

CIRCADIAN VARIABILITY OF RATE-PRESSURE PRODUCT IN ESSENTIAL HYPERTENSION WITH ENALAPRIL THERAPY

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A b s t r a c t

Rate-pressure product (systolic blood pressure x heart rate/100, RPP) is a major determinant of cardiac oxygen consumption. The aim of the study was to analyze the circadian RPP in essential hypertension with enalapril therapy. We examined 11 normotensives (C), 10 patients with essential hypertension (EH), 10 patients with essential hypertension after one-year enalapril therapy (12.5 mg in one morning dose, EH E) and 10 patients with renal hypertension (25 mg enalapril in one morning dose, N). Accutracker II was used for 24-h ambulatory blood pressure (BP) monitoring. From our results we can conclude that RPP showed large circadian variability in C, EH, EH E and N. The enalapril therapy did not normalize increased RPP in EH E at night.

Key words

Rate-pressure product, circadian variability, antihypertensive therapy

INTRODUCTION

In essential hypertension there is present an increased sympathetic activity, which increases further risk of cardiovascular morbidity and mortality. The effect of antihypertensive therapy is nowadays generally evaluated by means of ambulatory 24-hour blood pressure monitoring and the value of the decrease in blood pressure is taken as an ultimate goal of the treatment. This is correct in majority of patients because of correlation between blood pressure values and the development of organ pathological changes, e. g. hypertrophy of left ventricular mass and arterial smooth muscles. In patients with angina pectoris there was described the relation of heart rate and systolic blood pressure to the onset of pain in angina pectoris (1). Rate-pressure product is also called Robinson index. Rate-pressure product (systolic blood pressure x heart rate/100, RPP) is a major determinant of cardiac oxygen consumption (2). Therefore in cardiac patients it is necessary to reach not only the decrease in blood pressure but also the decrease in heart rate and also the oxygen consumption of the heart. The aim of the study was to analyze the circadian RPP in essential hypertension with enalapril therapy.

METHODS

Subjects:

We examined 11 normotensives (men, C), 10 patients with moderate essential hypertension without therapy (EH), 10 patients with essential hypertension after one-year enalapril therapy (12.5 mg in one morning dose, EH E) and 10 patients with nephrogenous hypertension with one-year enalapril therapy (25 mg enalapril in one morning dose, N).

The diagnosis of essential hypertension was determined according to WHO criteria. The patients were followed up in our clinic at least 3 years before the beginning of the study, the secondary hypertension was excluded and essential hypertension was established. The group of patients with nephrogenous hypertension was followed up at least 3 years in the nephrological department and the diagnosis was verified clinically and by examination of histological specimens.

The study was approved by Ethical Committee of the Masaryk University and informed consent was signed by all the patients.

Blood pressure measurement:

Accutracker II was used for 24-h ambulatory blood pressure (BP) and heart rate (HR) monitoring. Rate-pressure product (systolic blood pressure x heart rate/100, RPP) was calculated for 24-hour period. The statistical evaluation was carried out by means of Wilcoxon test.

RESULTS

The characteristics of the normotensives (C), untreated (EH) and treated hypertensives (EH E) and patients with nephrogenous hypertension (N) are shown in *Table 1*. They did not differ in age and basic anthropologic data. The results of SBP, DBP and RPP during 24 hours are given in *Table 2* and 3.

Fig. 1 to 4 illustrate the average changes of SBP and DBP during 24-h in all participants (mean \pm SD), *Fig. 5* to 8 the RPP during 24-h (mean \pm SD).

RPP showed large circadian variability in C, EH, EH E and N. The enalapril therapy did not normalize increased RPP in EH E at night.

DISCUSSION

The increase in sympathetic nervous activity is an important factor contributing not only to hypertrophy of left ventricular mass and arterial smooth muscles but also to the development of myocardial infarction and sudden cardiac death in patients with ischemic heart disease (3, 4, 9). The circadian variation of sympathetic nervous activity is reflected by the increase of the incidence of myocardial infarction and sudden cardiac death in the morning hours (5, 6). The increase of the incidence of both events start at 6 a.m. and reach the peak between 9 a.m. and midday. In the afternoon the incidence of both events is of about the half of the peak values. The aim of the chronotherapy of hypertension is to control blood pressure over the period of 24-h and to suppress the morning increase in the sympathetic activity.

