

## An open-label, prospective study comparing efficacy, tolerability and cost of therapy of losartan with enalapril in stage 1 and stage 2 hypertension

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### ABSTRACT

**Background:** Hypertension is a chronic disease which insidiously affects multiple systems in the body especially the cardiovascular and cerebrovascular systems. Also being a chronic disease the patient is required to take medications lifelong and this has financial implications. This study was attempted to evaluate drugs in two antihypertensive groups: Angiotensin II antagonist losartan v/s angiotensin converting enzyme inhibitor enalapril.

**Methods:** A total of 100 patients as per the selection criteria were enrolled in the study and allocated randomly to either group A (losartan group) or group B (enalapril group). The study period was for 12 weeks, during which regular assessments were done - first on recruitment and then at 2nd week, 4th week, 8th week, and 12th week. The assessment parameters were diastolic, systolic pressures and pulse rate. Routine investigations were performed during the 1st visit and after 12 weeks of the study period.

**Results:** There were no significant differences between the treatment groups with respect to baseline patient demographic data and clinical characteristics like systolic blood pressure, diastolic blood pressure and heart rate. The cost benefit ratio and less adverse effects (cough), can be appreciated in group A (losartan group).

**Conclusions:** Losartan and enalapril were well tolerated after 12 weeks of treatment with notable tolerability advantages of losartan especially with respect to the respiratory system (cough). The cost of therapy for losartan group was almost half the cost of therapy for enalapril group and hence being cost effective. Thus, losartan could be preferred as a suitable alternative to enalapril as an antihypertensive agent.

**Keywords:** Hypertension, Enalapril, Losartan

### INTRODUCTION

Hypertension is a common, chronic disorder which is associated with a significantly raised risk for cardiovascular and cerebrovascular events. Current Joint National Committee and British Hypertension Society guidelines emphasize that lowering elevated blood pressure (BP) reduces morbidity from stroke, myocardial infarction, congestive heart failure and renal failure.<sup>1,2</sup> Interference with the renin-angiotensin-aldosterone system (RAAS) is one of the several modalities to lower blood pressure (BP) in patients with hypertension.

The kidneys secrete the hormone renin to form angiotensin I (Ang I) from angiotensinogen, and in the

next step vasoconstrictive angiotensin II (Ang II) is formed by angiotensin converting enzyme (ACE) in several organ tissues. Apart from its physiological role in the regulation of glomerular filtration rate (GFR), sodium excretion<sup>3</sup> and in the early development of the kidney,<sup>4</sup> the renal effects of Ang II are also crucially involved in the development and maintenance of hypertension. The most important mechanisms proposed are renal vasoconstriction, increased proximal tubular sodium reabsorption and increased secretion of aldosterone.<sup>5</sup>

Two subtypes of Ang II receptors have been identified: (i) the AT1 receptor responsible for vasoconstriction and induction of smooth-muscle cell proliferation and migration, and (ii) the AT2 receptors whose functional roles are poorly defined, but they may exert

antiproliferative, proapoptotic, vasodilatory, and antihypertensive effects.<sup>6</sup> This leads to the consideration that a selective AT1 receptor antagonist could be useful in preventing angiogenesis as recently documented by Stoll.<sup>7</sup>

Losartan, the first orally active nonpeptide, specific Ang II AT1 receptor antagonist,<sup>8</sup> exhibited the assumed clinical pharmacology in healthy individuals,<sup>9</sup> and a blood pressure-lowering effect comparable to that of enalapril in essential hypertension.<sup>10</sup> In essential hypertension, fewer adverse effects of losartan in comparison with other antihypertensive drugs, especially ACE inhibitors, have been observed.<sup>11-12</sup> ACE inhibitors and angiotensin receptor blockers (ARBs) also slow down the progressive deterioration in renal function that reflects renal injury, particularly in patients with diabetic nephropathy.<sup>13-14</sup> Moreover, ACE inhibitors reduce cardiovascular mortality and morbidity in patients with increased cardiovascular risk,<sup>15</sup> left ventricular dysfunction, or congestive heart failure (CHF).<sup>16</sup> Similar data are now beginning to emerge with ARBs.<sup>17</sup> Hence there arises a debate over the comparative efficacy of ACE inhibitors and ARBs.<sup>18</sup>

Costs of medications for chronic conditions like hypertension continue to escalate, particularly for the elderly.<sup>19</sup> This has important ramifications for newer antihypertensives, as novel agents tend to be more expensive than older drugs. However, if patient compliance is enhanced through the improved tolerability of newer agents, and better BP control results from this, then these factors should be weighed against simple drug-acquisition costs.

