Ann. Acad. Med. Siles. (online) 2016; 70: 265–273
eISSN 1734-025X
DOI:10.18794/aams/66854

PRACA ORYGINALNA
ORIGINAL PAPER

Arterial blood pressure circadian rhythm in normotensive decompensated cirrhotic patients before and after single paracentesis

Rytm okołodobowy ciśnienia tętniczego krwi u normotensyjnych pacjentów z niewyrównaną marskością wątroby przed i po paracentezie

Czesław Marcisz[1], Arkadiusz Orzeł[2], Adriana Kowalik-Kabat[1], Halina Kulik[3], Joanna Balicka[3], Anna Olejko[4]

[1] Department of Gerontology and Geriatric Nursing, School of Health Sciences in Katowice, Medical University of Silesia in Katowice

[2] Department of Cardiology, Polish Medical Group, Chorzów

[3] Department of Nursing Propaedeutics, School of Health Sciences in Katowice, Medical University of Silesia in Katowice

[4] Department of Health Promotion and Environmental Nursing, School of Health Sciences in Katowice Medical University of Silesia in Katowice

ABSTRACT

INTRODUCTION: Decompensated liver cirrhosis is associated with hemodynamic changes including arterial blood pressure alterations. The aim of the study was to investigate the circadian rhythm variability of arterial blood pressure in relation to reninemia and aldosteronemia in cirrhotic patients with ascites, before and after paracentesis.

MATERIAL AND METHODS: The study was performed in 22 normotensive cirrhotics with ascites and 19 healthy controls. Ambulatory arterial blood pressure monitoring was conducted for 24 hours, cardiac output and systemic vascular resistance were determined and circulating renin and aldosterone concentrations were measured. In cirrhotics, the tests were repeated 24 hours after paracentesis.

RESULTS: It was demonstrated that as a consequence of paracentesis, the mesor values of systolic and diastolic blood pressure and heart rate decreased, whereas the amplitudes did not change in the cirrhotics. Moreover, in the cirrhotics' acrophases of blood pressure occurred earlier than in the controls. The day-night differences of mean pressure values were smaller in the cirrhotics than in the controls. The patients before paracentesis demonstrated higher cardiac output and lower systemic vascular resistance than healthy subjects. In cirrhotic patients the renin and aldosterone concentrations were higher and the aldosterone/renin ratio was lower than in the controls.

CONCLUSIONS: Arterial blood pressure circadian rhythm in normotensive patients with decompensated cirrhosis of the liver with ascites is characterized by a lowered decrease at nighttime that suggests the occurrence of non-dipping phenomenon. The reduction of ascites in patients with decompensated liver cirrhosis leads to a reduction in arterial blood pressure and does not eliminate the non-dipping phenomenon in its day-night rhythm. In normotensive cirrhotic patients with ascites before and after single paracentesis, a dissociation of the renin-aldosterone nexus occurs.

KEY WORDS

cirrhosis of the liver, aldosterone, diurnal rhythm of arterial blood pressure, paracentesis, renin

Received: 17.10.2016 **Revised:** 06.11.2016 **Accepted:** 08.11.2016 **Published online:** 12.12.2016

Address for correspondence: prof. dr hab. n. med. Czesław Marcisz, Department of Gerontology and Geriatric Nursing, School of Health Sciences in Katowice, Medical University of Silesia in Katowice, ul. Ziołowa 45/47, 40-635 Katowice, Poland, Mobile: +48 609 102 287, e-mail: klinwewtychy@poczta.onet.pl

STRESZCZENIE

WSTĘP: Niewyrównana marskość wątroby prowadzi do zaburzeń hemodynamicznych i zmian ciśnienia tętniczego krwi. Celem pracy było badanie zmienności okołodobowego rytmu ciśnienia tętniczego z uwzględnieniem reninemii i aldosteronemii u pacjentów z marskością wątroby z wodobrzuszem, przed i po paracentezie.
MATERIAŁ I METODY: Badania obejmowały 22 chorych na marskość wątroby z wodobrzuszem i 19 osób zdrowych stanowiących grupę kontrolną. Przeprowadzono 24-godzinny pomiar ciśnienia tętniczego krwi, określono objętość minutową serca, całkowity opór obwodowy naczyń oraz stężenie reniny i aldosteronu w surowicy. U chorych na marskość wątroby badania powtórzono po 24 godz. od wykonania paracentezy.
WYNIKI: W następstwie paracentezy mezory wartości ciśnienia skurczowego i rozkurczowego oraz tętna obniżyły się, amplituda zaś nie uległa zmianie. U chorych akrofazy ciśnienia krwi wystąpiły wcześniej niż w grupie kontrolnej. Różnice dzienno-nocne wartości ciśnienia krwi u chorych na marskość wątroby okazały się mniejsze niż u osób zdrowych. U chorych przed paracentezą objętość minutowa serca była większa, a całkowity opór obwodowy naczyń mniejszy niż u osób z grupy kontrolnej. W porównaniu z grupą kontrolną, reninemia i aldosteronemia były większe, natomiast wskaźnik aldosteron/renina mniejszy u chorych na marskość wątroby.
WNIOSKI: U normotensyjnych chorych na marskość wątroby z wodobrzuszem występuje zjawisko non-dipper. Paracenteza prowadzi do zmniejszenia ciśnienia tętniczego, lecz nie znosi zjawiska non-dipper. U chorych na marskość wątroby z wodobrzuszem obserwuje się rozkojarzenie reninowo-aldosteronowe zarówno przed, jak i po paracentezie.

