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IMPACT OF BEDTIME ANTIHYPERTENSIVE MEDICATION AND SLEEP QUALITY ENHANCEMENT ON NON-DIPPER HYPERTENSION

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Non-dipper hypertension characterized by a lack of nocturnal blood pressure reduction is associated with adverse cardiovascular outcomes and poor sleep quality.

The objective of the study is to evaluate efficacy of bedtime administration of antihypertensive drugs and the pharmacological treatment of the sleep quality.

Materials and methods. The study was conducted at Ivano-Frankivsk National Medical University, involving 65 patients divided into three groups. Group 1 (n=18) received a fixed combination of perindopril (8 mg) and indapamide (2.5 mg) in the morning. Group 2 (n=25) received the same medication in the evening. Group 3 (n=22) received the medication plus a combination of L-tryptophan and vitamins (Pineal-Tens) in the evening. Patients were monitored for three months using ambulatory blood pressure monitoring (Cardiosense BP) and arterial stiffness assessment (Siemens NX3 Elite ultrasound). Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Statistical analysis included Kruskal-Wallis, Chi-square, and Bonferroni tests.

Results. Baseline characteristics were well-matched across groups. Post-treatment, Groups 2 and 3 showed significant reductions in nighttime systolic and diastolic blood pressure compared to Group 1. Group 3 exhibited significant improvements in subjective sleep quality, sleep duration, and habitual sleep efficiency. The proportion of non-dippers significantly decreased in Groups 2 and 3, indicating better circadian blood pressure regulation. Arterial stiffness, measured by pulse wave velocity, significantly improved in Groups 2 and 3.

Conclusions:

Evening administration of antihypertensive drugs significantly reduces nighttime blood pressure.

The combination therapy with L-tryptophan and vitamins significantly improves sleep quality.

Bedtime administration helps restore normal circadian blood pressure patterns and reduces arterial stiffness.

Key words: non-dipper hypertension, bedtime antihypertensive therapy, sleep quality, arterial stiffness, circadian rhythm.

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ВПЛИВ ВЕЧІРНЬОГО ПРИЙОМУ АНТИГІПЕРТЕНЗИВНИХ ПРЕПАРАТІВ ТА ПОКРАЩЕННЯ ЯКОСТІ СНУ НА ГІПЕРТЕНЗІЮ ПРОФІЛЮ НОН-ДІППЕР

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Стаття присвячена оцінці ефективності вечірнього прийому антигіпертензивних препаратів та фармакологічного покращення якості сну у пацієнтів з гіпертензією профілю нон-діппер. У дослідженні взяли участь 65 пацієнтів, що були розділені на три групи. Група 1 отримувала периндоприл та індапамід вранці, група 2 – ввечері, а група 3 – ввечері разом з L-триптофаном і вітамінами (Пінеал-Тенс). Результати показали значне зниження нічного систолічного і діастолічного артеріального тиску у групах 2 і 3 порівняно з групою 1. Значні покращення у якості сну були відзначені у групі 3, включаючи збільшення тривалості сну та ефективності сну. Вечірній прийом антигіпертензивних препаратів допомагає нормалізувати циркадний ритм артеріального тиску та зменшує жорсткість артерій, що сприяє покращенню загального стану здоров'я пацієнтів.

Ключові слова: нон-діппер гіпертензія, вечірній прийом ліків, якість сну, артеріальна жорсткість, циркадний ритм.

Arterial hypertension is a prevalent condition characterized by elevated blood pressure levels, which can lead to severe cardiovascular complications if left untreated. Among the various subtypes of hypertension, non-dipper arterial hypertension has attracted considerable attention due to its unique pathophysiologic features and association with adverse clinical outcomes. Unlike dipper hypertension, where blood pressure naturally declines during nighttime sleep, non-dipper hypertension is marked by a less pronounced nocturnal dip or even a nighttime rise in blood pressure. This abnormal circadian blood pressure pattern has been linked to increased risks of stroke, myocardial infarction, and other cardiovascular events [1].

The impact of non-dipper hypertension extends beyond cardiovascular health, as it has been closely associated with poor sleep quality. Sleep quality is a critical determinant of overall health and well-being, influencing cognitive function, emotional stability, and physical health. Numerous studies have demonstrated that individuals with non-dipper hypertension often experience disrupted sleep patterns, including frequent awakenings, reduced sleep efficiency, and decreased overall sleep duration [2]. The bidirectional relationship between sleep quality and blood pressure regulation suggests that poor sleep may exacerbate hypertensive conditions, creating a vicious cycle that further impairs cardiovascular health [3].

The mechanisms underlying the association between non-dipper hypertension and poor sleep quality are multifaceted. One key factor is the dysregulation of the autonomic nervous system (ANS), which plays a pivotal role in maintaining circadian blood pressure rhythms. In non-dipper hypertensive individuals, sympathetic nervous activity remains elevated during nighttime, leading to persistently high blood pressure and disrupted sleep architecture [4]. Furthermore, increased arterial stiffness, a condition commonly observed in hypertensive patients, has been implicated in the disruption of sleep. Arterial stiffness, characterized by the reduced elasticity of the arterial walls, leads to impaired hemodynamic responses and elevated nocturnal blood pressure, further contributing to poor sleep quality [5].

