

The Circadian Pattern Of 24-Hour Ambulatory Blood Pressure And Heart Rate In The Cerebral Infarction Patients With Hypertension And Hypertensives Patients

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Abstract

Aims: Evaluation of the circadian rhythm of 24-hour ambulatory blood pressure and pulse rate in the cerebral infarction patients with hypertension and hypertensives patients with purpose prognostic, prevention and treatment in two group.

Objects and methods: This study included 140 cerebral infarction patients with hypertension, hospitalized for the first 7 days (mean age 65.5±10.4 years) and 143 primary hypertensive patients (mean age of 64.4±7.5 years). All had 24-h ambulatory recording, with measurement 30 every minutes in the daytime (6.00 am - 10.00 pm) and every 60 minutes at night (10.00 pm - 6.00 am).

Results: Blood pressure in patients with cerebral infarction oscillated significantly more than in hypertensive patients; mean standard deviation of systolic blood pressure (25.8 mmHg) and diastolic blood pressure (15.8 mmHg) in patients with cerebral infarction respectively was significantly higher than those with hypertension (20 mmHg and 12.1 mmHg) with $p < 0.01$. The rate of non-dipping blood pressure at night, the overload of systolic and diastolic blood pressure, morning surge blood pressure in patients with cerebral infarction was significantly higher than that of hypertensive patients (92.1; 75.5; 60.2; 57.8 versus 64.3; 60.1; 49.1; 36.3 respectively; $p < 0.01$).

Conclusion: It is necessary to monitor 24-hours ambulatory blood pressure in hypertensive patients and patients with cerebral infarction in the first week of admission to identify some phenomena such as nocturnal non-dipping blood pressure, the overload of blood pressure, especially morning surge blood pressure early to plan for prevention of target organ damage, particularly cerebral stroke in hypertensive patients.

Keywords: 24-hour ABPM, Circadian pattern, Cerebral infarction, Arterial hypertension

1. INTRODUCTION

Hypertension is an important cardiovascular risk factor, and is the leading cause of disability and death for the elderly in both developed and developing countries, is estimated to cause 7.1 million deaths worldwide³ accounting for 4,5% of the global burden of diseases¹³. Hypertension can lead to stroke, in which cerebral infarction accounts for the majority due to lack of monitoring. Some patients have their blood pressure

monitored daily, however using a regular sphygmomanometer instead of a 24-hour ambulatory blood pressure monitoring, as it would not be possible to measure the BP during sleep, unable to detect those hypertension episodes leading to cerebral infarction. On the other hand, patients with cerebral infarction also need to be monitored to detect a hypertensive crisis to prevent recurrent infarction. Therefore, it is necessary to compare the circadian rhythms of blood pressure between patients with hypertension and those in patients with cerebral infarction to find out the difference of 24-hour ambulatory blood pressure parameters with purpose to have the plan of prevention, treatment and prognostic for these two patients group.

2. PATIENTS AND METHODS

2.1. Study Setting and design

It is a descriptive cross-sectional study, convenience sampling. This study was conducted in Hue central hospital, Nghe An general hospital, Vinh Medical University hospital and Ha Tinh general hospital from 2012-2018.

2.2. Patients: This study included 140 cerebral infarction patients with hypertension hospitalized for the first 7 days (77 males, 63 females; mean age 65.5 ± 10.4 years) and 143 primary hypertensive patients (85 males, 58 females; mean age of 64.4 ± 7.5 years) were treated in hospital.

2.3. Methods: All patients had their 24-hour ambulatory blood pressure monitoring (24 h ABPM) every 30 minutes for 24 hour from 6 am to 10 pm and every 60 minutes at night from 10 pm to 6 am in the next morning by using Oscar 2 (Suntech, USA). The hypertensives patients without the cerebral stroke the patient did not take antihypertensive drugs during 1 day before and the day of measurement. The patients with cerebral infarction were taken their 24h ABPM in the first 7 days, without taking antihypertensive drugs (unless patients indicated due to hypertensive emergency). The patients of these two group were monitored closely, when the blood pressure raised, at the same time the patients has complications of hypertension then stop taking machine and give the patient medication (in fact in study process we did not record any patient with complication)

2.4. Study variables

Criteria of 24 hABPM variables^{1,2,4,7,8}:

Nocturnal Dipping(Nocturnal Dippers-Dipper)when both nocturnal Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)decreasedby > 10% compared to daytime levels.

*Nocturnal Non-dipping (Non-dipper)*when both nocturnal SBP and DBP decreased by $\leq 10\%$ compared to daytime levels.