SŁOWA KLUCZOWE
marskość wątroby, aldosteron, rytm okołodobowy ciśnienia tętniczego, paracenteza, renina

INTRODUCTION

Patients suffering from liver cirrhosis complicated by portal hypertension with ascites are accompanied by hemodynamic changes with hyperkinetic circulation and modification of arterial blood pressure [1,2]. A reduction of both effective blood volume and systemic vascular resistance was demonstrated in patients with decompensated liver cirrhosis [1]. In this disease, a vasoconstriction mechanism is activated via stimulation of renin-angiotensin-aldosterone system (RAAS) [3,4,5]. On the other hand, participation of factors causing arterial vessels to dilate, e.g. adrenomedullin, nitric oxide and calcitonin gene related peptide, increased [6,7,8]. In literature one may also find cases demonstrating that arterial blood pressure in patients with liver cirrhosis, or even decompensated liver cirrhosis, did not change or was elevated [1,9], sometimes taking a form of isolated systolic hypertension [10]. Incidence of arterial hypertension among cirrhotic patients is significantly lower than in the general population [11]. Reduction of arterial blood pressure was observed immediately after paracentesis [12] and within the duration of 24 [13] or 48 hours [14] after large volume paracentesis in cirrhotic patients with tense ascites.
Studies determining circadian variability of arterial blood pressure in cirrhotic patients appear to be interesting [13,15,16,17]. Evaluated variability of arterial blood pressure circadian rhythm during a 24-hour monitoring showed significantly lower reduction of systolic and diastolic blood pressure at night in cirrhotic patients than in healthy subjects [15,16]. The result is that cirrhotic patients were characterized by decreased pressure amplitude during the day and at night. It was shown that systolic, diastolic and mean arterial pressure decreased over 24-hour in cirrhotic patients after large volume paracentesis compared to the pre-paracentesis [13]. It is worth mentioning that the studies of the arterial blood pressure circadian rhythm concerned patients with reduced arterial blood pressure only [13,15,16].
The aim of the study was to investigate arterial blood pressure awake-asleep variation and reninemia and aldosteronemia in normotensive cirrhotic patients with ascites before and after single paracentesis.

MATERIAL AND METHODS

Subjects

The studies were performed in 22 normal blood pressure (daily mean systolic blood pressure = 120––139 mmHg, daily mean diastolic blood pressure = 80–89 mmHg) patients with liver cirrhosis with tense ascites and in 19 sex- and age-matched healthy controls. Table I shows characteristics of the examined subjects, biochemical test results determining hepatic and renal functions in both examined groups and Child-Pugh (CP) score as well as model for end-stage liver disease (MELD) score in cirrhotic patients.

Table I. Demographic and biochemical parameters in cirrhotic patients and healthy controls [mean(SEM)]
Tabela I. Wskaźniki demograficzne i biochemiczne u chorych na marskość wątroby i osób zdrowych

Parameter	Investigated groups	
	liver cirrhosis with ascites (n = 22)	controls (n = 19)
Sex (male/female)	14/8	13/6
Age (years)	54.9 ± 2.6	53.3 ± 1.6
Hemoglobin (mmol/L)	7.4 ± 0.2*	9.2 ± 0.2
Serum total protein (g/L)	70.2 ± 1.6	72.5 ± 1.0
Serum albumin (g/L)	41.2 ± 1.5*	58.4 ± 1.6
International normalized ratio (INR)	1.5 ± 0.1*	0.9 ± 0.1
Serum bilirubin (μmol/L)	57.2 ± 11.2*	10.9 ± 1.1
Serum alanine aminotransferase (IU/L)	35.5 ± 3.6*	27.9± 4.6
Serum aspartate aminotransferase (IU/L)	92.3 ± 12.5*	27.2 ± 3.3
Serum sodium (mmol/L)	134.1 ± 1.1*	141.0 ± 0.5
Serum potassium (mmol/L)	3.9 ± 0.1	4.2 ± 0.1
Serum creatinine (μmol/L)	84.3 ± 6.7	87.8 ± 3.8
Glomerular filtration rate (mL/min)	108,1 ± 8.3	98.7 ± 9.4
Child-Pugh score (A/B/C)	10.5 ± 0.2 (0/8/14)	–
MELD score	10.1 ± 1.0	–

