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Ambulatory blood pressure monitoring in essential hypertensive patients with acute ischaemic stroke

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Key words: *Essential Hypertension, Ischaemic Stroke, Ambulatory Blood Pressure Monitoring, Circadian index.*

Blood pressure (BP) has been identified as a risk factor for various health disorders, including stroke onsets. Hypertension is one of the crucial health problem among adult Ukrainian. Due to the importance of elevated BP in stroke causality, BP measurement remains critical. However, it is limited information about value in clinical practice of ambulatory blood pressure monitoring (ABPM) data in hypertensive patients with inadequately controlled BP with acute stroke compared with those individuals who has no vascular onset.

The aim of the study was to determine ABPM parameters in essential hypertensive patients with ischaemic hemisphere stroke.

Materials and methods. A total of 114 study participants were analyzed (mean age 62 (56;72) years, 40 % women). We divided them into two groups according to the level of 24-h systolic BP (SBP) and diastolic BP (DBP), and the results of clinical examination. The first group (n=83) were inadequately controlled essential hypertensive individuals with high systolic or/and diastolic BP level according to the ABMP results, and the second one (n=31) were EH patients with an acute hemispheric ischaemic stroke (IS). Diagnosis of stroke was confirmed with clinical examination and computed tomography scan or magnetic resonance imaging results, and ABPM was conducted in 4.2±2.3 days after the stroke onset.

Results. We had statistician difference ($p<0.001$) between groups of such parameters, as average SBP (diurnal, daytime, nighttime); diurnal pulse BP; SBP load ($p<0.05$); the diurnal AASI ($p<0.05$); circadian rhythm of DBP ($p<0.05$). No differences were found between the groups in morning surge calculated as speed and amplitude of the BP climbed in morning hours both for SBP (P=0.422 and P=0.395 respectively) and DBP (P=0.860 and P=0.337 respectively).

Conclusion. In the present study, we evaluated the ABPM parameters in inadequately controlled essential hypertensive individuals with and without acute ischaemic hemispheric stroke. There was no statistical difference in ABPM parameters as for diastolic BP (averages, BP load) and for systolic BP (some parameters of BP load, variability). Meanwhile, there was statistician difference in systolic BP profile (averages, BP load, and the circadian index), pulse BP and the diurnal AASI.

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Особливості показників добового моніторування артеріального тиску в гіпертензивних пацієнтів у гострому періоді ішемічного інсульту

С. П. Жеманюк

Гіпертензивна хвороба (ГХ) розглядається як значущий фактор ризику розвитку багатьох патологічних станів, зокрема інсульту, що має достатню доказову базу за результатами популяційних досліджень та низький рівень контролю серед дорослого населення України. Тому визначення показників артеріального тиску (АТ) набуває вагомого значення щодо діагностики та контролю лікування артеріальної гіпертензії. Добовий моніторинг артеріального тиску (ДМАТ) розглядається як перспективний метод дослідження пацієнтів, за допомогою якого визначаються маркери прогнозу розвитку як несприятливих подій, так і пошкодження органів-мішеней. У разі розвитку серцево-судинних катастроф (інсульту) змінюються параметри ДМАТ, але відомості щодо їхніх змін суперечливі.

Мета роботи – визначення особливостей добового профілю артеріального тиску у хворих на гіпертонічну хворобу, що ускладнена ішемічним півкульним інсультом.

Матеріали та методи. Для аналізу включили 114 пацієнтів (медіана віку – 62 (56;72) роки, 40 % – особи жіночої статі) зі встановленою ГХ, у яких за даними ДМАТ зафіксовано підвищення усереднених показників добового профілю систолічного АТ (САТ) та/або діастолічного АТ (ДАТ) (≥130 мм рт. ст. і ≥80 мм рт. ст. відповідно). До першої групи увійшло 83 хворих на ГХ, до другої – 31 гіпертензивний пацієнт зіставного віку з ішемічним півкульним інсультом (ІІ) у гострому періоді.

