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THE EFFECTIVENESS OF CHRONOTHERAPY IN HYPERTENSIVE PATIENTS WITH AN INSUFFICIENT DEGREE OF SLEEP-TIME SYSTOLIC BLOOD PRESSURE DECLINE

Petrenko O. V., Yabluchansky M. I.
V. N. Karazin Kharkiv National University, Kharkiv, Ukraine

Blood pressure (BP) circadian rhythm violation, manifested as an insufficient degree of its sleep-time relative decline, is an independent cardiovascular risk factor. The main method of the correction is chronotherapeutic approach, when at least one antihypertensive drug is taken at bedtime. However, most researchers focus on normalizing the daily profile of systolic blood pressure (SBP) and do not pay enough attention to changes in the daily profile of diastolic blood pressure (DBP) and blood pressure in general. The aim of the study was to evaluate the influence of the chronotherapeutic approach on the SBP and DBP levels and the DBP daily profile in hypertensive patients with an insufficient degree of sleep-time relative SBP decline. The study included 12 patients with arterial hypertension (AH) with an insufficient degree of sleep-time relative SBP decline. Participants were divided into two groups: group 1 included patients who take at least one antihypertensive drug at bedtime, group 2 – patients who take all antihypertensive drugs in the morning. All patients underwent 24-hour blood pressure monitoring using the computer system «Cardiosens» (KhAI Medica, Ukraine, with the oscillometric method of BP measuring) when enrolling in the study and after 3 months. The type of SBP and DBP diurnal profile, the mean values of SBP, DBP and hyperbaric indices were determined and compared between groups 1 and 2 at each visit, as well as within groups between visits. The results showed that the SBP daily profile normalization in patients with insufficient degree of sleep-time relative SBP decline from group 2 was achieved only in 11 % of cases, and in group 1 SBP and DBP daily profile normalized in 1/3 patients. In some patients from group 2 SBP and DBP daily profile converted into the overdipper type, while in group 1 overdippers did not appear at the end of the study. It was concluded that conversion of daily DBP profile to overdipper as a consequence of bedtime drug administration requires a review of the accepted treatment strategy.

KEY WORDS: arterial hypertension, chronotherapy, daily blood pressure profile, nondipper

ЕФЕКТИВНІСТЬ ХРОНОТЕРАПИИ ГІПЕРТОНІЧНОЇ ХВОРОБИ У ПАЦІЄНТІВ З НЕДОСТАТНІМ СТУПЕНЕМ НІЧНОГО ЗНИЖЕННЯ СИСТОЛІЧНОГО АРТЕРІАЛЬНОГО ТИСКУ

Петренко О. В., Яблучанський М. І.
Харківський національний університет імені В. Н. Каразіна, м. Харків, Україна

Порушення добового ритму артеріального тиску (АТ), що проявляється у недостатній мірі його нічного зниження, є незалежним чинником ризику серцево-судинних захворювань. Основним методом його корекції є хронотерапевтичний підхід, коли хоча б один антигіпертензивний препарат призначається на ніч. Однак більшість дослідників фокусуються на нормалізації добового профілю систолічного артеріального тиску (САТ) і не приділяють достатньої уваги змінам добового профілю діастолічного АТ (ДАТ) і АТ в цілому. Метою дослідження було оцінити вплив хронотерапевтичного підходу на рівень САТ і ДАТ та добовий профіль ДАТ у пацієнтів з гіпертонічною хворобою (ГХ) з недостатнім ступенем нічного зниження САТ. У дослідження увійшли 12 хворих на ГХ з недостатнім ступенем нічного зниження САТ. Учасники були розділені на дві групи: до групи 1 увійшли пацієнти, що приймають хоча б один гіпотензивний препарат на ніч, в групу 2 – пацієнти, що приймають все гіпотензивні препарати вранці. Всім пацієнтам проводилося добове моніторування АТ з використанням комп'ютерної системи «Кардіосенс» (ХАІ Медика, Україна, з осцилометричним методом вимірювання АТ) на початку дослідження та через 3 міс. Визначали тип добового профілю САТ і ДАТ, середні значення САТ, ДАТ та показників навантаження підвищеним тиском і порівнювали між собою в групах 1 та 2 на кожному візиті, а також всередині груп між візитами. Результати показали, що нормалізація добового профілю САТ у пацієнтів з недостатнім ступенем його нічного зниження з групи 2 було досягнуто лише в 11 % випадків, а в групі 1 добовий профіль САТ і ДАТ нормалізувався у 1/3 пацієнтів. В групі 2 у частині пацієнтів добовий профіль САТ і ДАТ