*p < 0.05 vs. control group

Diagnosis of liver cirrhosis was based on clinical examination, biochemical as well as imaging tests and, wherever possible, histopathologi cal examination. Fourteen patients with postalcoholic cirrhosis and 8 patients with a history of hepatitis B or C were included in the study. Patients with alcoholic liver cirrhosis have been consuming more than 50 g of alcohol daily for at least 5 years. For at least 10 days prior to the examination the patients have not consumed alcohol. Only the subjects that did not exhibit alcohol withdrawal symptoms were included in the study. In order to determine the degree of liver failure, CP classification [18] and MELD score [19] were used. The patient group included 8 subjects with CP class B and 14 subjects with CP class C. All examined subjects were patients of the Department of Internal Medicine of Silesian Medical University in Katowice.
Patients with hepatorenal syndrome, encephalopathy above grade 1, bacterial infections, gastrointestinal bleeding in the last 3 months, overt heart failure, heart defects, impaired segmental myocardial contractility, arterial hypertension in medical history, malignant tumors, diabetes, endocrinological diseases and subjects that did not consent to perform the study were excluded from the study.

The study protocol was approved by Bioethics Committee of Medical University of Silesia in Katowice (Approval No.: NN-6501-150/07).

Methods

A 24-hour ambulatory arterial blood pressure monitoring (ABPM) was performed in all study subjects. Hemodynamic parameters including: systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR), cardiac output (CO) and systemic vascular resistance (SVR) were also determined. Upon termination of the 24-hour ABPM, examined patients' blood was drawn from median cubital vein between 7:30 AM and 8:00 AM, on empty stomach, in the sitting position, for approximately 30 minutes in order to determine blood cells morphology, protein electrophoresis, bilirubin, alanine and aspartate aminotransferases, alkaline phosphatase, gamma-glutamyl transpeptidase, prothrombin, INR, creatinine, sodium, potassium, serum C-reactive protein, blood glucose and concentrations of plasma renin and serum aldosterone. In order to measure renin concentrations, blood was drawn into EDTA vials that had been cooled and immediately centrifuged at 4°C for 10 minutes at 3000 rpm. Centrifuged plasma and serum for measuring aldosterone were placed in a freezer at -30°C till the time when measurements were to be performed. A radioimmunologic method with Cisbio Bioassays reagent (Great Britain) was used to measure plasma renin concentration. Range of renin concentration values considered as normal was: supine = 1.1–20.2 pg/mL, upright = 1.8–59.4 pg/mL. A radioimmunologic method with Radim S.p.A. reagent (Italy) was used to measure serum aldosterone concentration (reference value at rest = 10–160 pg/mL, in motion = 35–300 pg/mL). Glomerular filtration rate was calculated with the use of modification of diet in renal disease (MDRD) formula [20].
In cirrhotic patients with ascites, studies of hemodynamic and biochemical parameters were performed before paracentesis during diet including daily sodium dose of 60 mmol and were repeated after reduction of ascites following single paracentesis with drainage of 5 liters of fluid from abdominal cavity without albumin infusion. Paracentesis was performed in a semi-recumbent position with a 0.7–0.9 thick and ≥ 40 mm long needle under ultrasonography guidance. Repeated studies of biochemical parameters have been performed after 24 hours since the paracentesis. Patients' weight was determined in the mornings after emptying urine bladder, during the entire monitoring period. Diuretic administration and beta-blockers were discontinued at least 5 days before paracentesis.
On the second day after paracentesis, a 24-hour ABPM was re-performed by means of HolCARD

system with a CR-06 recorder programmed by a compatible computer system that allows for printing out the results. Frequency of measurements was programmed for every 15 minutes during the day (06:00 AM–10:00 PM) and every 30 minutes during the night (10:00 PM–06:00 AM). On the basis of obtained measurements, maximal and minimal values for arterial blood pressure and HR during the day and night were established. Mean values for SBP and DBP, mean arterial pressure [MAP = DBP + (SBP-DBP)/3] and HR were calculated separately for day and night. Daily mean arterial pressure (dMAP) and nocturnal mean arterial pressure (nMAP) were determined and then, percentage changes of nMAP to dMAP were calculated according to the equation: ΔMAP% = (1 - nMAP/dMAP) x 100 (%). ΔMAP% lower than 10% determines occurrence of non-dipping profile, whereas ≥ 10% – dipping [21].

The 24-hour ABPM was followed by transthoracic echocardiography performed by means of ALOKA SSD-4000 with a 4V2 (2.5–5 MHz) ultrasonic transducer and simultaneous ECG recording. The tests were performed during shallow breathing. Obtained results were averaged on the basis of five full cardiac cycles. Hemodynamic parameters were determined, i.e.: stroke volume (SV) based on the equation: SV = CSA (aortic cross-sectional area) x VTI (velocity time integral) [mL], cardiac output (CO) from the equation: CO = SV x HR [mL/min] and SVR from the equation: SVR = (MAP – right atrial pressure)/CO x 80 [mmHg x min/mL]. All echocardiograms were interpreted by A.O., who had no knowledge of the clinical and laboratory data.