Thus, the aim of the present study was to compare the effects of the Ang II type 1 receptor antagonist losartan with enalapril on blood pressure (BP) after 12 weeks of treatment in patients with stage 1 and stage 2 hypertension, as defined by the current JNC 7 guidelines.<sup>1</sup> Another aim of the present investigation was to evaluate the tolerability and cost of therapy of these two drugs in this special group of patients.

## METHODS

### *Patient selection*

The study was conducted in the Out-Patient Department of Medicine, Rural Tertiary Care Teaching Hospital, Vadodara, Gujarat. Approval from the institutional ethics committee was obtained and all the information with regard to identity of patients and physicians was strictly kept confidential.

A total of 100 patients as per the selection criteria were enrolled in the study in two equal groups (group A and group B). The inclusion criteria for selection of patients were as follows: Patients of either sex with age 18 years and above; patients who have been either newly

diagnosed with stage 1 hypertension (SBP/DBP = 140-159/90-99 mmHg) or stage 2 hypertension (SBP/DBP =  $\geq 160/ \geq 100$  mmHg) or those who had discontinued antihypertensive medication voluntarily for more than 4 weeks. They had no active medical problems other than essential hypertension and received no other drug therapy that might affect blood pressure.

Patients on other antihypertensive therapy; patients with history of secondary hypertension, stroke, myocardial infarction, congestive heart failure, arrhythmias, diabetes mellitus, allergy to ACE inhibitors and concomitant use of drugs (major psychotropic agents, antidepressants, regular use of non steroidal anti-inflammatory agents, high-dose aspirin) that could affect blood pressure were excluded from the study. Patients with impaired liver function defined as SGOT (serum glutamic oxaloacetic transaminase) or SGPT (serum glutamic pyruvic transaminase)  $>2$  times the normal limit; impaired kidney function confirmed by serum creatinine  $>2$ mg/dl; women of childbearing potential or who were breastfeeding were also excluded.

### *Study design*

The study was prospective, open, observational, non-interventional, parallel and comparative in nature. All the patients in the study were explained clearly about the purpose and nature of the study in the language they understood. They were included in the study only after obtaining a written informed consent. We used a case record form for gathering information regarding the treatment.

Fifty patients receiving tablet losartan potassium (50 mg once a day orally for 12 weeks) were assigned to group A and fifty patients receiving tablet enalapril maleate (10 mg once a day orally for 12 weeks) were assigned to group B. Pharmaceutical equivalence was affirmed by prescribing the same brand of drug to all the patients in the respective groups. The drugs were readily available in the hospital pharmacy throughout the study period. The allotment of the patients to either group was assigned randomly by the treating physician. The study was conducted for a period of 12 weeks with subsequent follow ups at 2 weeks, 4 weeks, 8 weeks and 12 weeks. At each visit detailed history and complete clinical examination was performed. Routine investigations were done at the beginning and at the end of the study.

### *Observation methods*

At each visit, complete clinical examination was performed which included: recording of systolic and diastolic blood pressure (BP) of each patient using a mercury sphygmomanometer by the auscultation method (Kortokoff phase V for diastolic BP). The BP was recorded in a sitting position after 5 minutes of rest. The pulse rate was determined during 30 seconds in sitting position.

Investigations such as hemogram, SGOT, SGPT, random blood sugar, serum creatinine and urine examination were performed during the first visit and after 12 weeks of the study period.

Cost of therapy for both the groups was evaluated at the end of the study. Analysis of enalapril maleate (10mg) and losartan potassium (50mg) tablets available in Indian market was performed with the help of an Indian drug index, Drug Today October-December 2010 issue, for variation in cost for the brands available.

The primary efficacy end point was the change from baseline diastolic BP; secondary end point included change from baseline in systolic BP. Dropouts of the patients if any, were noted and those patients were not included in the study for statistical analysis.

