan increased excretion of SUA and decreased the SUA level in both healthy and hypertensive subject. ⁽⁷⁾ The uricosuric effect of losartan result from its inhibitory action on the urate / anion exchanger of the renal proximal tubular epithelial cells, ⁽⁸⁾ Enomoto et al ⁽⁸⁾ found that the uric acid transporter URAT₁ is involved in the reabsorption of UA from lumen to cystol along the proximal tubule. They showed that UA transport via URAT₁ was inhibited by uricosuric benzbromarone. ⁽⁹⁾ Lansortan has a uricosuric effect, this is due to its molecular deposition (or physical property), ⁽⁹⁾ recently losartan show to target the urate anion exchange URAT₁ and inhibit water-uptake by this transport, thus reducing urate reabsorption from proximal tubules. ⁽¹⁰⁾ Angiotensin converting enzyme (ACE) inhibitors and calcium channel blockers have modest uricosuric effect, but do not decrease SUA level. ⁽¹¹⁾ In this study the hypothesis that losartan compared with enalapril, would lower SUA level in hypertensive patients, was tested.

Methods

Participants: This study was carried out over four weeks, followed up, eighty patients (43 female and 37 male) age between (51-81 years), with newly diagnosis of mild to moderate essential hypertension. Forty one apparently healthy subjects (22 female and 19 male), age from 50-80 years as control, are participant in this study, the trial protocol was approved by local ethics committees. The exclusive criteria from this study patients with renal and hepatic impairment, myocardial infarction, angina, heart failure and patients receiving any drugs that affect SUA (e.g. aspirin and allopurinol). The patients divided as follows:

Group 1: forty patients were treated with losartan 50mg/day.

Group 2: forty patients were treated with enalapril 20mg/day.

Control group: : forty one apparently healthy subjects.

All patients in each group were followed up for four weeks.

Procedures

Patient with newly diagnosed mild to moderate hypertension who do not receive any treatment for their high blood pressure in Ibn-Sina Teaching Hospital in Mosul city were recruited to this study. All patients were followed up for four weeks which is the study follow-up period. Systolic and diastolic blood pressure and serum uric acid levels were measured for each patient before and the end of the study. Similar parameters were done at base line for healthy control subjects. Blood pressure measured by using mercury sphygmomanometers. ⁽¹⁰⁾ Serum uric acid levels was measured by an enzymatic uricos method. ⁽¹¹⁾

Statistical analysis

All the values were taken as mean \pm SD and percentage. The effect of losartan and enalapril on measured

parameters(before and after therapy) were compared using paired t-test. Comparison of measured parameters between control and each of patients before therapy with losartan and enalapril were compared using unpaired t-test.

P-value \leq 0.05 was considered statistically significant. ⁽¹²⁾

Results

In this study, a total number of 80 patients were randomized, both sexes were enrolled with 41 healthy individual as control. The patients were divided in two groups of 40 patients; they were given treatment for 4 weeks. Group 1: given 50mg losartan. Group 2: given 20mg enalapril at the end of the study, the results of two groups were compared they showed significant changes effect

in serum uric acid level and blood pressure as illustrated in following tables. Table (1): Shows the effects of losartan therapy on the serum uric acid level and blood pressure illustrate a significant difference before and after treatment. Table (2): Illustrate effect of enalapril therapy on the serum uric acid level shown no significant before and after treatment, but significant difference in blood pressure. Tables (3): Shown comparison between control and patient before and after losartan therapy, it showed no significant difference in serum uric acid level, but significant difference in blood pressure. Table (4): Illustrate comparison between control and each patient before and after enalapril therapy. It showed no significant difference in serum uric acid level, but they found significant difference in blood pressure.

Table (1): Effects of losartan therapy on the serum uric acid level and blood pressure using paired t-test.

Parameters	Mean \pm SD		P-value
	Before therapy	After therapy	
Uric acid (mmol/L)	448.07 \pm 93.47	348.3 \pm 75.41	< 0.05
SBP (mmHg)	159.78 \pm 10.25	142.15 \pm 12.70	< 0.05
DBP (mmHg)	92.38 \pm 5.44	79.83 \pm 4.34	< 0.05

P<0.05 is significant

Table (2): Effects of Enalapril therapy on the serum uric acid level and blood pressure using paired t-test.