перейшов в тип овердіпер, в той час як в групі 1 овердіперів по закінченню дослідження не виявилося. Зроблено висновки, що зміна типу добового профілю ДАТ на овердіпер як наслідок призначення гіпотензивних на ніч вимагає перегляду прийнятої лікувальної стратегії.

КЛЮЧОВІ СЛОВА: гіпертонічна хвороба, хронотерапія, добовий профіль артеріального тиску, нондіпер

ЭФФЕКТИВНОСТЬ ХРОНОТЕРАПИИ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНИ У ПАЦИЕНТОВ С НЕДОСТАТОЧНОЙ СТЕПЕНЬЮ НОЧНОГО СНИЖЕНИЯ СИСТОЛИЧЕСКОГО АРТЕРИАЛЬНОГО ДАВЛЕНИЯ

Петренко Е. В., Яблучанский Н. И.
Харьковский национальный университет имени В. Н. Каразина, г. Харьков, Украина

Нарушение суточного ритма артериального давления (АД), проявляющееся в недостаточной степени его ночного снижения, является независимым фактором риска сердечно-сосудистых заболеваний. Основным методом его коррекции является хронотерапевтический подход, когда хотя бы один антигипертензивный препарат назначается на ночь. Однако большинство исследователей фокусируются на нормализации суточного профиля систолического АД (САД) и не уделяют достаточного внимания изменениям суточного профиля диастолического АД (ДАД) и АД в целом. Целью исследования было оценить влияние хронотерапевтического подхода на уровень САД и ДАД и суточный профиль ДАД у пациентов с гипертонической болезнью (ГБ) с недостаточной степенью ночного снижения САД. В исследование вошли 12 больных ГБ с недостаточной степенью ночного снижения САД. Участники были разделены на две группы: в группу 1 вошли пациенты, принимающие хотя бы один гипотензивный препарат на ночь, в группу 2 – пациенты, принимающие все гипотензивные препараты утром. Всем пациентам проводилось суточное мониторирование АД с использованием компьютерной системы «Кардиосенс» (ХАИ Медика, Украина, с осцилло-метрическим методом измерения АД) при включении в исследование и через 3 мес. Определяли тип суточного профиля САД и ДАД, средние значения САД, ДАД и показателей нагрузки повышенным давлением и сравнивали между собой в группах 1 и 2 на каждом визите, а также внутри групп между визитами. Результаты показали, что нормализация суточного профиля САД у пациентов с недостаточной степенью его ночного снижения из группы 2 была достигнута лишь в 11 % случаев, а в группе 1 суточный профиль САД и ДАД нормализовался у 1/3 пациентов. В группе 2 у части пациентов суточный профиль САД и ДАД перешёл в тип овердиппер, в то время как в группе 1 овердипперов по окончанию исследования не оказалось. Сделаны выводы, что изменение типа суточного профиля ДАД на овердиппер как следствие назначения гипотензивных препаратов на ночь требует пересмотра принятой лечебной стратегии.

КЛЮЧЕВЫЕ СЛОВА: гипертоническая болезнь, хронотерапия, суточный профиль артериального давления, нондиппер

INTRODUCTION

With the introduction of ambulatory blood pressure monitoring (ABPM) into clinical practice, the daily variability of blood pressure (BP) and its changes become important in the management of patients with arterial hypertension (AH) [1–3]. The BP circadian rhythm is considered normal, when its daily values exceed the night ones by 10–20 % [4].