Blood Pressure overload rate was the % rate of measurment times with hight blood pressure in 24 hours, daytime and nighttime.

*Morning surge BP (MSBP)*when SBPand DBP increase at least 20/15mmHg from lowest BPduring sleep to mean BP after the first 2 hours after waking up⁸.

All collected data were analyzed with SPSS 20 software. Qualitative variables were represented by frequency and percentage, while quantiative were discribed by mean value and standard deviation (mean \pm SD). Rates were compared by using the chi-square test, while mean values were compared through Student's test. A p-value <0.05 was considered statistically significant.

Baseline of cerebral infraction with hypertension and hypertensive patients

Variability	Cerebral infraction patient			Hypertensive patient		
	Male (77)	Female(63)	Total (140)	Male (85)	Female(58)	Total(143)
Age (year)	63,8 \pm 9,8	67,7 \pm 10,7	65,5 \pm 10,4	64.41 \pm 7.53	67.69 \pm 7.11	65.67 \pm 7.47
Hight (cm)	162,7 \pm 3,5	152,7 \pm 2,2	158,2 \pm 5,9	163.22 \pm 4.25	152.38 \pm 3.31	158.06 \pm 6.68
Weight(kg)	51,9 \pm 8,0	46,1 \pm 7,9	49,3 \pm 8,5	56.52 \pm 10.02	48.93 \pm 7.96	52.95 \pm 9.81

3. RESULTS

3.1. Blood pressure (BP) and heart rate (HR) variability every hour in hypertensive patients

Blood pressure in patients with hypertension rises at 9–10 am, 5–7 pm. BP drops at 1–2 pm, dipping from 22:00, lowest at 3–4 am and then increases gradually at 5–6 am. Heart rates share a similar pattern with BP, increasing with SBP at 8–9 am, at 5–7 pm and then gradually decreasing and bottoms at 3–4 am. The mean standard deviation for SBP is 20.0 mmHg, for DBP is 12.1 mmHg and the heart rate also fluctuate along with BP.

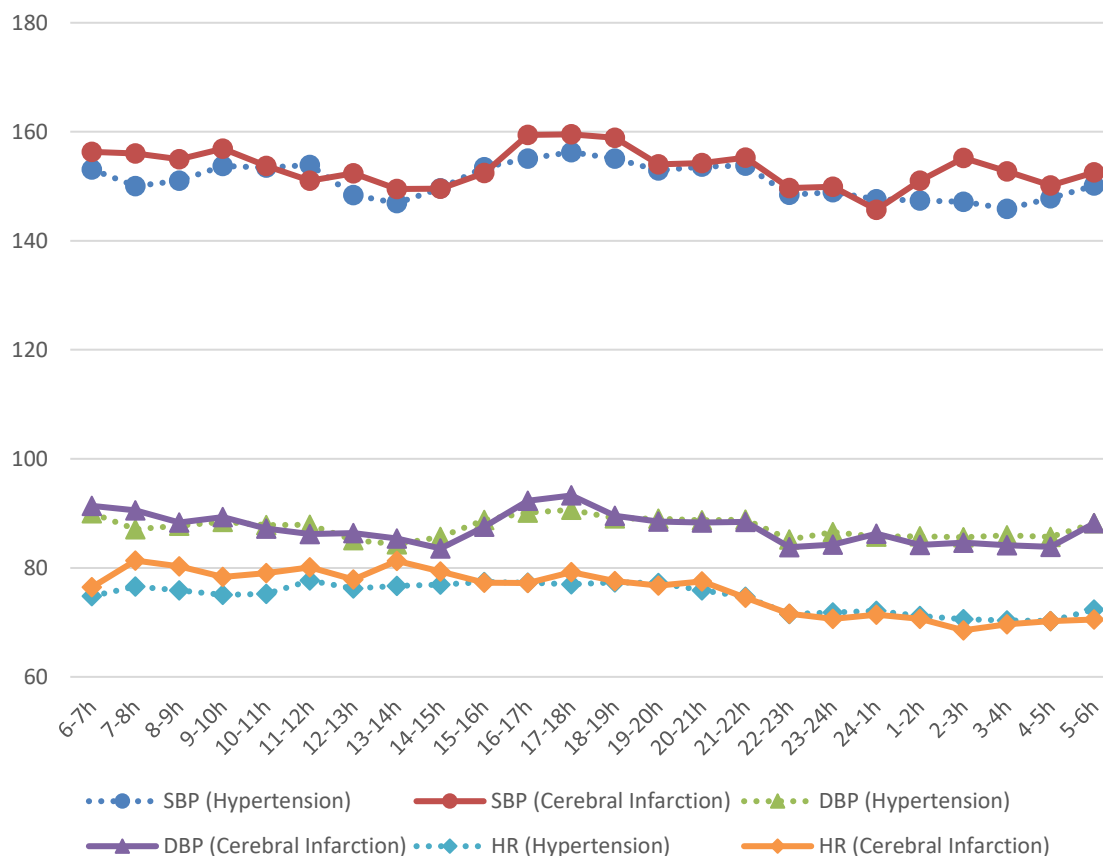


Figure 1: 24-Hour Blood Pressure and Heart Rate Variability in hypertensive patients and cerebral infarction