All observed or volunteered adverse events were recorded at any point of the study and designated by the physician according to the WHO-UMC causality scale as definite or probable or possible.

#### Statistical methods

For nominal categorical comparisons (e.g. demographics), Fisher's exact t-test was used. Qualitative data on adverse effects were analyzed by using the Z-test for difference between proportions. Quantitative data were analyzed by using the Z-test for difference between means. A  $p \leq 0.05$  was considered statistically significant.

## RESULTS

#### Patient characteristics

There were no significant differences between the treatment groups with respect to baseline patient demographic data and clinical characteristics like systolic BP, diastolic BP and heart rate.

A total of 92 patients completed the study [47 (51.08%) in Losartan and 45 (48.91%) in Enalapril group] and 8 patients dropped out (3 in Losartan and 5 in Enalapril group). Age averaged  $49 \pm 7$  years and body mass index  $25.4 \pm 3.1$  kg/m<sup>2</sup>. Median duration of hypertension was 8 months (range from 1 to 132). Thirty patients had previously been treated for hypertension, 18 were current smokers.

#### Blood pressure

In the enalapril treated group, the mean diastolic BP at baseline was  $99.63 \pm 3.53$  mmHg (Table 1). Once the treatment started, the diastolic BP reduced to  $90.79 \pm 2.65$  mmHg,  $87.94 \pm 2.71$  mmHg,  $86.15 \pm 1.53$  mmHg,  $85.10 \pm 1.54$  mmHg at 2 weeks, 4 weeks, 8 weeks, and 12 weeks, respectively. The reduction in diastolic BP was found to be statistically significant ( $p < 0.001$ ) at 2 weeks,

4 weeks, 8 weeks and 12 weeks of treatment when compared to the baseline diastolic BP.

**Table 1: Diastolic BP (mmHg) during enalapril and losartan treatment.**

| Visit          | Enalapril<br>10mg<br>(mean±SD) | Losartan<br>50mg<br>(mean±SD) | p-value |
|----------------|--------------------------------|-------------------------------|---------|
| Baseline       | 99.63 ± 3.53                   | 99.3 ± 4.18                   | >0.05   |
| After 2 weeks  | 90.79 ± 2.65                   | 91.37 ± 2.25                  | >0.05   |
| After 4 weeks  | 87.94 ± 2.71                   | 88.78 ± 2.35                  | >0.05   |
| After 8 weeks  | 86.15 ± 1.53                   | 85.49 ± 1.82                  | >0.05   |
| After 12 weeks | 85.10 ± 1.54                   | 83.37 ± 1.16                  | <0.001  |

In the enalapril treated group, the mean systolic BP at baseline was  $156.61 \pm 12.52$  mmHg (Table 2). Once the treatment started, the systolic BP reduced to  $147.46 \pm 10.47$  mmHg,  $139.83 \pm 8.79$  mmHg,  $130.21 \pm 7.74$  mmHg,  $126.38 \pm 6.27$  mmHg at 2 weeks, 4 weeks, 8 weeks, and 12 weeks, respectively. The reduction in systolic BP was found to be statistically significant ( $p < 0.001$ ) at 2 weeks, 4 weeks, 8 weeks and 12 weeks of treatment when compared to the baseline systolic BP.

In the losartan treated group, the mean diastolic BP at baseline was  $99.3 \pm 4.18$  mmHg (Table 1). Once the treatment started, the diastolic BP reduced to  $91.37 \pm 2.25$  mmHg,  $88.78 \pm 2.35$  mmHg,  $85.49 \pm 1.82$  mmHg,  $83.37 \pm 1.16$  mmHg at 2 weeks, 4 weeks, 8 weeks, and 12 weeks, respectively. The reduction in diastolic BP was found to be statistically significant ( $p < 0.001$ ) at 2 weeks, 4 weeks, 8 weeks and 12 weeks of treatment when compared to the baseline diastolic BP.