Our data demonstrate that the 24-hour profile of rate-pressure product much better correlates with the incidence of sudden cardiac death and myocardial infarction than the blood pressure curves. This finding can reflect the fact that sympathetic nervous activity is a major determinant of blood pressure. The

Table 1
Characteristics of the subjects and patients

	N	age (years)	height (cm)	body weight (kg)
C	11	48 ± 6	180 ± 6	82 ± 5
EH	10	49 ± 5	179 ± 8	83 ± 6
EH E	10	49 ± 5	178 ± 5	86 ± 5
N	10	49 ± 9	176 ± 5	85 ± 3

Table 2
24-h mean (± SD) values of systolic blood pressure (SBP), diastolic blood pressure (DBP)
and rate - pressure product (RPP) in subjects and patients

	SBP(mmHg)	DBP(mmHg)	HR(cpm)	RPP(mmHg.cpm/100)
C	121 ± 10	74 ± 8	75 ± 11	93.18 ± 12.08
EH	147 ± 12**	88 ± 9**	80 ± 9	117.59 ± 17.76**
EH E	129 ± 9	80 ± 7	83 ± 11	107.32 ± 15.70
N	127 ± 8	74 ± 6	80 ± 8	102.29 ± 8.54

(Statistical significance versus C: * - p<0.05, ** - p<0.01)

Table 3
Daytime mean (± SD) and night-time mean (± SD) values of rate - pressure product (RPP)
in subjects and patients

	Daytime mean RPP(± SD)	Night-time mean RPP(± SD)
	07:00 - 24:00	01:00 - 06:00
C	101.44 ± 15.06	68.50 ± 3.14
EH	125.44 ± 18.33**	94.16 ± 16.06**
EH E	113.78 ± 14.67	88.00 ± 18.82*
N	109.11 ± 9.76	81.83 ± 4.91

(Statistical significance versus C: * - p<0.05, ** - p<0.01)

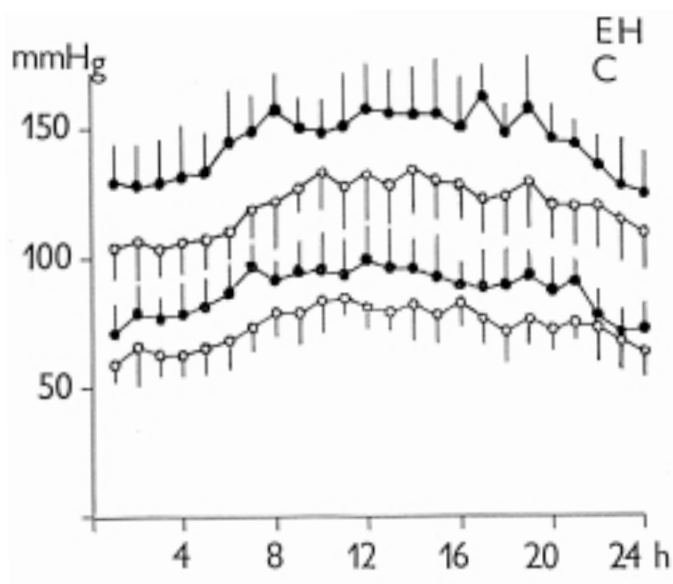


Fig. 1.
24-h blood pressure profiles in controls (C) and patients with essential hypertension without therapy (EH).