In 1988, O'Brien and co-authors first showed that the violation of the BP circadian rhythm, manifested in an insufficient degree of its nightly decline, increases the risk of stroke in patients with AH [5]. This type of BP profile was called «nondipper». Further studies conducted in this direction confirmed that an insufficient reduction in systolic BP (SBP) at night is an independent risk factor for cardiovascular diseases [3]. According to the data of different authors, the frequency of occurrence the «nondipper» type of BP profile among patients with AH is about 50 % [6–7].

The main method of correction of this circadian rhythm disruption is the chronotherapeutic approach, when at least one antihypertensive drug in a full daily dose is prescribed at bedtime [8]. It is believed that the shift of the intake of antihypertensive drugs of all major groups from morning to evening time allows restoring the normal daily BP rhythm in 30–60 % of «nondippers» according to the data of different authors [8–9]. However, most researchers focus on the normalization of SBP daily profile and do not pay enough

attention to changes in diastolic blood pressure profile [9].

OBJECTIVE

To assess the impact of the chrono-therapeutic approach on the level of SBP and ВИЗ daily profile in patients with AH with insufficient degree of sleep-time relative SBP decline.

MATERIALS AND METHODS

The research was carried out within the framework of the research work «Pharmacological and interventional approaches to the treatment of patients with cardiac arrhythmias, arterial hypertension», state registration number 0116U000973.

In the settings of the outpatient clinic № 24 in Kharkiv, 44 patients with AH aged from 41 to 78 years were examined. For further analysis, patients with an insufficient degree of sleep-time relative SBP decline (< 10 %) according to ABPM were selected.

The study included 12 people with the «nondipper» type of SBP daily profile – 7 women (58 %) and 5 men (42 %). The first stage of AH was diagnosed in 1 patient (8 %), the second – in 8 (67 %), the third – in 3 (25 %). The first degree of AH was diagnosed in 7 patients (58 %), the second – in 2 (17 %). Three patients (25 %) had controlled AH, with preserving the target values of SBP and DBP throughout the 24 hours. Nocturnal hypertension was diagnosed in 9 cases (75 %).

Participants were divided into two groups. Group 1 included 3 patients (25 %) taking at least one antihypertensive drug at bedtime, group 2 included 9 patients (75 %) taking all antihypertensive drugs in the morning. To achieve target BP levels, patients, if necessary, underwent correction of antihypertensive therapy – increasing the dose, replacing or adding drugs. The regimen of antihypertensive drugs intake was not changed.

Exclusion criteria were secondary arterial hypertension, hemodynamically significant valvular heart disease, cardiomyopathy of any origin, chronic heart failure of III clinical stage or IV functional class by NYHA, any acute conditions (infections, trauma, operations) during the previous 3 months, chronic diseases in decompensated stage or exacerbation, oncological diseases, as well as any circumstances that make it difficult to perform ABPM.

All patients underwent ABPM when included in the study – 1 visit, and after 3 months – 2 visit. The monitoring was carried out using the computer system «Cardiosens» (KhAI Medica, Ukraine) with an oscillometric method of BP measurement. The monitoring was performed in the conditions of a typical patient day, with the preservation of domestic physical and psychoemotional loads. The cuff was placed on the non-dominant hand. According to Ambulatory Blood Pressure Monitoring International Recommendations 2013 [4], BP was measured with an interval of 15 minutes during the period of awake and 30 minutes during the sleep time. Periods of the day and night was defined on the basis of the patient's diary. When assessing ABPM data, in accordance with Ambulatory Blood Pressure Monitoring International Recommendations 2013 [4], manual data extraction was performed – the following measurements were excluded from the analysis: SBP > 250 or < 70 mm Hg; DBP > 150 or < 40 mm Hg; pulse pressure > 150 or < 20 mm Hg; heart rate > 200 or < 20 per minute.