In the losartan treated group, the mean systolic BP at baseline was  $158.54 \pm 11.33$  mmHg (Table 2). Once the treatment started, the systolic BP reduced to  $149.15 \pm 12.13$  mmHg,  $149.77 \pm 8.41$  mmHg,  $132.86 \pm 7.93$  mmHg,  $127.90 \pm 6.51$  mmHg at 2 weeks, 4 weeks, 8 weeks, and 12 weeks, respectively. The reduction in systolic BP was found to be statistically significant ( $p < 0.001$ ) at 2 weeks, 4 weeks, 8 weeks and 12 weeks of treatment when compared to the baseline systolic BP.

When the reduction in diastolic BP in the two groups was compared at 2 weeks, 4 weeks, 8 weeks (Table 1), there was no significant difference between the groups ( $p > 0.05$ ). The mean reduction in diastolic BP achieved with losartan at 12th week was significantly higher ( $p < 0.001$ ). When the reduction in systolic BP in the two groups was compared at 2 weeks, 4 weeks, 8 weeks and 12 weeks (Table 2), there was no significant difference between the two groups ( $p > 0.05$ ).

**Table 2: Systolic BP (mmHg) during enalapril and losartan treatment.**

| Visit          | Enalapril 10mg (mean±SD) | Losartan 50mg (mean±SD) | p-value |
|----------------|--------------------------|-------------------------|---------|
| Baseline       | 156.61 ± 12.52           | 158.54 ± 11.33          | >0.05   |
| After 2 weeks  | 147.46 ± 10.47           | 149.15 ± 12.13          | >0.05   |
| After 4 weeks  | 139.83 ± 8.79            | 149.77 ± 8.41           | >0.05   |
| After 8 weeks  | 130.21 ± 7.74            | 132.86 ± 7.93           | >0.05   |
| After 12 weeks | 126.38 ± 6.27            | 127.90 ± 6.51           | >0.05   |

### Adverse events

Fifteen patients had at least one AE during the active treatment phase (Table 3), 3(6.37%) in the losartan group, and 12(26.66%) in the enalapril group that were assessed as being possibly, probably or definitely related to the study drug. Both treatment groups showed a similar incidence of AEs for all body systems with respect to the different levels of drug relationship except for the respiratory system, for which the incidence of cough was significantly higher 6(13.33%), in the enalapril group ( $p<0.05$ ), however the difference in the frequency of AEs regarding other body systems between the groups was not statistically significant ( $p>0.05$ ). There were no patients with serious AEs.

**Table 3: Most common clinical adverse experiences.**

| Adverse event    | Enalapril 10mg (n=45) | Losartan 50mg (n=47) |
|------------------|-----------------------|----------------------|
| Asthenia/fatigue | 3(6.66%)              | 2(4.25%)             |
| Nausea           | 1(2.22%)              | 0(0%)                |
| Headache         | 1(2.22%)              | 1(2.12%)             |
| Skin rash        | 1(2.22%)              | 0(0%)                |
| Cough            | 6(13.33)              | 0(%)                 |
| <b>Total</b>     | <b>12(26.66%)</b>     | <b>3(6.37)</b>       |

### Cost of therapy

Cost of a single tablet of enalapril prescribed to the patients in the study was Rs 2.37/ tablet and accordingly the cost of therapy for 12 weeks came out to be Rs 199.08. Cost of a single tablet of losartan prescribed to the patients in the study was Rs 1.10/ tablet and accordingly the cost of therapy for 12 weeks came out to be Rs 92.40.

Analyses of the cost of tablets in the drug index, taking the lowest and highest priced brands of losartan and enalapril, we found that, it ranged from Rs 1.10 to Rs 10.50 per tablet for losartan and Rs 1.20 to Rs 5.20 per tablet for enalapril.

### DISCUSSION

This study was designed to compare the antihypertensive efficacy and tolerability of losartan, an Ang II type 1 receptor antagonist and enalapril, an ACE inhibitor in patients with stage 1 and stage 2 hypertension.

For the antihypertensive efficacy end-points, notably the DBP, no significant difference ( $p>0.05$  value) between losartan and enalapril was observed with respect to the distribution of patients in the different categories of antihypertensive response. Although losartan is reported to develop its maximal antihypertensive effect after 4 to 6 weeks of treatment,<sup>20</sup> the reduction in DBP was significantly higher with losartan than after enalapril administration after week 12 of the study. The degree of BP reduction by losartan observed in our study is comparable to results of other studies in patients with hypertension, indicating that this angiotensin receptor antagonist is in fact as potent as an ACE inhibitor in lowering BP.