Statistical analysis

The obtained results were statistically compiled with the use of Statistica v. 7.1 PL program produced by Stat Soft and MedCalc Software v.11.3.3.0. Shapiro-Wilk test was used to evaluate whether a given parameter was characterized by a distribution close to or diverging from the norm. Then, paired and unpaired Student's t-tests for normal distribution data and Mann-Whitney-Wilcoxon test for data distribution diverging from the norm were used. Correlation coefficient (r) was calculated by means of Pearson test or Spearman's rank test. It used a single cosinor method for the statistical evaluation of parameters of circadian BP or HR rhythms. For validated rhythm, the following parameters were estimated: mesor (a rhythm-adjusted mean), the acrophase (the lag from a reference time to the crest time of the best fitting cosine curve) and the amplitude (one-half of the difference between the peak and nadir of BP or HR rhythm). A statistical significance $p \leq 0.05$ was accepted in statistical calculations.

RESULTS

Study of arterial blood pressure variability and its daily rhythm showed that in cirrhotic patients with tense ascites mesor values of SBP, DBP and MAP were comparable to the ones determined in healthy control groups (Tab. II). Following paracentesis, the mesor values were reduced ($p < 0.001$) and became significantly lower than the ones observed in the control group ($p < 0.001$). Differences between mean values of arterial blood pressure and HR components determined during the day and at night turned out to be significantly lower in cirrhotic patients, before and after paracentesis, than the ones observed in control group subjects ($p < 0.001$; Tab. II). It was demonstrated that proportional decrease in MAP at night, when compared to the one determined during the day (ΔMAP%), was also significantly lower in these patients than in the control group ($p < 0.001$; Tab. II). 18 out of 22 cirrhotic patients showed a decrease in MAP < 10% during nighttime sleep and were categorized as non-dippers, while the remaining 4 showed ≥ 10% and were categorized as dippers. The prevalence rates of non-dippers in these patients were 82%. Amplitude values in SBP and DBP daily rhythm in cirrhotic patients, before and after paracentesis, and in controls were comparable (Tab. II). Peak pressure values referred to as acrophases occurred during the day between 12:00 PM and 4:00 PM. In cirrhotic patients there occurred shifts in acrophases: SBP, DBP and MAP occurred respectively 140, 85 and 121 minutes earlier than in healthy subjects ($p < 0.05$–0.001; Tab. II). Mean HR in daily rhythm was higher in cirrhotic patients than in controls ($p < 0.001$; Tab. II).

Examined hemodynamic parameters determining CO and SVR significantly differed in cirrhotic patients with tense ascites; CO was higher and SVR was lower in comparison to the values obtained in control group subjects ($p < 0.05$; Tab. III). Hemodynamic parameter values after paracentesis showed only a tendency towards normalization.

Plasma renin concentration and aldosteronemia were significantly higher in cirrhotic patients before and after paracentesis when compared with the control group ($p < 0.05$–0.001; Tab. III). Concentration of renin significantly increased after paracentesis ($p < 0.05$). Aldosterone/renin ratio was lower in cirrhotic patients than in controls ($p < 0.001$; Tab. III). The parameter was further decreasing after paracentesis ($p < 0.05$).

Table II. Circadian rhythm of arterial blood pressure and heart rate in cirrhotic patients with ascites before and after paracentesis and healthy controls [mean(SEM)]
Tabela II. Okołodobowy rytm ciśnienia tętniczego krwi i częstości akcji serca u chorych na marskość wątroby z wodobrzuszem przed i po paracentezie oraz u osób zdrowych [średnia(SEM)]

Parameter		Investigated groups		
		liver cirrhosis with ascites (n = 22)		Controls (n = 19)
		before paracentesis	after paracentesis	
Systolic blood pressure (mmHg)	mesor	126.8 (0.6)	118.6 (0.6)†‡	127.3 (0.5)
	daytime/	130.5 (0.7)/	122.4 (0.7)/	134.3 (0.8)/
	nighttime	120.4 (1.1)	112.1 (1.0)	116.6 (1.0)
	Δ	10.1 (0.8)†	10.3 (0.8)†	17.8 (0.9)
	amplitude	6.5 (0.9)	6.4 (0.9)	8.1 (0.8)
	acrophase (h)	13.27 (0.45)†	13.6 (0.59)*	15.6 (0.45)
Diastolic blood pressure (mmHg)	mesor	82.3 (0.4)	74.4 (0.4)†‡	82.3 (0.4)
	daytime/	84.5 (0.5)/	77.0 (0.5)/	86.5 (0.4)/
	nighttime	78.2 (0.8)	70.8 (0.7)	75.1 (0.7)
	Δ	6.2 (0.6)†	5.9 (0.5)†	11.5 (0.5)
	amplitude	4.7 (0.6)	4.1 (0.6)	5.6 (0.5)
	acrophase (h)	12.63 (0.49)*	13.40(0.51)	14.05(0.47)
Mean arterial pressure (mmHg)	mesor	97.1 (0.4)	89.1 (0.4)†‡	97.2 (0.4)
	daytime/	100.1 (0.5)/	92.0 (0.6)/	102.4 (0.5)/
	nightime	92.3 (0.9)	84.4 (0.8)	88.9 (0.8)
	ΔMAP%	7.6 (0.4)†	8.1 (0.5)†	13.2 (0.7)
	amplitude	5.3 (0.6)	4.9 (0.6)	6.4 (0.6)
	acrophase (h)	12.10 (0.49)*	12.53 (0.56)*	14.12 (0.47)
Heart rate (beats/min)	mesor	84.1 (0.4)†	78.1 (0.4)†‡	65.9 (0.4)
	daytime/	86.2 (0.6)/	79.2 (0.5)/	69.1 (0.5)/
	nighttime	80.5 (0.8)	76.2 (0.6)	60.5 (0.6)
	Δ	5.6 (0.6)†	3.1 (0.6)†	8.7 (0.5)
	amplitude	3.8 (0.6)	3.9 (0.6)	5.3 (0.6)
	acrophase (h)	14.53 (0.58)	14.57 (0.56)	13.03 (0.53)