3.2. BP and HR every hour in patients with cerebral infarction having hypertension

Blood pressure in patients with cerebral infarction changes, significantly fluctuating during the daytime (Figure 1). The standard deviation of hourly BP within 24 hours in patients with high cerebral infarction in 24 hours were over 23 mmHg with an average of 25.8 mmHg in terms of SBP and over 13 mmHg with an average of 15.8 mmHg in terms of DBP. Especially during nighttime from 10 pm - 6 am still higher than 145/85 mmHg, not reduced by over 10% compared with daytime BP. Blood pressure in patients with cerebral infarction having many peaks during the day at 6–7 am, 9 am–12 pm and from 3–7 pm. There are some times the BP decreased from 12 – 3 pm, the average BP during sleep is lower but not significant, with its lowest at 3–4 am (145.9 mmHg). The standard deviation of heart rate during the hours is also high during all hours are over 13 beats/minute. Some peaks along with BP, HR between consecutive hours of the day is relatively stable. Heart Rate during nighttime from 10 pm–6 pm is not over 10% lower than during the day (nocturnal non-dipping). Heart Rate during nighttime were all over 70 beats/minute.

3.3. Dipping, non-dipping pattern, severe parameters of 24-hour ABPM (BP load, BP morning surge) in hypertensive patients and cerebral infarction patients

The percentage of nocturnal dipping was higher in the hypertensive group than that in the cerebral infarction group having hypertension (HTN) (Table 1).

Table 1. *Value decreasing of nocturnal BP in hypertensive patients and cerebral infarction.*

BP (mmHg)	Daytime Average	Nighttime Average	Δ day-night	% dipping
SBP (1) HTN	155.0±18.4	148.4±20.8	6.6 ±14.2	3.8 ±8.9
SBP (2) Cerebral infarction	153.0 ± 20.4	148.4± 22.1	4.6 ± 10.9	0.32 ±6.8
p(1-2)	>0.05	>0.05	>0.05	<0.01
DBP (1) HTN	88.7±10.5	85.3±12.9	3.4 ±10.1	4.0 ±9.6
DBP (2) Cerebral infarction	88.4± 12.2	86.7 ± 13.3	1.7± 7.9	- 0.67 ±8.1
p(1-2)	>0.05	>0.05	>0.05	<0.01

The prevalence of non-dipping at night and reverse blood pressure was significantly higher in patients with cerebral infarction having hypertension (Table 2). In patients with nocturnal dipping it starts from 22h, the SBP and DBP decreased lower than that of the daytime, the weakest at 0-1h. In the non-dipping group, it starts from 10 pm–6 pm, the BP is still as high as that of the daytime.

Table 2. *Dipping and non-dipping, BP reverse, the rate of severe parameters of 24 h ABP in the group of HTN and cerebral infarction*

Variables	HTN (1)	Cerebral infarction (2)	p (1-2)
Nocturnal dipping	35.7%	7.9%	<0.01
Nocturnal non-dipping	64.3%	92.1%	<0.01
BP reverse	12.6%	32.9%	<0.01
SBP Overload ≥50%	57.0%	82.3%	<0.01
DBP Overload ≥50%	52.4%	61.5%	<0.01
Morning surge BP %	36.3%	57.8%	<0.01
Systolic BP load %	60.1 ±23.0	75.0 ± 26.8	< 0.01
Diastolic BP load %	49.1±26.0	60.2± 28.0	< 0.01

The percentage of BP load in the group of patients with cerebral infarction having hypertension significantly higher than the group with hypertension. The rate of severe systolic overload was significantly higher in the cerebral infarction group than the hypertension group (p <0.01). The rate of severe diastolic overload was significantly higher in the cerebral infarction group than the hypertension group (p <0.05). The rate of morning surge blood pressure was significantly higher in the cerebral infarction group than the hypertension group (p<0.05) (Table 3).