No serious AEs occurred in this study. The two treatment groups demonstrated no significant difference with respect to the incidence of AEs for other body systems except respiratory system in which the losartan group presented without any AE of cough as compared to enalapril group in which 6 (13.33%) patients presented with cough, thus indicating a better tolerability of losartan.

Both the approaches to block the renin-angiotensin system produce an increase in plasma renin activity (presumably related to interruption of the negative feedback of angiotensin II on renin release). This may be particularly relevant for the Ang II antagonist because the ensuing elevation of circulating Ang II levels would stimulate the unblocked type 2 receptors, and antagonise type 1 receptor actions by mediating vasodilatation and antiproliferation.<sup>21</sup>

It has even been shown in certain cell types that, stimulation of the type 2 receptors trigger kinin generation and NO-production, suggesting kinin-mediated effects of angiotensin II antagonists.<sup>22</sup> However, the biological importance of these effects in human essential hypertension is still being debated.<sup>23</sup>

The limitations of the current study were as follows: the small number of patients involved in the study; use of parallel study instead of a cross-over study, in which each patient serves as his own control and hence the response to the drugs can be compared in the individual patient; sitting BP measurement instead of ambulatory BP. The

latter is shown to be a better measure, since it is devoid of the white coat effect and has been shown to be highly reproducible on repeated measurements over a short period of time.<sup>24</sup>

Available data show that losartan has efficacy similar to that of enalapril in terms of blood pressure control, but also has improved tolerability, leading to improved patient persistence in the long term and a lesser need for switching treatment.

In the present study, cost-benefit evaluation showed that losartan had an economic advantage over enalapril with the patient saving upto Rs 100 for the period of 12 weeks. This amount is significant with respect to the average Indian population. There is a high variation in cost between different brands available within the same group. Further studies should be performed to evaluate difference in therapeutic efficacies between the drugs under same group but different brands to see how much do they differ and whether that much difference can be weighed against the less cost of therapy with the cheaper brands.

It is important to be aware of the huge expense incurred by treatment that is not taken regularly and correctly. It should also be considered that treatment in the real world is more difficult and complex than in a clinical trial environment. Data concerning the benefits of treatment are usually derived from controlled clinical trials whose setting is completely different from everyday clinical practice. Such trials commonly last no longer than 3-5 years and are typically of a much shorter duration, a period of time in which BP reduction is the main parameter by which the benefits of treatment are measured. However, other beneficial treatment related effects (e.g. on left ventricular hypertrophy and atherosclerosis) that are more typical of newer antihypertensives cannot be fully evaluated in terms of morbidity and mortality over such a short period of time..

## CONCLUSION

In patients with stage 1 and stage 2 hypertension, 12 weeks of treatment with losartan or enalapril produced similar antihypertensive effect. Losartan and enalapril were similarly well tolerated after 12 weeks of treatment with notable tolerability advantages of losartan especially with respect to the respiratory system. As expected, the major advantage of losartan over ACE inhibitors was the lower incidence of cough. The cost of therapy for losartan group was almost half the cost of therapy for enalapril group thus being cost effective to the patients. Thus, losartan could be preferred as a suitable alternative to enalapril as an antihypertensive agent.

Since it is well known that consistent antihypertensive therapy can delay the progression of renal disease<sup>25</sup> Ang II receptor type 1 antagonists such as losartan should be considered as drugs of first choice for antihypertensive

treatment more often in the future, and not only when ACE inhibitors are not tolerated.

Further studies in this area will increase awareness of the true cost-effectiveness of losartan as compared to enalapril therapies amongst different brands from reputed pharmaceuticals available in the market with varying price range and whether they actually differ in therapeutic efficacy with the cheaper brands available, and this will ultimately benefit both patients and healthcare providers.