Mesor = a rhythm-adjusted mean; amplitude = one-half of the difference between the peak and nadir of rhythm; acrophase = the lag from a reference time to the crest time of the best fitting cosine curve; Δ = difference between daytime and nighttime; ΔMAP% = percentage changes of nocturnal mean arterial pressure to daily mean arterial pressure; *p < 0.05; †p < 0.001 vs. control group; ‡p < 0.001 vs. before paracentesis

A positive correlation was found between renin and aldosterone concentrations: in control group ($r = 0.77$; $p < 0.001$), in normotensive cirrhotic patients before paracentesis ($r = 0.82$; $p < 0.001$) and after paracentesis ($r = 0.47$; $p < 0.05$). Significant correlations between MELD score and reninemia ($r = 0.47$; $p < 0.05$) as well as aldosterone/renin ratio ($r = -0.47$; $p < 0.05$) were showed in cirrhotic patients before paracentesis. Increases in reninemia and aldosteronemia that occurred after paracentesis were covariable ($r = 0.61$; $p < 0.01$).

Table III. Hemodynamic parameters and reninemia and aldosteronemia in cirrhotic patients with ascites before and after paracentesis and healthy controls [mean (SEM)]
Tabela III. Wskaźniki hemodynamiczne, reninemia i aldosteronemia u chorych na marskość wątroby z wodobrzuszem przed i po paracentezie oraz u osób zdrowych [średnia (SEM)]

Parameter	Investigated groups		
	liver cirrhosis with ascites (n = 22)		controls (n = 19)
	before paracentesis	after paracentesis	
Systolic blood pressure (mmHg)	129.4 (0.7)	121.8 (0.6)†‡	132.5 (0.5)
Diastolic blood pressure (mmHg)	83.7 (0.5)	76.7 (0.5)†‡	84.6 (0.4)
Heart rate (beats/min)	88.4 (0.3)†	81.2 (0.4)†‡	68.7 (0.4)
Cardiac output (L/min)	7.4 (0.4)*	7.1 (0.6)	5.9 (0.3)
Systemic vascular resistance (mm Hg x min/mL)	952.4 (70.6)†	969.0 (90.1)§	1382.2 (79.8)
Plasma renin level (pg/mL)	128.3 (41.2)†	182.3 (43.4)†$	12.0 (3.7)
Serum aldosterone level (pg/mL)	498.0 (79.1)*	592.5 (71.7)§	300.0 (48.8)
Aldosterone/renin ratio	16.8 (4.2))†	10.7 (3.2))†$	40.7 (6.3)

*p < 0.05; §p < 0.01; †p < 0.001 vs. control group; $p < 0.05; ‡p < 0.001 vs. before paracentesis