The results of ABPM were excluded from analysis in the following cases: ≥ 30 % of invalid measurements; absence of BP measurements for 2 hours or more; unusual for the patient daily activity during monitoring; a night sleep period of less than 6 or more than 12 hours [4].

The degree of relative sleep-time BP decline was calculated using the formula: *(100 × [mean daily BP – mean BP] / mean daily BP).*

Depending on the value of this ration the following types of daily BP profile were defined: «dipper» - physiological decrease in BP during the night – sleep-time relative BP decline 10–20 %; «overdipper» – an excessive fall in BP at night, sleep-time relative BP decline > 20 %; «nondipper» – the lack of BP reduction at night, sleep-time relative BP decline < 10 %; «night-peaker» - night-time BP more than during daily activity, sleep-time relative BP decline < 0 [4].

The mean values of SBP, DBP and hyperbaric indices for SBP and DBP were determined for 24 hours and periods of day and night and compared in groups 1 and 2 at each visit, as well as within groups between visits.

For each ABPM parameter the arithmetic mean (M), the median (Me), and the standard deviation (Sd) were determined. Proportions of

types of the daily BP profile were determined in percent (P).

A comparison of the data obtained in groups 1 and 2 at each stage of the study was performed using the unpaired Student's t-test for parameters with normal distribution and the Mann-Whitney U-test for free-distributed parameters. Comparison of data obtained at the beginning and at the end of the study in groups 1 and 2, and in general for all enrolled patients was performed using paired Student's t-test for parameters with normal distribution and Wilcoxon signed-rank test for parameters with a free distribution. To compare the proportions the angular transformation method with F-test was used.

RESULTS AND DISCUSSION

At the first visit, the mean sleep-time values of SBP and DBP exceeded the recommended threshold levels in both groups (Table 1), as well as the 24-h SBP mean in group 2 and 24-h DBP mean in group 1. The awake means of SBP and DBP remained within the normal range in both groups. The values of pulse pressure (PP) exceeded the recommended levels in both groups during all monitoring periods. The awake, sleep-time and daily mean values of the SBP and DBP time index (TI) were higher than normal in both groups, and all of them in both groups were higher at night than in daytime. The mean values of SBP and DBP hyperbaric index (HBI) exceeded recommended values during all monitoring periods in both groups.

It was noteworthy that the mean values of SBP, PP and SBP hyperbaric indices during all monitoring periods were higher in group 2, but mean values of DBP and DBP hyperbaric indices – in group 1.

The mean values of SBP and DBP sleep-time relative BP decline did not exceed 10 % in both groups, but were mostly reduced in group 2– both for SBP and DBP.

When comparing the studied indices of ABPM in the awake, sleep-time and 24-h periods no significant differences between the groups were seen (Table 1).

Table 1

ABPM indices in groups 1 and 2, visit 1

Monitoring periods	ABPM indices	Patients groups					
		group 1, n = 3			group 2, n = 9		
		M	Me	Sd	M	Me	Sd
24 hours	SBP, mm Hg	130	129	11.5	132	130	12.3
	DBP, mm Hg	81	83	7.2	75	73	9.7
	PP, mm Hg	49	46	9.5	56	57	7.0
	SBP TI, %	45	42	29.1	52	48	27.1
	DBP TI, %	44	46	28.5	29	29	22.0
	SBP HBI, mm Hg / h	134	89	143.0	178	146	149.8
	DBP HBI, mm Hg / h	97	109	84.1	68	51	63.4
Awake	SBP, mm Hg	131	130	12.1	133	128	12.8
	DBP, mm Hg	82	84	6.7	77	73	10.4
	PP, mm Hg	49	45	9.6	56	55	8.4
	SBP TI, %	40	31	31.6	45	29	30.5
	DBP TI, %	40	44	28.1	24	31	25.2
	SBP HBI, mm Hg / h	73	25	95.5	98	8	104.3
	DBP HBI, mm Hg / h	47	61	37.2	36	13	42.4
Sleep- time	SBP, mm Hg	126	126	10.0	129	131	11.2
	DBP, mm Hg	76	77	7.1	71	72	8.1
	PP, mm Hg	51	48	8.3	58	60	6.2
	SBP TI, %	53	61	27.0	65	65	29.1
	DBP TI, %	51	49	29.2	45	60	27.6
	SBP HBI, mm Hg / h	60	64	52.0	80	73	63.7
	DBP HBI, mm Hg / h	50	48	48.2	31	28	24.3
Sleep-time relative SBP decline,%		4	3	1.1	3	5	5.5
Sleep-time relative DBP decline,%		9	9	1.0	7	11	7.4