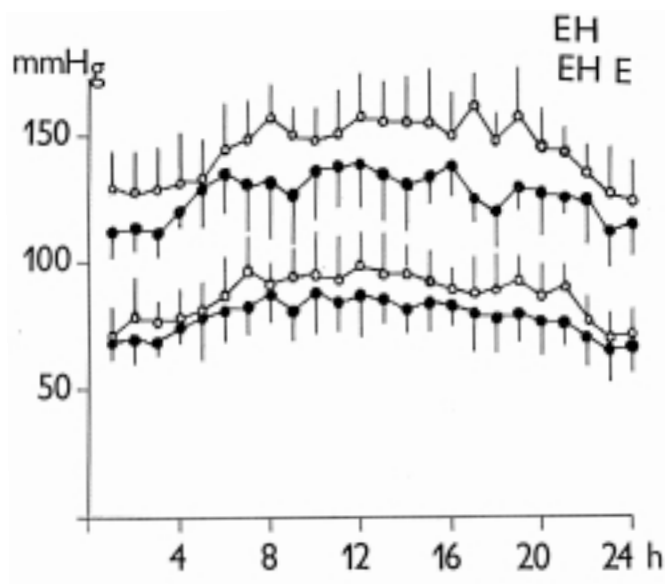


Fig. 2.
24-h blood pressure profiles in patients with essential hypertension without therapy (EH) and patients with essential hypertension with enalapril therapy (EH E).

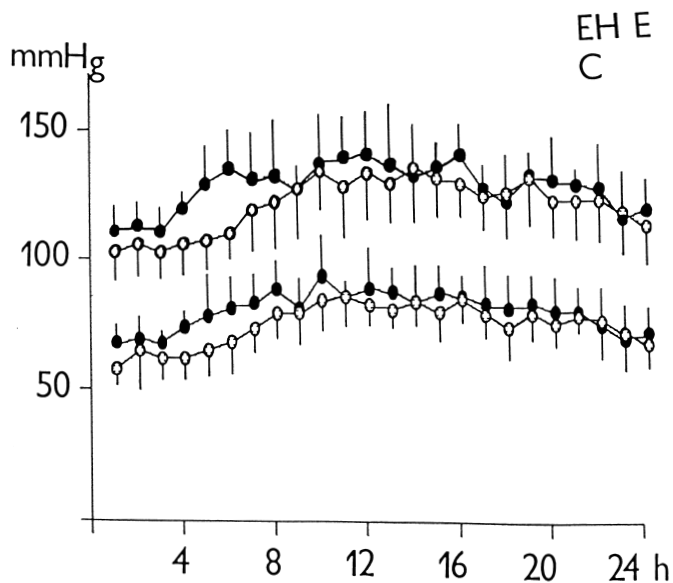


Fig. 3.
24-h blood pressure profiles in controls (C) and patients with essential hypertension with enalapril therapy (EH E).

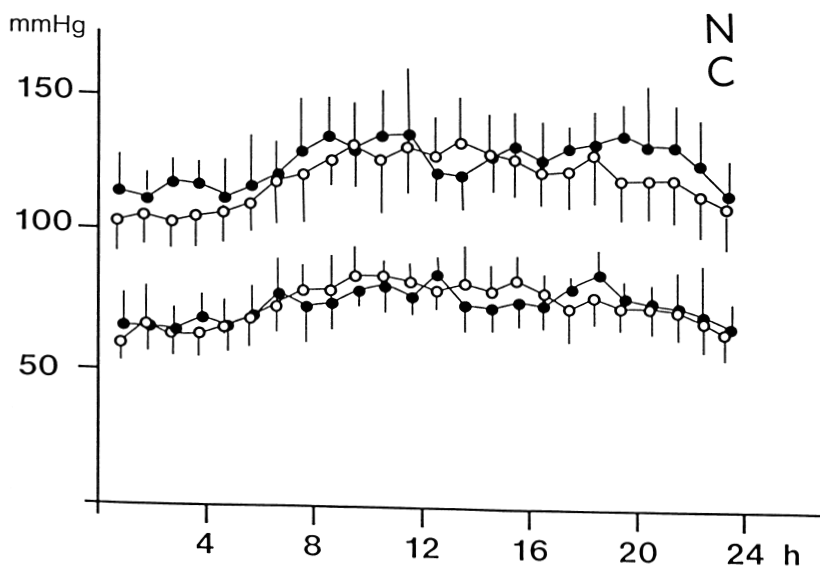


Fig. 4.
24-h blood pressure profiles in controls (C) and patients with nephrogenous hypertension with enalapril therapy (N).