Результати. Групи були статистично відмінними ($p<0,001$) за показниками усереднених значень САТ (за добовий, денний і нічний періоди); пульсового АТ (ПАТ) за добовий проміжок часу. За показниками навантаження гіпертензією статистична відмінність ($p<0,001$) спостерігалась за індексом часу САТ (за добовий і денний проміжок часу); за індексом площі САТ і нормалізованим індексом площі САТ за всіма часовими проміжками ($p<0,05$). Щодо варіабельності АТ, статистична розбіжність ($p<0,001$) виявлена тільки для ДАТ за нічний проміжок. За показниками індексу амбулаторної жорсткості судинної стінки виявлено вірогідну відмінність ($p<0,05$) показника за добовий, нічний часові проміжки. За циркадним ритмом відмінність у групах отримано лише за показником ДАТ. Поряд з тим не виявлено вірогідної статистичної відмінності у групах за показниками ранкового підйому САТ, ДАТ і показниками циркадного індексу САТ.

Висновки. Хворі на ГХ із неконтрольованими показниками АТ за ДМАТ мають схожий профіль АТ порівняно з когортою пацієнтів зіставного віку з ішемічним півкульним інсультом у гострому періоді практично за всіма показниками ДМАТ. Так, діастолічні показники АТ (усереднені показники, показники навантаження тиском), систолічні показники АТ (індекси навантаження тиском, варіабельність АТ) статистично не відрізнялись у групах. Натомість різницю за показниками ДМАТ виявили за систолічним профілем АТ (усередненими показниками, більшістю індексів навантаження тиском), за пульсовим АТ за добу, а також за новими індексами ДМАТ (амбулаторним індексом жорсткості судинної стінки за добовий і денний періоди) та циркадним ритмом за ДАТ.

Ключові слова: *гіпертонічна хвороба, ішемічний інсульт, добовий моніторинг артеріального тиску, циркадний індекс.*

Запорізький медичний журнал. – 2016. – №6 (99). – С. 25–29

Особенности показателей суточного мониторирования артериального давления у гипертензивных пациентов с ишемическим инсультом в остром периоде

С. П. Жеманюк

Гипертоническая болезнь (ГБ) рассматривается как значимый фактор риска развития многих паталогических состояний, включая инсульт, имеющий достаточную доказательную базу по результатам популяционных исследований и низкий уровень контроля среди

взрослого населения Украины. В связи с этим определение показателей артериального давления (АД) приобретает ведущее значение в установлении диагноза и контроле лечения. Суточное мониторирование АД (СМАД) рассматривается как перспективный неинвазивный инструментальный метод исследования пациентов, с помощью которого изучаются маркеры прогноза развития как неблагоприятного исхода, так и риска развития поражения органов-мишеней. При развитии сердечно-сосудистой катастрофы (инсульт) происходят изменения ряда параметров СМАД, сведения о которых весьма противоречивы.

Цель работы – определение особенностей суточного профиля артериального давления у больных гипертонической болезнью, осложнённой ишемическим полушарным инсультом.

Материалы и методы. В исследование включили 114 пациентов (медиана возраста – 62 (56;72) года; 40 % – лица женского пола) с ГБ, у которых по данным СМАД были зафиксированы высокие усреднённые показатели суточного профиля систолического АД (САД) и/или диастолического АД (ДАД) (≥130 мм рт. ст. и ≥80 мм рт. ст. соответственно). В первую группу вошли 83 пациента с ГБ с неконтролируемой гипертензией, во вторую – 31 гипертензивный пациент в остром периоде ишемического полушарного инсульта.

Результаты. Группы статистически отличались (p<0,001) по усреднённым показателям САД (за суточный, дневной и ночной периоды); пульсовому АД (ПАД) за суточный период времени. По показателям нагрузки гипертензией статистическое различие (p<0,001) наблюдалось по индексу времени САД (за суточный и дневной временные периоды); индексу площади САД и нормализированному индексу площади САД во всех временных интервалах (p<0,05). По показателям индекса амбулаторной жёсткости сосудистой стенки были выявлены достоверные различия (p<0,05) за суточный и ночной периоды времени. По результатам распределения показателей циркадного ритма отличие выявлено только по ДАД. В то же время не получено достоверной статистической разницы в показателях утреннего подъёма как САД и ДАД, так и циркадного индекса САД.