Parameters	Mean \pm SD		P-value
	Before therapy	After therapy	
Uric acid (mmol/L)	398.7 \pm 110.72	378.73 \pm 104.7	< 0.05
SBP (mmHg)	163.05 \pm 10.67	136.25 \pm 11.08	< 0.05
DBP (mmHg)	98.88 \pm 8.83	82.8 \pm 8.23	< 0.05

N.S: Not Significant

Table (3): Comparison of serum uric acid level and blood pressure between control and each patient before and after Losartan therapy

parameters	Mean \pm SD		After drug (n=40)
	Control (n=41)	Before drug (n=40)	
Uric acid (mmol/L)	352.98 \pm 63.24	448.07 \pm 93.47	348.3 \pm 75.41
SBP (mmHg)	125.98 \pm 7.35	159.78 \pm 10.25	142.15 \pm 12.70
DBP (mmHg)	76.95 \pm 7.06	92.38 \pm 5.44	79.83 \pm 4.34

P<0.05 is significant
Using unpaired t-test

Table (4): Comparison of serum uric acid level and blood pressure between control and each patient before and after Enalapril therapy

parameters	Mean \pm SD		After drug (n=40)
	Control (n=41)	Before drug (n=40)	
Uric acid (mmol/L)	352.98 \pm 63.24	398.7 \pm 110.72	378.73 \pm 104.7
SBP (mmHg)	125.98 \pm 7.35	163.05 \pm 10.7	136.25 \pm 11.08
DBP (mmHg)	76.95 \pm 7.06	98.88 \pm 8.83	82.8 \pm 8.23

P<0.05 is significant
Using unpaired t-test

Discussion

In this study, it was found that both losartan and enalapril are effective in reducing blood pressure (BP), However; enalapril is more effective. On other hand losartan reduce serum uric acid (SUA)level significantly, but enalapril do not. This finding are inconsistent with the results of many studies, San-Chiang et al, ⁽¹³⁾ compared losartan with lisinopril and amlodopine, they reported a significant reduction in BP with losartan in mild to moderate hypertension with four weeks of treatment. Faeiz and Renaud ⁽¹⁴⁾ reported similar observations that losartan decrease BP significantly when compared with placebo, during eight weeks treatment-trial. Gradman et al, ⁽¹⁵⁾ and Fegard et al, ⁽¹⁶⁾ reported, by compared losartan with enalapril in

patients with mild to moderate hypertension, they found both were effect in reducing BP, however they found enalapril was more effective , this is due to role of enalapril in bradykinine, which is a potent vasodilator/ in contrast to losartan, which is not. In the LIFE study shown that reducing SUA level is associated with beneficial effect on outcomes in these treatment of hypertension and cardiovascular events,⁽¹⁷⁾ SUA level is closely related to renal function and to hypertension. ^(18,19) Increase SUA level in hypertension may be caused by decreased renal urate clearance independent of change in glomeruli filtration, which may mediated by an increase in serum lactate, ⁽²⁰⁾ that inhibit secretion of urate by the tubular anion-exchange transport system. Another possibility is that reduced uric

acid excretion may be linked to increase proximal tubular reabsorption of Na⁺, and water is conducted by the same transport system.⁽²¹⁾ In 2nd LIFE study, it was shown that 24% reduction in outcome measure (cardiovascular death, myocardial infarction and stroke) in the losartan group, which can be explained by the difference in SUA level over the course of the study,⁽²²⁾ these result suggest that the uricosuric quality of losartan may be an added benefit of this particular angiotensin receptor blocker. The novel concept that salt-dependent hypertension result from renal microvascular injury with local ischemia could provide a pathogenic link with hypertension,⁽²³⁾ increase SUA level in human, is associated with renal vasoconstriction,⁽²⁴⁾ and is positively correlated with plasma rennin activity in hypertensive subjects.⁽²⁵⁾ A novel mechanism has recently been suggested in a rodent model by which UA can stimulate the development of hypertension.^(26,27) Renal lesion and hypertension could be prevented by lowering UA levels and treatment with angiotensin-converted enzyme inhibitor.⁽²⁸⁾ Previously, it was shown that losartan induced a significant decrease in SUA level in patients with hypertension and gout.⁽²⁹⁾ Other studies, revealed that addition of losartan to allopurinol to gout and hypertension patients caused a significant decrease in SUA level.⁽³⁰⁾ In the present study there was a significant reduction in SUA level with losartan and this finding in agreement with many studies,^(29,30) the study of Takahoshi et al showed reduction of 11% in SUA level in combination therapy, i.e. losartan and allopurinol, and 15% reduction in SUA level by losartan alone. The result of this study correlated with Takahoshi in respect of monotherapy.⁽³⁰⁾ The results of the present study are in accordance with

that of Weber et al, who reported that mean values of SUA level reduced by losartan at bore line. Minghelli et al⁽³¹⁾ evaluates the uricosuric effect of losartan in hypertensive patients and revealed that plasma UA level decreased significantly after four weeks of treatment. A significant increase in UA excretion was observed only with losartan, support the results of present study.⁽³¹⁾ Since serum urate is elevated in renal dysfunction of inappropriate diet and may be marker for cardiovascular disease. Thiazide is often co-prescribed with losartan, the uricosuric effect of losartan may be useful to counteract any rise in urate or increase in risk of gout.

Conclusion

The present study showed that the use of both losartan and enalapril resulted in smooth reduction in BP which is in favor of enalapril, However; losartan showed a greatest reduction in SUA as compared to enalapril.

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