DISCUSSION

The main aim of this study was to examine the circadian rhythm variability of arterial blood pressure in normotensive cirrhotic patients with tense ascites, before and after single paracentesis. A significantly smaller reduction of systolic and diastolic blood pressure has been observed at night in these patients in comparison with the control group, what suggests occurrence of non-dipping phenomenon in liver cirrhosis. Decreased differences between mean values of blood pressure during day and night persisted also after 24 hours from the paracentesis of 5 liters of fluid. Other studies showed that awake-asleep variation of blood pressure in hypotensive cirrhotic patients was also lower than in the controls [15,16]. Reduced awake-asleep variation of blood pressure and HR may be associated with impaired autonomic nervous system activity and has already been described in cirrhotic patients [22,23]. Moreover, it stems from the literature that circadian rhythm disorders of some hemodynamic parameters, such as HR, CO and portal blood flow [6,24], occurred in liver cirrhosis and could influence modification of day-night blood pressure rhythm. Author's own research revealed significantly smaller reduction of blood pressure at night than during the day in circadian variability of MAP rhythm in normotensive cirrhotic patients both before and after single paracentesis, respectively: 7.6% and 8.1%; in the compared control group the reduction was 13.2%. The similar results were obtained by Carl et al. [13], who proved that in cirrhotic patients with ascites MAP decreased by 7% from day to night. These observations make it possible to conclude that cirrhotic patients were non-dippers. Other authors, who had observed in circadian arterial blood pressure rhythm of cirrhotic patients with or without ascites smaller differences between pressures during the day and at night than in subjects with a negative history of liver and cardiovascular diseases, reached similar conclusions [15,16,17]. Pathomechanism of non-dipping blood pressure profile is not fully known yet, however, this phenomenon has occurred in excessive extracellular fluid volume, hyperaldosteronism and disturbances of the autonomic nervous system [25]. In our study, it should be emphasized that single paracentesis has led to a decrease in systolic and diastolic blood pressure, probably in a volume mechanism, and it also should be noted that no albumin was applied after paracentesis. Reduction of arterial blood pressure was observed immediately after paracentesis [12] and after the lapse of 24 or 48 hours [13,14] in cirrhotic patients with tense ascites. Additionally, there were no cases of post-paracentesis circulatory dysfunction in any of the examined patients. Another observation showed that the reduction of ascites in approximately 5.6 liters in hypotensive cirrhotic patients has not led to the decrease in systolic and diastolic blood pressure [26], probably because 8 g albumin infusion was used for every liter of reduced fluid.

In author's own research, cirrhotic patients were characterized by rapid HR that was significantly reduced after paracentesis, but did not reach values of the observed controls. HR was reduced less significantly at night in cirrhotic patients than in healthy subjects. Maintained elevated values of HR at nighttime during diurnal rhythm in cirrhotic patients were also demonstrated by another study [6]. Decreased amplitude in HR day-night variability in cirrhotic patients is probably caused by sympathetic and parasympathetic nervous system imbalances with an increase in sympathetic nervous system activity [22].

Cosinor analysis of blood pressure circadian rhythm showed that amplitudes of SBP, DPB, MAP and HR in examined cirrhotic patients, before and after single paracentesis, did not differ in comparison with the group of healthy subjects. Mesor values of arterial blood pressure components in normotensive cirrhotic patients before paracentesis and in controls were comparable. As a consequence of ascites reduction by means of paracentesis, mesor values of SBP, DPB, MAP and HR decreased. Demonstrating that acrophase of arterial blood pressure components has occurred 85–140 minutes earlier in cirrhotic patients before paracentesis than in controls should be emphasized. This shift was reduced to 39–120 minutes due to ascites reduction. Mechanism of this phenomenon is unknown.

Significant increase in CO value and a decrease in SVR were demonstrated in cirrhotic patients, what corresponded with results obtained by Henriksen et al. [1] in normotensive cirrhotic patients in Child-Pugh class B and C. Parameters did not change significantly after paracentesis, despite slowdown of HR, which determines CO. On the basis of obtained test results determining left ventricular ejection function one may conclude that this function has been intensified in cirrhotic patients with ascites and remained this way after singular drainage of 5 liters of ascetic fluid from abdominal. Peltekian et al. [27] also did not observe any changes in cardiac index after 48 h from single 5 liters paracentesis without albumin infusion in cirrhotic patients with ascites resistant to diuretics. Significant changes in peripheral haemodynamics, which are characterized mainly by hyperkinetic circulation, occur in liver cirrhosis [1]. A key role in mechanism of this phenomenon is to be played by dilatation of vascular bed, which in turn leads to rapid HR and increase in CO, i.e. changes that have been demonstrated in the examined patients. A reduction of SVR, typical for hyperkinetic circulation, was observed in these patients.

Comparison of healthy subjects with patients suffering from liver cirrhosis revealed that the latter ones had increased plasma renin concentration and aldosteronemia as well as reduction of aldosterone/renin ratio. Other authors obtained similar results and showed an increase in plasma renin and aldosterone concentration in cirrhotic patients with ascites [4,28]. Further significant increase in reninemia and a decrease in aldosterone/renin ratio values as well as clear tendency towards hyperaldosteronemia were observed as a consequence of reduction of ascites with approximately 5 liters. Nasr et al. [14] described almost twofold increase in plasma renin activity during the 6^{th} day after drainage of approximately 10 liters of ascetic fluid from abdominal cavity of patients with decompensated liver cirrhosis; similarly, Vila et al. [5] demonstrated an increase in plasma renin activity and aldosteronemia at the 6^{th} day after paracentesis in cirrhotic patients with effective hypovolemia. Observed reninemia and aldosteronemia following paracentesis are probably connected with reduction of effective circulating volume in compensatory mechanism. It should be noted that similarly to healthy subjects, in cirrhotic patients before and after paracentesis a highly positive correlation between aldosteronemia and reninemia occurred, while gains in concentration of these hormones after reduction of ascites were covariable. It means that feedback between renin and aldosterone release was maintained in decompensated liver cirrhosis. However, a decrease in aldosterone/renin ratio in cirrhotic patients could support weakened production of aldosterone. This phenomenon indicated dissociation of renin-aldosterone nexus and was independent of fluid reduction in abdominal cavity. One could assume that this dissociation was connected with disturbance of a stage of renin-aldosterone pathway, e.g. deficiency of angiotensinogen, whose synthesis was lowered in patients with decompensated liver cirrhosis [4,29] and angiotensinogen mRNA expression decreased in cirrhotics animals [30]. Correlation of renin-aldosterone system with the level of liver failure may be supported by covariability between MELD score and reninemia (positive correlation) and aldosterone/renin ratio (negative correlation), presented in our study.