Выводы. Пациенты с ГБ с неконтролируемыми показателями АД по данным СМАД имеют похожий профиль артериального давления по сравнению с лицами с острым полушарным ишемическим инсультом. Так, в отношении диастолического АД (усреднённые показатели, показатели нагрузки давлением), систолического АД (некоторые показатели нагрузки давлениям, вариабельность АД) группы статистически не отличались. Однако существенная разница в показателях СМАД была получена по систолическому профилю АД (усреднённые показатели АД, большинство показателей нагрузки давлением), пульсовому АД за сутки, а также в отношении некоторых новых индексов СМАД (амбулаторный индекс жёсткости сосудистой стенки за суточный и ночной периоды времени).

***Ключевые слова**: гипертоническая болезнь, ишемический инсульт, суточное мониторирование артериального давления, циркадный индекс.*

Запорожский медицинский журнал. – 2016. – №6 (99). – С. 25–29

Hypertension is one of the crucial health problem among adult Ukrainian population affecting 55.8 % [1]. Blood pressure (BP) has been identified as a risk factor for various health disorders, including stroke onsets, approximately a half of which are attributed to high BP [12]. It was shown that the benefit of BP reduction on stroke incidence or recurrence, population attributable risk calculations place hypertension as the single factor explaining the highest percentage of stroke risk [18]. Furthermore, hypertension can influence to the high level of stroke mortality and a high frequency of disability [3].

Due to the importance of elevated BP in stroke causality, BP measurement remains critical. The ambulatory blood pressure monitoring (ABPM) is a modern method due to international and local recommendations for investigation of hypertension [2,17]. Use of the ABPM to determine the presence of raised BP is becoming standard practice in developed countries [18]. Noticeably, it has been reported that ABPM is superior predictor of future cardiovascular events than clinic BP measurement [5]. However, it is limited information about value in clinical practice of ABPM data in hypertensive patients with inadequately controlled BP with acute stroke compared with those individuals who has no vascular onset.

In the present study, we sought the confirmation that hypertensive patients with acute hemisphere ischaemic stroke (IS) would have a considerable difference in the ABPM parameters compared with inadequately controlled essential hypertensives (EHs).

For this purpose, we measured ABPM data in inadequately controlled EH individuals with or without acute hemisphere ischaemic stroke.

Materials and methods

The study protocol was approved by the Medical ethics committee of the Zaporizhzhia State Medical University, and the study was conducted according to the Helsinki Declaration. We examined patients admitted to the Zaporizhzhia clinical hospital № 6 (stroke, cardiology, intensive care units), which is the city stroke center and also the clinical base of the Department of Propedeutics of Internal Diseases, Zaporizhzhia State Medical University (the chief of the Department V. V. Syvolap). A researcher provided written and oral information on the study before the examination. Information on demographics and clinical characteristics was extracted from patients' medical records and purpose-designed questions in the questionnaire. The measurement of brachial BP has been performed using aneroid-type sphygmomanometer and a health professional auscultating the Korotkoff sounds. All the patients underwent ABPM.

ABPM was recorded using a bifunctional device (Incart, S.-P., R. F.). After the baseline examination participants were fitted with it on their nondominant arm if there were no considerable difference of BP results. Appropriate cuff bladder size was determined based on arm circumference. BP was measured at 15-min intervals from 07:01 to 23:00 and at 30-min intervals from 23:01 to 07:00. For analyzing matter, we defined awake and asleep periods as the fixed periods of time (from midnight to 06:00 $_{AM}$ for nighttime and from nighttime to 06:00 $_{AM,}$ respectively). Analysis was carried out using an oscillometric method. Moreover, we categorized patients based on night/day ratio [10] separately for SBP and DBP as (1) rising or absence of dipping (ratio >1.0); (2) mild dipping (0.9< ratio ≤1.0); (3) dipping (0.8< ratio ≤0.9); and (4) extreme dipping (ratio ≤0.8).

Quality of the ABPM studies was defined by the length of time that the monitor was actually worn (≥21 hours) and the number of successful BP recordings (≥1 valid BP measured per two hours were acceptable for analysis, so that there were 14 measures for daytime and at least 7 measurements – for nighttime period) [10].