Notes: M – mean value, Me - median, Sd – standard deviation, SBP – systolic blood pressure, DBP – diastolic blood pressure, PP – pulse pressure, TI – time index, HBI – hyperbaric index

In group 1, all patients had a daily DBP profile nondipper. In group 2, frequencies of the daily DBP profiles dipper and nondipper were approximately the same. The overdipper daily profile at the first visit was not met in any of the groups (Table 3).

After 3 months all patients underwent repeated ABPM. Overall, we achieved a reduction of all ABPM parameters the target values of SBP and DBP for all monitoring periods, except sleep-time DBP values, which have been reduced, but did not normalize. Statistically significant differences at the level of $p < 0.05$ were achieved for awake, sleep-time and 24-h means of DBP, sleep-time SBP means and DBP HBI. Sleep-time relative SBP and DBP decline has improved as compared with the initial data, but they are still did not exceed 10 % (Table. 2).

Table 2

Comparison of the main ABPM indices at visits 1 and 2

Monitoring periods	ABPM indices	Visits					
		visit 1, n = 12			visit 2, n = 12		
		M	Me	Sd	M	Me	Sd
24 hours	SBP, mm Hg	131	130	11.6	128	127	9.2
	DBP, mm Hg	77	76	9.2	74 *	75	7.4
	PP, mm Hg	55	56	7.9	54	54	6.5
	SBP TI, %	50	45	26.4	42	38	25.8
	DBP TI, %	33	33	23.3	27	22	23.4
	SBP HBI, mm Hg / h	167	118	143.0	112	116	78.3
	DBP HBI, mm Hg / h	75	59	66.3	51	30	51.4
Awake	SBP, mm Hg	133	129	12.1	130	129	10.0
	DBP, mm Hg	78	79	9.7	75 *	76	7.8
	PP, mm Hg	54	55	8.9	54	54	7.9
	SBP TI, %	43	30	29.4	38	25	30.3
	DBP TI, %	28	23	25.7	23	19	20.8
	SBP HBI, mm Hg / h	92	29	98.5	58	30	58.7
	DBP HBI, mm Hg / h	39	26	39.8	27	20	23.7
Sleep- time	SBP, mm Hg	128	129	10.5	123 *	125	9.8
	DBP, mm Hg	72	73	7.9	68 *	67	8.4
	PP, mm Hg	56	57	7.2	54	53	6.4
	SBP TI, %	62	63	27.9	49	46	33.5
	DBP TI, %	47	54	26.7	41	35	36.7
	SBP HBI, mm Hg / h	75	69	59.3	54	60	45.8
	DBP HBI, mm Hg / h	36	38	30.4	25 *	8	32.2
Sleep-time relative SBP decline,%		3	4	4.7	5	6	8.2
Sleep-time relative DBP decline,%		8	10	6.4	9	11	8.9

*Notes: M – mean value, Me – median, Sd – standard deviation, SBP – systolic blood pressure, DBP – diastolic blood pressure, PP – pulse pressure, TI – time index, HBI – hyperbaric index; * p < 0.05*