Covariability of arterial blood pressure and the examined hormones was not shown during the study of associations between values of arterial blood pressure components, reninemia and aldosteronemia. Similar results were obtained by Tzamouranis et al. [17], who did not observe correlations between serum renin and aldosterone concentration and mean circadian systolic and diastolic blood pressure in patients with liver cirrhosis and ascites. It could be assumed that both renin and aldosterone do not influence significantly the circadian arterial blood pressure in normotensive patients with decompensated liver cirrhosis. However, confirmation of this assumption would require more in-depth studies, at least regarding the simultaneous determination of arterial blood pressure circadian rhythm and concentration of RAAS components.

CONCLUSION

Arterial blood pressure circadian rhythm in normotensive patients with decompensated liver cirrhosis with ascites is characterized by lowered decrease at nighttime that suggests occurrence of non-dipping phenomenon. Reduction of ascites in patients with decompensated liver cirrhosis leads to reduction of arterial blood pressure and does not eliminate the non-dipping phenomenon in its day-night rhythm. In normotensive cirrhotic patients with ascites before and after single paracentesis, a dissociation of renin-aldosterone nexus occurs.

Conflict of interest

The authors declare no conflicts of interests.

Author's contribution

Study design – Cz. Marcisz, A. Orzeł
Data collection – A. Kowalik-Kabat, J. Balicka, A. Olejko
Data interpretation – Cz. Marcisz, A. Orzeł
Statistical analysis – H. Kulik
Manuscript preparation – Cz. Marcisz, A. Orzeł
Literature research – Cz. Marcisz, A. Kowalik-Kabat, H. Kulik

REFERENCES

1. Henriksen J.H., Fuglsang S., Bandtsen F., Møller S. Arterial hypertension in cirrhosis: arterial compliance, volume distribution, and central haemodynamics. Gut 2006; 55: 380–387.

2. Meng H.C., Lin H.C., Tsai Y.T. Relationships between the severity of cirrhosis and haemodynamic values in patients with cirrhosis. J. Gastroenterol. Hepatol. 1994; 9: 148–153.

3. Bernardi M., Trevisani F., Santini C., De Palma R., Gasbarrini G. Aldosterone related blood volume expansion in cirrhosis before and during the early phase of ascites formation. Gut 1983; 24: 761–766.

4. Kuiper J.J., Boomsma F., van Buren H., de Man R., Danser A.H.J., van den Meiracker A.H. Components of the renin-angiotensin-aldosterone system in plasma and ascites in hepatic cirrhosis. Eur. J. Clin. Invest. 2008; 38: 939––944.

5. Vila M.C., Solà R., Molina L., Andreu M., Coll S., Gana J., Marquez J., Palá J., Bory F., Pons S., Szescielinski L., Jimenez W. Hemodynamic changes in patients developing effective hypovolemia after total paracentesis. J. Hepatol. 1998; 28: 639–645.

6. Genesca J., Segura R., Gonzalez A., Catalan R., Marti R., Torregrosa M., Cereto F., Martinez M., Esteban R., Guardia J. Nitric oxide may contribute to nocturnal hemodynamic changes in cirrhotic patients. Am. J. Gastroenterol. 2000; 95: 1539–1544.

7. Henriksen J.H., Møller S., Schifter S., Bendtsen F. Increased arterial compliance in decompensated cirrhosis. J. Hepatol. 1999; 31: 712–718.

8. Kojima H., Tsujimoto T., Uemura M., Takaya A., Okamoto S., Ueda S., Nishio K., Miyamoto S., Kubo A., Minamino N., Kangawa K., Matsuo H., Fukui H. Significance of increased plasma adrenomedullin concentration in patients with cirrhosis. J. Hepatol. 1998; 28: 840–846.

9. Sharma P., Kumar A., Jha S., Mishra S.R., Sharma B.C., Sarin S.K. The haemodynamic response to propranolol in cirrhosis with arterial hypertension: a comparative analysis with normotensive cirrhotic patients. Aliment. Pharmacol. Ther. 2010; 32: 105–112.

10. Winkler C., Hobolth L., Krag A., Bendtsen F., Møller S. Effect of treatment with β-blocker and aldosterone antagonist on central and peripheral haemodynamics and oxygenation in cirrhosis. Eur. J. Gastroenterol. Hepatol. 2011; 23: 334–342.