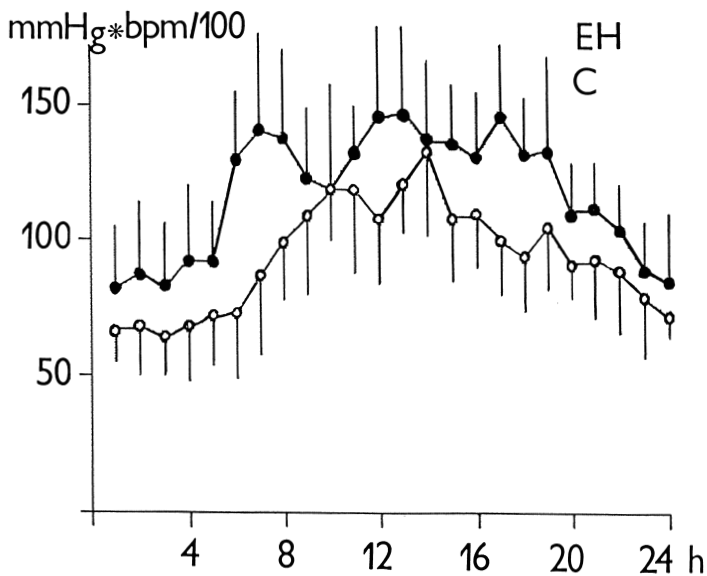


Fig. 5.
24-h rate-pressure product (RPP) profiles in controls (C) and in patients with essential hypertension without therapy (EH).

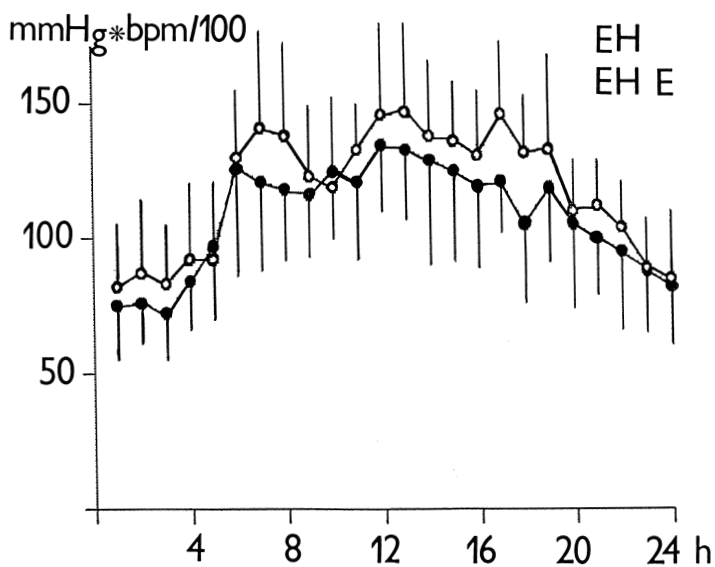


Fig 6.
24-h rate-pressure product (RPP) profiles in patients with essential hypertension without therapy (EH) and patients with essential hypertension with enalapril therapy (EH E).

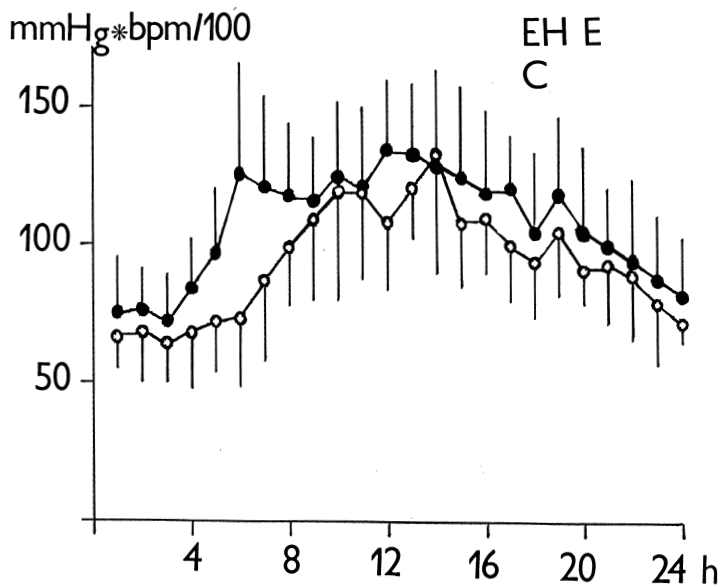


Fig 7.