At the second visit in group 1 daily and awake SBP and DBP target values were achieved, while sleep-time SBP and DBP means normalization was failed, and the average values of SBP over the night period did not change at all (tab. 4). Changes in the PP were insignificant – within 1–2 mm Hg. The hyperbaric indices decreased in comparison with the initial values, but did not restore to normal. A statistically significant decrease was achieved only for 24-h values of DBP TI at the level of $p < 0.05$. Awake mean values of SBP and DBP hyperbaric indices were able to decrease as close as possible to the recommended standards, and sleep-time DBP hyperbaric indices – to transfer to borderline values. The daily SBP and DBP profile succeeded to normalize in 1/3 patients (Table. 3).Mean values of sleep-time relative SBP and DBP decline decreased, to a greater extent for SBP (Table 4).

Table 3

BP daily profiles in groups 1 and 2 at the 2nd visit

Type of daily BP profile		Patients groups			
		group 1, n = 3		group 2, n = 9	
		visit 1	*visit 2*	*visit 1*	*visit 2*
SBP	**dipper**	-	33 %	-	11 %
	nondipper	100 %	67 %	100 %	78 %
	night-picker				
	overdipper	-	-	-	11 %
DBP	**dipper**	-	33 %	56 %	56 %
	nondipper	100 %	67 %	44 %	33 %
	night-picker				
	overdipper	-	-	-	11 %

Table 4

ABPM indices in groups 1 and 2, visit 2

Monitoring periods	ABPM indices	Patients groups					
		group 1, n = 3			group 2, n = 9		
		M	Me	Sd	M	Me	Sd
24 hours	**SBP, mm Hg**	126	127	1,2	129	131	10,7
	DBP, mm Hg	78	76	4.0	73[i]	73	7.9
	PP, mm Hg	48	49	3,6	57*	55	5,8
	SBP TI, %	29	78	15,1	47	49	27,9
	DBP TI, %	34•	38	29,5	25	22	22,5
	SBP HBI, mm Hg / h	78	37	58,1	124	128	83,7
	DBP HBI, mm Hg / h	67	107	66,9	46	28	49,0
Awake	**SBP, mm Hg**	126	58	2,5	131	130	11,3
	DBP, mm Hg	80	126	3,8	74[i]	74	8,4
	PP, mm Hg	47	47	4,5	57*	55	7,2
	SBP TI, %	17	16	3,2	45	46	32,4
	DBP TI, %	25	27	22,0	22	14	21,8
	SBP HBI, mm Hg / h	19	19	9,1	71	35	62,9
	DBP HBI, mm Hg / h	27	28	25,3	26	19	24,7
Sleep- time	**SBP, mm Hg**	126	129	8,5	122[i]	121	10,5
	DBP, mm Hg	74	71	8,3	66	65	8.0
	PP, mm Hg	52	49	5,2	55	53	6,8
	SBP TI, %	51	67	40,7	48	43	33,6
	DBP TI, %	49	52	44,0	38	12	36,4
	SBP HBI, mm Hg / h	60	88	49,8	53	36	47,4
	DBP HBI, mm Hg / h	39	30	42,0	20	2	29,6
Sleep-time relative SBP decline, %		1	- 4	8,5	7	6	7,9
Sleep-time relative DBP decline, %		8	8	6,8	10	11	9,8

Notes: M – mean value, Me – median, Sd – standard deviation, SBP – systolic blood pressure, DBP – diastolic blood pressure, PP – pulse pressure, TI – time index, HBI – hyperbaric index; *p < 0,05 comparing groups 1 and 2 at visit 2, •p < 0,05 comparing visits 1 and 2 of group 1, p < 0,05 comparing visits 1 and 2 of group 2

In group 2, at the second visit, it was possible to reduce and achieve the target values of SBP and DBP during all monitoring periods, except the mean sleep-time values of SBP. Concerning 24-h and awake values of DBP and sleep-time SBP values a statistically significant decrease was achieved at the level of $p < 0.05$. Mean sleep-time PP values decreased in comparison with baseline, but did not return to normal, but, on the contrary, daily and awake PP means increased, albeit insignificantly. Also, it was possible to reduce the hyperbaric indices. DBP TI and HBI, as well as SBP TI succeeded to transferee to the borderline values during all monitoring periods, but SBP HBI even decreased in comparison with the baseline, but remained high throughout the 24 hours (Table 4). The sleep-time relative SBP and DBP decline increased, and for DBP it was reached the level of 10 %, which already corresponds to the dipper type. The number of SBP non-dippers in group 2 decreased by 22 % and DBP non-dippers by 11 % (Table 3).