Upon completion of the 24-h ABP recording, the data was downloaded and analyzed statistically to calculate BP averages for systolic BP (SBP) and diastolic BP (DBP) for different time periods (i. e., 24-h, daytime and nighttime) as well as BP loads, BP variations and ABPM indexes and coefficients. In particularly, the BP load was calculated as the proportion of BP ≥135/85 mm Hg during the day period and BP ≥120/75 mm Hg during the night period [17,18]. And the BP variability was calculated manually as standard deviation of SBP and DBP over a 24-h period, daytime and night periods for each patient [18]. The AASI was calculated manually as one minus diastolic (DBP) versus systolic blood pressure (SBP); the Sym_Slope was calculated as slope SBP-versus-DBP divided by correlation coefficient (r); the Sym_AASI was founded as 1-1(1-AASI)/r in linear regression analysis as described [9,16].

Statistical analysis was performed using the Statistica version 6.0 (StatSoft, Tulsa, OK., U.S.A.). The various BP values and relationships between them were compared and calculated after excluding patients with inadequately controlled BP. The Shapiro-Wilk test was used to test for deviation from normality. Categorical data are presented as percentages and continuous data as mean ± standard deviation or medians and interquartile ranges as appropriate after testing for normality of distribution. Comparisons between groups were done using the Student *t*, the Mann-Whitney *U* and χ^2 tests as appropriate. Two-tailed P values <0.05 were considered statistically significant.

Results and its discussion

In flow chart (*Fig. 1*), it is presented the stages of patients including to the analysis. We enrolled individuals older 18 years with previously documented EH, with sinus rhythm on electrocardiogram (ECG) monitoring, with valid ABPM results.

The study population reported here includes 114 patients, the median age of study population was 62 (56; 72) years and 40 % were female. We classified the subjects into two groups according to the results of clinical examination and ABPM results. The first group (n=83) were inadequately controlled essential hypertensive individuals with high systolic or/and diastolic BP level according to the ABMP results and the second one (n=31) were EH patients with an acute hemispheric IS, diagnosis confirmed with clinical examination and computed tomography scan or magnetic resonance imaging results, and ABPM was conducted in 4.2±2.3 days after the stroke onset.

Age and sex did not differ between the groups of EHs and EH individuals with IS (P=0.110 and P=0.931, respectively). There was a steady increase in the overwhelming ABPM parameters. Particularly, the averages SBP24-hour and DBP24-hour were elevated in all hypertensive patients, however, only for SBP24-hour there were statistical difference (P<0.001) as it is seen in *Table 1*.

The results of the analysis also show that groups were significantly different only in averages of SBP and pulse BP (PBP). Diastolic BP averages were not shown significantly different between groups. There were increased results in IS group for diurnal SBP (P<0.001), daytime SBP (P<0.001) and nighttime SBP (p<0.001) as compared with the group of EH participants without IS. In addition, for diurnal PBP, results obtained in IS patients were significantly greater than obtained in inadequately controlled BP patients (P<0.001).

It was demonstrated statistical difference in BP loads only for SBP parameters. Percentage of BP augmentation for the diurnal period and daytime periods was considerably higher in the second group with IS (P<0.001 and P=0.001, respectively). Also, the square normalized indexes (SBP_{Nsq}) of hypertension for all periods (for diurnal, daytime and nighttime) were more in IS patients group compared with the other group of EH individuals (84.6 %, 76.9 %, 93.8 % respectively) with significant difference between two groups (P<0.05). Both the square indexes (SBP_{Sq}) of hypertension (for diurnal and nighttime periods) and the time index of hypertension (for diurnal period and daytime) were 94.2 %, 16.9 % and 26.7 %, 28.8 % increased respectively and showed significant difference between groups (P<0.05).

At the same time, only DBP data for nighttime period achieved significance (P<0.001) after analysis of SBP and DBP variability.

Notably, only the AASI for 24-h period and the AASI for nighttime period were significantly higher in IS individuals (P=0.016 and P<0.015 respectively). Meanwhile, there was no statistical difference in other new calculated ABPM indexes between groups (Sym_AASI_{24}, (P=0.068); Sym_slope_{24}, (P=0.068)).