11. Rajesh P.P., Srinivasan R., Jayanthi V. Prevalence of arterial hypertension in cirrhosis of liver. Saudi. J. Gastroenterol. 2009; 15: 65–66.

12. Cabrera J., Falcon L., Gorriz E., Pardo M.D., Granados R., Quinones A., Maynar M. Abdominal decompression plays a major role in early postparacentesis haemodynamic changes in cirrhotic patients with tense ascites. Gut 2001; 48: 384–389.

13. Carl D.E., Ghosh S., Cheng J., Gehr T.W., Stravitz R.T., Sanyal A. Post-paracentesis circulatory derangements are related to monocyte activation. Liver Int. 2014; 34: 1001–1007.

14. Nasr G., Hassan A., Ahmed S., Serwah A. Predictors of large paracentesis induced circulatory dysfunction in patients with massive hepatic ascites. J. Cardiovasc. Dis. Res. 2010; 1: 136–144.

15. Møller S., Christensen E., Henriksen J.H. Continuous blood pressure monitoring in cirrhosis. Relations to splanchnic and systemic haemodynamics. J. Hepatol. 1997; 27: 284–294.

16. Møller S., Wiinberg N., Henriksen J.H. Noninvasive 24-hour ambulatory arterial blood pressure monitoring in cirrhosis. Hepatology 1995; 22: 88–95.

17. Tzamouranis D.G., Alexopoulou A., Dourakis S.P., Stergiou G.S. Relationship of 24-hour ambulatory blood pressure and heart rate with markers of hepatic function in cirrhotic patients. BMC Gastroenterology 2010; 10: 143–150.

18. Pugh R.N., Murray-Lyon I.M., Dawson J.L., Pietroni M.C., Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br. J. Surg. 1973; 60: 646–649.

19. Wiesner R.H., McDiarmid S.V., Kamath P.S., Edwards E.B., Malinchoc M., Kremers W.K., Krom R.A., Kim W.R. MELD and PELD: application of survival models to liver allocation. Liver Transpl. 2001; 7: 567–580.

20. Pöge U., Gerhardt T., Stoffel-Wagner B., Klehr H.U., Sauerbruch T., Woitas R.P. Calculation of glomerular filtration rate based on cystatin C in cirrhotic patients. Nephrol. Dial. Transplant. 2006; 21: 660–664.

21. Manabe Y., Murakami T., Iwatsuki K., Narai H., Warita H., Hayashi T., Shoji M., Imai Y., Abe K. Nocturnal blood pressure dip in CADASIL. J. Neurol. Sci. 2001; 193: 13–16.

22. Lazzeri C., La Villa G., Laffi G., Vecchiarino S., Gambilonghi F., Gentilini P., Franchi F. Autonomic regulation of heart rate and QT interval in nonalcoholic cirrhosis with ascites. Digestion 1997; 58: 580–586.

23. Trevisani F., Sica G., Mainquà P., Santese G., De Notariis S., Caraceni P., Domenicali M., Zacà F., Grazi G.L., Mazziotti A., Cavallari A., Bernardi M. Autonomic dysfunction and hyperdynamic circulation in cirrhosis with ascites. Hepatology 1999; 30: 1387–1392.

24. Alvarez D., Golombek D., Lopez P., de las Heras M., Viola L., Sanchez S., Kolker M., Mastai R. Diurnal fluctuations of portal and systemic hemodynamic parameters in patients with cirrhosis. Hepatology 1994; 20: 1198–1203.

25. Birkenhäger A.M., van den Meiracker A.H. Causes and consequences of a non-dipping blood pressure profile. Neth. J. Med. 2007; 65: 127–131.

26. Kogan J., Turkot S., Golzman B., Oren S. Small artery compliance in cirrhotic patients during total paracentes. Isr. Med. Assoc. J. 2005; 7: 233––236.

27. Peltekian K.M., Wong F., Liu P.P., Logan A.G., Sherman M., Bendis L.M. Cardiovascular, renal, and neurohumoral responses to single large-volume paracentesis in patients with cirrhosis and diuretic-resistant ascites. Am. J. Gastroenterol. 1997; 92: 394–399.

28. Møller S., Bendtsen F., Henriksen J.H. Determinants of the renin-angiotensin-aldosterone system in cirrhosis with special emphasis on the central blood volume. Scand. J. Gastroenterol. 2006; 41: 451–458.

29. Plouin P.F., Cudek P., Arnal J.F., Guyene T.T., Corvol P. Immunoradiometric assay of active renin versus determination of plasma renin activity in the clinical investigation of hypertension, congestive heart failure and liver cirrhosis. Horm. Res. 1990; 34: 138–141.

30. Lu P., Liu H., Yin H., Yang L. Expression of angiotensinogen during hepatic fibrogenesis and its effect on hepatic stellate cells. Med. Sci. Monit. 2011; 17: BR248–256.