Thus, it was possible to achieve the target SBP and DBP 24-h and awake means in both groups, while sleep-time SBP and DBP mean values were failed to normalize in group 1. In group 2 the sleep-time SBP and DBP mean values decreased, although we achieved target values only for DBP (Table 4). A more pronounced decrease in sleep-time relative SBP and DBP decline was found in group 2. In group 1 the 24-h SBP values were reduced to a greater extend then in group 2.

It was notable the PP changes. In group 1, at the second visit, there was a PP decrease in daytime and an increase at night, in group 2, on the contrary, an increase in daytime and a decrease in night. When comparing the PP levels in groups 1 and 2 on the second visit, the differences were statistically significant at the level of $p < 0.05$ (Table 4). In general, in group 1, PP decreased compared to baseline, and in group 2 increased.

In group 2 at the second visit it was possible not only to reduce the main ABPM indices, but also to achieve lower values in comparison with group 1 (Table 4).

Sleep-time relative SBP and DBP decline succeeded to increase and made close to dipper profile only in group 2, while in group 1, on the contrary, it increased, aspiring to an even more unfavorable night-picker type of daily BP profile. Although normalization of the SBP and DBP daily profile was achieved in a larger proportion of patients in group 1, these differences were statistically insignificant (Table 3–4).

It is believed that in patients with AH, the administration of at least one antihypertensive drug at bedtime leads to more pronounced BP decrease at night and contributes to the daily profile normalization [8–9]. Hermida et al., 2005, 2007 [10–11] provide data on the daily SBP profile normalization in 75 % of patients with AH in those who takes drugs at bedtime. But it does not take into account that as a result of antihypertensive therapy DBP is also reduced, and this both BP indices are important in management and prognosis in patients with AH [12].

In our study, the normalization of SBP daily profile in patients with an insufficient sleep-time relative SBP decline from group 2 was achieved only in 11 % of cases. Patients of group 1 had better results – the daily profile of SBP and DBP was normalized in 1/3 of patients. Also, at the end of the study, it was found that in group 2 in a part of the patients the daily profile of both SBP and DBP converted to the overdipper type, while in the group 1 there were no overdippers at the end of the study.

In accordance with these results, the question of antihypertensive drugs administration at bedtime in hypertensive patients with SBP non-dipper profile should be considered open, since in some cases this leads not to normalization of the daily BP profile, but to its transition to the overdipper type.

The data obtained in our study show that the chronotherapeutic approach in management of patients with AH should not consist in the strict antihypertensive drugs administration at bedtime, but be based on a thorough evaluation of the patient's chronoprofile and the daily profile not only of the SBP, but the DBP also.

CONCLUSIONS

1. Hypotensive therapy in patients with AH with SBP nondipper profile irrespectively of the medication regimen leads not only to a decrease in BP, but also to the normalization of its daily profile.

2. The use of antihypertensive drugs at bedtime in such patients to a greater extent

reduces sleep-time BP, and morning administration – awake BP, and SBP daily profile normalization is better in patients, who takes antihypertensive drugs in the morning then at bedtime.

3. Transition of diurnal DBP profile into overdipper as a consequence of the bedtime antihypertensive drug administration requires revision of this treatment strategy.

PROSPECTS FOR FUTURE STUDIES

It seems advisable to study the administrating time effects on the daily DBP profile in hypertensive patients with an insufficient sleep-time relative DBP decline.

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