The groups were statistically different only in DBP data concerning analysis of circadian indexes (*Table 2*). Particularly, there were substantially more mild dipping in DBP pattern in participants with IS as compered with the other group of EHs (39 % vs. 19 %; P<0.029).

No differences were found between the groups in morning surge calculated as speed and amplitude of the BP raising in morning hours both for SBP (P=0.422 and P=0.395 respectively) and DBP (P=0.860 and P=0.337 respectively).

Discussion

BP tends to remain high in the hours and days after acute stroke. It was found that BP elevated in 84 % of patients in the acute phase of stroke [11]. BP levels are closely associated with clinical outcome in individuals with acute IS [13]. As noted in a

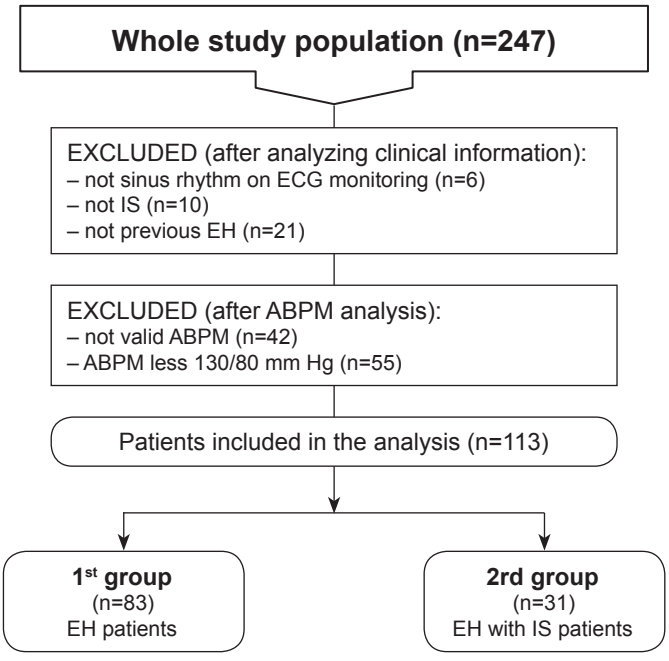

Fig. 1. Flow chart of study population.

Notes: ABMP – ambulatory blood pressure monitoring; ECG – electrocardiogram; EH – essential hypertension; IS – ischaemic hemispheric stroke.

Skalidi et al. study [7] increased SBP values are associated with formation of brain edema. Both stroke-specific and non – specific external stimuli as well as other transient factors may contribute to BP changes in participants with acute stroke. However, it is noticeably, that BP recorded during sleep or in the early morning is more predictive of first or recurring stroke events than daytime SBP, especially in the elderly [9]. Observational studies show that both extremely high and extremely low BP on admission correlates with death or dependency in acute stroke participants [11]. Recently, in a cohort study it was found that both daytime and nighttime BP predicted all cardiovascular events in general population. However, nighttime BP, adjusted for daytime BP independently predicted mortality (total, cardiovascular, and non-cardiovascular) [14].

It was also demonstrated that BP load is an independent predictor of hypertensive target organ damage and adverse cardiovascular risk profile according to the study results, where subjects with a higher SBP load, adjusted for average diurnal SBP, were found to have increased relative myocardial wall thickness and total peripheral vascular resistance [15].

A recent study in stroke cohort population showed the loss of nocturnal BP dipping [9], which may lead to worse target organ damage and facilitates recurrent stroke. Modest preservation of nocturnal BP dipping and the physiological circadian BP pattern may induce a protective effect on cerebral circulation in IS patients.