24-h rate-pressure product (RPP) profiles in controls (C) and patients with essential hypertension with enalapril therapy (EH E).

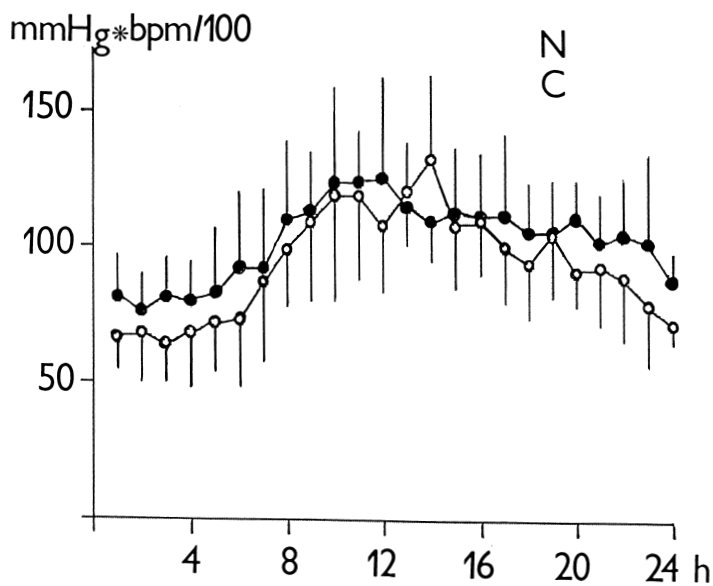


Fig. 8.

24-h rate-pressure product (RPP) profiles in controls (C) and patients with nephrogenous hypertension with enalapril therapy (N).

baroreflex is probably the mechanism increasing the heart rate during the nifedipine therapy and this can be the reason for the increase of mortality after nifedipine. The decrease in blood pressure in morning hours during the enalapril treatment is accompanied by a lower heart rate increase as indicated by the decrease of rate-pressure product after enalapril treatment in comparison to non-treated patients.

The relatively low increase in rate-pressure product in the morning hours of enalapril treated patients with nephrogenous hypertension probably reflects the fact that the cause of hypertension is not the increased sympathetic activity in this group of patients. This fact is supported by our finding of normal baroreflex heart rate sensitivity in patients with nephrogenous hypertension in comparison to the essential hypertension (7, 8).

In conclusion, the non-invasive methods used in this study may facilitate the study of myocardial ischemia in patients with essential hypertension. The 24-h measurements of blood pressure and the evaluation of RPP might eventually become an appropriate tool for identification of optimal strategies in the different therapy of arterial hypertension and demonstrate a favorable prognostic outcome.

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CIRKADIÁNNÍ VARIABILITA PRODUKTU FREKVENCE-TLAK U ESENCIÁLNÍ HYPERTENZE LÉČENÉ ENALAPRILEM

S o u h r n

Produkt frekvence tlak (systolický krevní tlak x srdeční frekvence/100, RPP) je hlavním determinantem utilizace kyslíku srdečním svalem. Cílem studie bylo analyzovat cirkadiánní RPP u esenciální hypertenze léčené enalapilem. Vyšetřili jsme 11 normotoniců (C), 10 pacientů s esenciální hypertenzí bez léčby (EH), 10 pacientů s esenciální hypertenzí léčených enalapilem 1 rok (12.5 mg v jedné ranní dávce, EH E) a 10 pacientů s nefrogenní hypertenzí (25 mg enalaprilu v jedné ranní dávce, N). Pro 24-h ambulantní monitorování krevního tlaku byl použit Accutacker II. Z našich výsledků vyplývá, že RPP vykazoval velkou cirkadiánní variabilitu u C, EH, EH E a N. Léčení enalapilem nenormalizovalo RPP u EH E v noci.

Acknowledgement

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