4. DISCUSSION

4.1. Blood pressure and heart rate variability during daytime

Following our result, SBP and DBP in people with hypertension often over 130/ 80mmHg at all hours of the day even when sleeping from 10 pm–6 am the next morning. The standard deviation was uneven between hours but averaged 20 mmHg for SBP and 12.1 mmHg for DBP in hypertension. Meanwhile, the standard deviation for the cerebral infarction group having hypertension was 25.8 mmHg for SBP and 15.8 mmHg, which was significantly higher than that of people with hypertension (Table 1). Thus it can be said that blood pressure in patients with cerebral infarction fluctuated more than that in patients having hypertension without a cerebrovascular accident. The limited standard deviation for normal people according to Niels Gobin et al. ¹⁴ was over 12-15mmHg, according to E Brien was 10-15 mmHg for daytime BP and 5-10 mmHg for nighttime average in hypertensive patients ².

Through our research we have found that in people with hypertension, their BP bottomed at 2 times like normal people and hypertensive patients showed that at 1 – 2 pm and 2 –3 am having many peaks during the day, there were 2 times like normal people, usually 9 - 11 am and 15 - 6 pm but there were 3 more times of increasing BP: 9 – 10 pm, 5 – 6 am and 6 - 7 am. And in patients with cerebral infarction having

hypertension, there was an increase of BP at 6-7h, 9 am–12 pm, 15 – 19h. There were some low times, such as at 12 – 15h, the average during sleep time was lower but not significant, and bottomed at 3–4 am. This BP change was related to the occurrence of cardiovascular events at the above hours. A prospective study⁵ on 132 patients with hospitalized strokes for day and night rhythm changes showed that up to 40% was at high risk of myocardial infarction, 29% was at high risk of cardiac death, 49% increasing the risk of stroke and 47% having a stroke from 6 – 12h. In contrast, in another report⁵ the highest chance of a stroke occurred between 22:00 and 2:00 am. The high frequency of stroke due to hypertension at 6 am - 12 am and 10 pm - 2 am is associated with nocturnal non-dipping BP and morning surge BP.

4.2. Nocturnal dipping, non-dipping blood pressure

Several studies have mentioned nocturnal dipping, non-dipping blood pressure (dipper or non-dipper). The incidence of non-dipping BP increased along with complication in hypertensive patients especially in a cerebral vascular accident as showed in our research. Hatem Fahan et al.⁶ compared BP monitoring on ABPM and measuring BP in risk assessment and treatment of hypertension on 104 patients with hypertension showed that the incidence of non-dippers in hypertensive patients were 64.4%. Our research results (Table 1) showed that daytime BP was 6.6/3.4 mmHg higher at night in hypertensive patients, but nighttime BP decreased by less than 10% compared to daytime (3.8% for SBP and 4.0% for DBP). The percentage of non-dippers in the hypertensive group was 64.3%, while the proportion of dippers was only 36.7%. Among non-dipping patients in the hypertensive group, 12.6% (18 patients) has a reversed BP. Meanwhile, in the group of patients with cerebral infarction, the rate of non-dippers during nighttime was 92.1%, the rate of dippers was only 7.9%, the rate of reverse blood pressure was 32.9% (46 patients). The reverse of BP was the phenomenon that explained why there was a high proportion of patients usually had a cerebral stroke at night (Table 2).

4.3. The rate of 24-hour Blood Pressure Overload

BP overload was the rate of times that BP was exceeding BP threshold during 24-hour measuring BP, day-night cycle. In a normal person, the BP overload ratio under 25%, which means that less than 25% of the measurements have high BP above the threshold^{9,12, 14}. The rate of BP overload was related to the prognosis of hypertension, especially to cardiovascular events such as peripheral arterial disease, kidney, eye and brain damage¹¹. Following Ohasama study¹, in Japan followed from 4.1 to 9.2 years showed that cardiac death related to BP overload during 24 hours, every 5% increase in SBP or day-night ratio of DBP would increase 20% risk of cardiac death. Our research results (Tables 3) showed that in patients with cerebral infarction, the mean SBP overload rate was $75.0 \pm 26.8\%$, diastolic was $60.2 \pm 28\%$ significantly higher than that in hypertension group: $60.1 \pm 23\%$ for SBP and $49.1 \pm 26.0\%$ for DBP. Along with nocturnal non-dipping BP, reverse BP was a sign indicating the loss of circadian rhythm in hypertension patients and one of the risk factors causing target organ damage, especially stroke. This results confirmed that hypertensive patients with cerebral infarction had significantly higher rates of reverse blood pressure than hypertension group.