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## REFERENCES

1. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report Of The Joint National Committee On Prevention, Detection, Evaluation, And Treatment Of High Blood Pressure: the JNC 7 Report. JAMA 2003;289:2560-72.
2. Ramsay L, Williams B, Johnston G, et al. Guidelines for management of hypertension: report of the third working party of the British Hypertension Society. J Hum Hypertens 1999;13:569-92.
3. Ballermann BJ. Vasoactive peptides and the kidney. In: Brenner BM, Rector FC, editors. The kidney. Philadelphia: WB Saunders, 1991:510-83.
4. Friberg P. The renin-angiotensin system in neonatal rats: Induction of renal abnormality in response to ACE inhibition or angiotensin II antagonism. Kidney Int 1994;45:485-92.
5. Mitchell KD, Braam B, Navar LG. Hypertensinogenic mechanisms mediated by renal actions of the renin-angiotensin system. Hypertension 1992;19(1 Suppl):I18-27.
6. Carey RM, Howell NL, Jin XH, Siragy HM. Angiotensin type 2 receptor-mediated hypotension in angiotensin type 1 receptor-blocked rats. Hypertension 2001;38:1272-7.
7. Stoll M. The angiotensin AT2 receptor mediates inhibition of cell proliferation in coronary endothelial cells. J Clin Invest 1995;95:651-7.
8. Timmermann PB, Carini DJ, Chiu AT. The discovery of a new class of highly specific nonpeptide angiotensin II receptor antagonists. Am J Hypertens 1991;4:275S-281S.
9. Burnier M, Waeber M, Brunner HR. Clinical pharmacology of the angiotensin II receptor antagonist losartan potassium in healthy subjects. J Hypertens 1995;13:S23-S28.

10. Gradmann AH, Arcuri KE, Goldberg AI, et al. A randomized, placebo-controlled, double-blind, parallel study of various doses of losartan potassium compared with enalapril maleate in patients with essential hypertension. *Hypertension* 1995;25:1345-50.
11. Goldberg AI, Dunlay MC, Sweet CS, et al. Safety and tolerability of losartan potassium, an angiotensin II receptor antagonist, compared with hydrochlorothiazide, atenolol, felodipine ER, and angiotensin-converting enzyme inhibitors for the treatment of systemic hypertension. *J Am J Cardiol* 1995;75:793-5.
12. Lacouciere Y, Lefebvre J, Nakhle G, et al. Association between cough and angiotensin converting enzyme inhibitors and angiotensin II antagonists: the design of a prospective, controlled study. *J Hypertens* 1994;12:S49-S53.
13. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;345:861-9.
14. Lewis EJ, Hunsicker LG, Bain RP, et al. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. *N Engl J Med* 1993;329:1456-62.
15. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342:145-53.
16. Garg R, Yusuf S, for the Collaborative Group on ACE Inhibitor Trials. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. *JAMA* 1995;273:1450-6.
17. Cohn JN, Tognoni G, for the Val-HeFT Investigators. Effects of the angiotensin receptor blocker valsartan on morbidity and mortality in heart failure: The Valsartan Heart Failure Trial (Val-HeFT). *Circulation* 2000;267:2672-6.
18. Ball SG, White WB. Debate: angiotensin-converting enzyme inhibitors versus angiotensin II receptor blockers—a gap in evidence-based medicine. *Am J Cardiol* 2003;91:15-21.
19. Davis M, Poisal J, Chulis G, et al. Prescription drug coverage, utilization, and spending among Medicare beneficiaries. *Health Aff (Millwood)*. 1999;18:231-43.
20. Nelson E, Arcuri K, Ikeda L, et al. Efficacy and safety of losartan in patients with essential hypertension. *Am J Hypertens* 1992;5:19A-20A.
21. Horiushi M, Akishita M, Dzau VJ. Recent progress in angiotensin II type 2 receptor research in the cardiovascular system. *Hypertension* 1999;33:613-21.
22. Gohlke P, Pees C, Unger T. AT2 receptor stimulation increases aortic cyclic GMP in SHRSP by a kinin dependent mechanism. *Hypertension* 1998;31:349-55.
23. Birkenhager WH, de Leeuw PW. Non-peptide angiotensin type 1 receptor antagonists in the treatment of hypertension. *J Hypertens* 1999;17:873-81.
24. Staessen H et al. The diurnal BP profile. A population study. *Am J Hypertens* 1992;5:386-92.
25. Strutz F, Müller GA. Renal fibrogenesis and progression. In: Nielsen EG, Couser WC, editors. *Immunologic renal diseases*. Philadelphia, New York: Lipincott-Raven, 1997:705-26.

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