reduce SBP significantly (Co, 133 ± 5; SNX, 144 ± 8; ET-A, 132 ± 8; ET-AB, 140 ± 6 mmHg; NS). Urinary protein excretion was increased 20-fold in untreated SNX animals after 12 weeks compared with controls (P < 0.01). Both ET receptor antagonists were able to reduce proteinuria in SNX rats, whereas the selective ET_A receptor antagonist reduced proteinuria to a greater extent than the combined ET_AB receptor antagonist (proteinuria: CO, 6 ± 2; SNX, 92 ± 9; ET-A, 27 ± 2; ET-AB, 43 ± 6 mg/24 h; P < 0.01). The hypertrophy of the heart in untreated SNX rats was prevented significantly by both ET receptor antagonists. The plasma aldosterone showed an activation in untreated SNX rats, being completely antagonized by ET_AB but not by ET_A receptor antagonist.

Summary

The present study suggests that ET-1 is involved in the pathogenesis of uraemic cardiac hypertrophy and in the progression of renal failure in rats with subtotal nephrectomy examined after an intermediate period of 12 weeks of renal failure. Furthermore, proteinuria is reduced by the selective ET_A receptor antagonist more than by the unselctive ET_AB receptor antagonist, without reducing the blood pressure. ET receptor blockade might preserve renal function by reduction of protein excretion. In addition, ET receptor antagonists influence the aldosterone system. In our animal studies, the medication was well tolerated. Our study results provide a possible therapeutic approach using ET receptor antagonists for cardiac hypertrophy and renal protein excretion by blockade of endogenous ET-1.

Further human studies are needed to show whether this protection of the heart and kidney might influence the survival and life expectancy of patients suffering from chronic renal failure, of patients on dialysis or after kidney transplantation.


**Decreased diurnal blood pressure variability and low dehydroepiandrosterone sulfate levels in patients with renal hypertension, and after kidney transplantation**

I. Barna, K. Földes, M. Szathmári, L. Gerő and R. de Châtel

First Department of Medicine, Semmelweis University Medical School, Budapest, Hungary

The decrease in diurnal rhythm of blood pressure and low plasma dehydroepiandrosterone sulfate (DHEAS) levels are strong predictors of cardiovascular morbidity and mortality [1,2]. In our earlier study, we found a close correlation between serum DHEAS levels and diurnal indices in normotensive volunteers and in patients with essential hypertension [3]. The aim of the study was to determine the relationship between the level of DHEAS and the diurnal blood pressure variability in patients with renal hypertension (RH)
and after kidney transplantation (TPX). The ambulatory blood pressure monitoring and assessment of diurnal variability were performed with a Meditech-02 ABPM device; blood pressure and heart rate were measured every 20 min during the day and every 30 min at night. Each patient kept a log on the events of the day, the times of drug intake, if any, and the time of getting up and going to bed. The determination of DHEAS was done by a radioimmunoassay technique [4]. The prevalence of reversed systolic/diastolic diurnal indices was 2/2% in normotension, 25/25% in RH and 48/33% in TPX patients ($P<0.001$ with $\chi^2$ test). We found significant correlations between systolic and diastolic indices, and serum DHEAS levels in the total population. These relationships were also significant when analysing normotensive subjects, RH subjects and TPX patients separately (Table 1).

Mean diurnal systolic/diastolic indices (SI/DI) were 12/17% for normotensives, 8/12% in RH, and 3/5% after TPX. The mean DHEAS was significantly different between normotensive, RH and TPX patients (4.7 vs 3.0 vs 1.5 $\mu$mol/l), respectively ($P<0.001$) (Figure 1).

These findings indicate that low DHEAS and decreased SI/DI are often associated with each other, indicating increased cardiovascular risk, which is particularly dominant in patients after renal transplantation.

### Table 1.

<table>
<thead>
<tr>
<th></th>
<th>$n$</th>
<th>DHEAS/SI</th>
<th>DHEAS/DI</th>
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<tr>
<td></td>
<td>$r$</td>
<td>$P$</td>
<td>$r$</td>
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<tr>
<td>Total population</td>
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<td>Normotension</td>
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<td>After transplantation</td>
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<td>0.370</td>
<td>0.340</td>
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### References