4.4. Morning surge blood pressure

Our research results in Table 3 showed that in hypertensive patients, the rate of morning surge BP was 36.3% significantly lower than that of patients with cerebral infarction having hypertension. This results suggested that morning surge BP was one of the factors causing cerebral infarction in the morning. The phenomenon of morning surge BP can be the cause of a stroke or cerebral hemorrhage, explaining that stroke often occurred in the early morning as patients hospitalized from 6 to 12 hours accounted for 47%⁸. A study in the United Kingdom¹¹ on 1187 subjects with an average age of 59.3 showed that the rate of morning surge BP was 47.09% (559 patients). Kario et al. in Japan^{9, 10} have shown that elderly people with morning surge BP had a high incidence of multifocal cerebral infarction (57% vs 33%; $p = 0.001$) and high risk of stroke (19% vs 7.3%, $p=0.004$). Redon et al. showed that, in treated patients, morning surge BP accounted for 52-72%. Morning surge BP and morning hypertension were factors that increased mortality and cardiac death in the early hours of the morning¹².

5. CONCLUSION

It is necessary to monitor 24-hour ambulatory blood pressure in hypertensive patients and patients with cerebral infarction in the first week of admission to identify some phenomena such as nocturnal non-dipping blood pressure, the overload of blood pressure, especially morning surge blood pressure early to plan for prevention of target organ damage, particularly cerebral stroke in hypertensive patients.

REFERENCES

1. Ohkubo T, Hozawa A, Yamaguchi J, Kikuya M, Ohmori K, Michimata M, Matsubara M, Hashimoto J, Hoshi H, Araki T, Tsuji I, Satoh H, Hisamichi S, Imai Y. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24-h blood pressure: the Ohasama study. *J Hypertens*. 2002;20, 11:2183-9. DOI: 10.1097/00004872-200211000-00017. PMID: 12409956
2. Eoin O' Brien, Ambulatory Blood Pressure Monitoring: 24-h blood pressure control as a therapeutic goal for improving cardiovascular prognosis. *Medicographia*. 2010; 32, 3:241-249.
3. Norm Campbell et al. Canadian Hypertension Education Program recommendations, An annual update, *Canadian Family Physician- Le Medecin de famillecanadien*, 2010: 649-653.
4. Abanti Chaudhuri et al. Role of Twenty-Four- Hour Ambulatory Blood Pressure Monitoring in Children on Dialysis, *Clin J Am SocNephrol*. 2011: 1-7.
5. Gupta. A, H. Shetty (2005) Circadian Variation in Stroke a Prospective Hospital-Based Study, *Int J ClinPract*. 2005;59(11):1272-1275.
6. Hatem Farhan, Mona Al-Hasani, Mohamed Misbah, and Mansour Sallam. Comparative Study of Ambulatory Blood Pressure Monitoring and Clinic Blood Pressure Measurement in the Risk Assessment and Management of Hypertension. *Sultan QaboosUniv Med J*. 2010; 10(3): 370–376.
7. Hiroshi Ijriet al. Cardiacarrhythmias and Left Ventricular Hypertrophy in Dipper and Non-dipper Patient With Essential Hypertension. *Japanese Circulation Journal*.2000; 64: 499-504.
8. Iqbal. P and Louise Stevenson. Cardiovascular Outcomes in patients with normal and abnormal 24-hour ambulatory blood pressure monitoring. *International Journal of Hypertension*. 2011.4 pages.
9. Kario K. Caution for Winter Morning Surge in Blood Pressure: A Possible Link With Cardiovascular Risk in the Elderly. *Hypertension*; 2006;47:139-140.
10. Kazuomi Kario, Morning Surge in Blood Pressure and Cardiovascular Risk: Evidence and Perspectives. *Hypertension*. 2010; 56:765-773.
11. Madin. K, P. Iqbal. Twenty-four-hour ambulatory blood pressure monitoring: a new tool for determining cardiovascular prognosis. *The Fellowship of Postgraduate Medicine*; 2006;82:548-551.
12. Josep Redon. The importance of 24-hour ambulatory blood pressure monitoring in patients at risk of cardiovascular events. *High Blood Press Cardiovasc Prev*. 2013;20(1):13-8. DOI: 10.1007/s40292-013-0006-3.
13. Thomas Truelsen et al. Global burden of cerebrovascular disease. *Cerebrovascular diseases*. 2000:1-67.
14. Niels Gobin et al. (2012), Mesureambulatoire de la pressionartérielle sur 24 heures, *Forum Medical Suisse*.2012; 12. (31-32):600-607.