Several longitudinal epidemiological studies have shown the predictive value of arterial stiffness as intermediate end point, i.e. the greater the arterial stiffness, the greater the number

Table 1

Ambulatory blood pressure components between groups

Classification of ABPM parameters		ABPM parameters	1 group with EH (n=83)	2 group with IS (n=35)	P Value
Recommended	Average BP	SBP_{24}, mm Hg	142 (137;150)	155 (145;177)	<0.001
		DBP_{24}, mm Hg	81 (75;87)	82 (74;96)	0.518 (NS)
		SBP_{day}, mm Hg	145 (139;154)	156 (145;178)	<0.001
		SBP_{night}, mm Hg	136 (124;145)	151 (133;165)	<0.001
		PBP_{24}, mm Hg	63 (54;69)	70 (65;83)	<0.001
New one	BP load	SBP_{24}, %	71 (56;88)	94 (76;99)	<0.001
		SBP_{day},%	69 (53;88)	93 (72;100)	0.001
		SBP_{night},%	86 (56;100)	100 (82;100)	<0.001
		$SBP_{24,\ time,}$ %	75 (64;92)	95 (78;100)	<0.001
		$SBP_{day,\ time,}$ %	73 (58;91)	94 (78;100)	<0.001
		$SBP_{24,\ Sq}$, mm h	292 (188;458)	567 (334;1077)	<0.001
		$SBP_{day,\ Sq}$, mm h	219 (137;338)	153 (78;253)	0.001
		$SBP_{night,\ Sq}$, mm h	83 (31;137)	97 (41;154)	<0.001
		$SBP_{24,\ Nsq}$ mm h	13 (8;20)	24 (14;43)	<0.001
		$SBP_{day,\ Nsq}$ mm h	13 (8;20)	23 (11;43)	0.002
		$SBP_{night,\ Nsq}$ mm h	16 (6;25)	31 (14;45)	<0.001
	AASI	$AASI_{24}$	0.47±0.15	0.56±0.24	0.016
		$AASI_{night}$	0.44 (0.26;0.60)	0.62 (0.33;0.87)	<0.015
	VBP	DBP_{night}, mmHg	9 (6;11)	12 (8;15)	<0.001

Notes: Values are mean±SD; median (1^{st}; 3^{rd} quartile) or n (%). AASI – ambulatory arterial stiffness index; DBP – diastolic blood pressure; EH – essential hypertension; IS – ischaemic stroke; Nsq – normalized square index; SBP – systolic blood pressure; Sq – square index; VBP – blood pressure variability.

Table 2

Circadian index parameters

BP ratio	Circadian index	1 group with EH (n=83)	2 group with IS (n=31)	P value
SBP	Rising or absence of dipping, n (%)	13 (16)	9 (29)	0.122 (NS)
	Mild dipping, n (%)	35 (42)	15 (48)	0.567 (NS)
	Dipping, n (%)	29 (35)	6 (20)	0.126 (NS)
	Extreme dipping, n (%)	6 (7)	1 (3)	0.422 (NS)
DBP	Rising or absence of dipping, n (%)	15 (18)	9 (29)	0.202(NS)
	Mild dipping, n (%)	16 (19)	12 (39)	0.029
	Dipping, n (%)	38 (46)	9 (29)	0.104 (NS)
	Extreme dipping, n (%)	14 (17)	1 (3)	0.052(NS)

of cardiovascular events [11] and found as one of the strong predictor of stroke and cardiovascular mortality [4]. Recently, in meta-analysis it was concluded that this index predicts independently future clinical events, particularly stroke onset [6]. Increased arterial stiffness is associated with higher cardiovascular risk, and carotid stiffness was shown to be a predictor of incident stroke, independent of other cardiovascular risk factors and of aortic stiffness as estimated by carotid-femoral pulse wave velocity [8].

A number of clinical studies propose prognostic value of ABPM parameters as the result of population studies, however, it is not clear the additional value of ABPM data in individuals who are on the acute phase of cardiovascular (CV) event or have already influenced by CV events, like stroke, for the clinical situation.

Conclusions

1. Overall, in the present study we have found statistical difference in all groups of ABPM parameters, as recommended by the European guidelines as new ones, like the AASI. Noticeably, none of the average and load for diastolic BP parameters, and variability and the circadian index for systolic BP is shown statistical difference between the groups. Meanwhile, there was statistical difference in systolic BP profile (averages, BP load, the circadian index), pulse BP and the AASI. However, the new described indexes of ABPM not show difference in the groups, except the AASI.

2. Future studies should provide ABPM data on a wider range of populations and diseases, as well as consensus of reference values.

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