Given the significant health implications of non-dipper hypertension and its impact on sleep quality, effective treatment strategies are essential. Current therapeutic approaches primarily focus on antihypertensive medications and lifestyle modifications aimed at achieving optimal blood pressure control and improving sleep quality. Pharmacological treatments, including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers, and diuretics, have been shown to effectively reduce blood pressure and restore a more favorable circadian rhythm in non-dipper hypertensive patients [6]. However, the choice of medication should be tailored to individual patient profiles, considering factors such as comorbid conditions and medication tolerance, as was highlighted in large studies, in particular in the TIME study [7; 8].

In addition to pharmacotherapy, non-pharmacological interventions play a crucial role in managing non-dipper hypertension and enhancing sleep quality. Regular physical activity has been demonstrated to lower blood pressure and improve sleep patterns through its beneficial effects on autonomic function and metabolic health [9]. Dietary modifications, particularly the adoption of a diet rich in fruits, vegetables, whole grains, and low in sodium, can also contribute to better blood pressure control and improved sleep [10]. Body weight management, especially in individuals with obesity, is another critical aspect, as weight reduction has been associated with significant improvements in both hypertension and sleep quality [11].

Moreover, specific behavioral therapies, including cognitive-behavioral therapy for insomnia (CBT-I), can be effective in addressing sleep disturbances and promoting better sleep hygiene [12]. Additionally, addressing arterial stiffness through targeted interventions, such as aerobic exercise and medications like statins, may further enhance sleep quality and reduce the burden of non-dipper hypertension [13].

The objective of the study is to evaluate efficacy of bedtime administration of antihypertensive drugs and the pharmacological treatment of the sleep quality.

Materials and methods. The present study was conducted at the clinical bases of Ivano-Frankivsk National Medical University. The study protocol was reviewed and approved by the Ethics Committee of Ivano-Frankivsk National Medical University (protocol No. 137/23, 24.10.2023). All patients provided written informed consent before participation. The study adhered to the principles outlined in the Declaration of Helsinki, ensuring the ethical treatment of all participants.

A total of 65 patients with diagnosed non-dipper arterial hypertension were enrolled in the study. The patients were divided into three groups:

Group 1: 18 patients received a fixed combination of perindopril (8 mg) and indapamide (2.5 mg) administered in the morning.

Group 2: 25 patients received a fixed combination of perindopril (8 mg) and indapamide (2.5 mg) administered in the evening.

Group 3: 22 patients received a combination of perindopril (8 mg) and indapamide (2.5 mg) plus a combination of L-tryptophan and vitamins (Pineal-Tens) administered in the evening.

Patients included in the study were required to meet the following criteria:

Diagnosed with non-dipper arterial hypertension

Aged between 18 and 75 years

Provided informed consent

Exclusion criteria included:

Secondary hypertension

Significant cardiovascular events within the past six months

Chronic kidney disease (stage 3 or higher)

Severe hepatic impairment

Pregnancy or breastfeeding

The follow-up period for all patients was three months. During this time, patients underwent regular ambulatory blood pressure monitoring using the Cardiosense BP device (XAI-Medica, Ukraine). Blood pressure measurements were taken at 30-minute intervals during the day and 60-minute intervals during the night.

Arterial stiffness was evaluated using the Siemens NX3 Elite ultrasound machine (Siemens, Germany). The

technique employed for this assessment followed the protocol detailed in the study by J. Calabia, P. Torguet, M. Garcia, et al (Fig. 1) [14].

Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). This index is a validated questionnaire that assesses various aspects of sleep quality, including sleep duration, sleep disturbances, sleep latency, daytime dysfunction, and overall sleep satisfaction. The PSQI scores range from 0 to 21, with higher scores indicating poorer sleep quality.

Statistical analysis was performed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Kruskal-Wallis Test was used to compare the differences in continuous among the three groups. Chi-Square Test was applied to compare categorical variables. Bonferroni Correction was used for post-hoc analysis to identify specific group differences when the overall test was significant. A p-value of <0.05 was considered statistically significant for all analyses.

Results. The baseline characteristics of the study participants are summarized in Table 1.

The gender distribution showed a higher proportion of males in Group 1 (66.7%) and Group 3 (63.6%) compared to Group 2 (40.0%). While the gender distribution varied across the groups, the p-value of 0.14 indicates that these differences were not statistically significant. The median age of patients was comparable across the groups, with no significant differences (p=0.713). Most patients in all groups had not received previous antihypertensive treatment, with 83.3% in Group 1, 80.0% in Group 2, and 77.3% in Group 3 being treatment-naive. The differences were not statistically significant (p=0.893). The median BMI was similar across all groups, with no significant differences observed (p=0.728). Waist circumference, another important measure related to cardiovascular risk, showed no significant differences among the groups (p=0.829). The median sleep duration was similar among the groups, with Group 1 having a median of 8.44 hours, Group 2 with 8.23 hours, and Group 3 with 8.29 hours. There were no significant differences (p=0.743).

Overall, the baseline characteristics indicate that the three groups were well-matched in terms of gender distribution, age, previous treatment history, BMI, waist circumference, and sleep duration. These similarities ensure that any observed differences in treatment outcomes can be more confidently attributed to the interventions rather than baseline disparities among the groups.

The results of the ABPM and pulse wave velocity (PWV) for the three groups of patients are presented in Table 2.

Before treatment, the daytime systolic blood pressure (SBP) was comparable across all groups. Post-treatment, all groups showed a reduction in daytime SBP. The reduction was more pronounced in the evening medication groups (Groups 2 and 3), although the differences between groups were not statistically significant. This suggests that while all treatments were effective in lowering

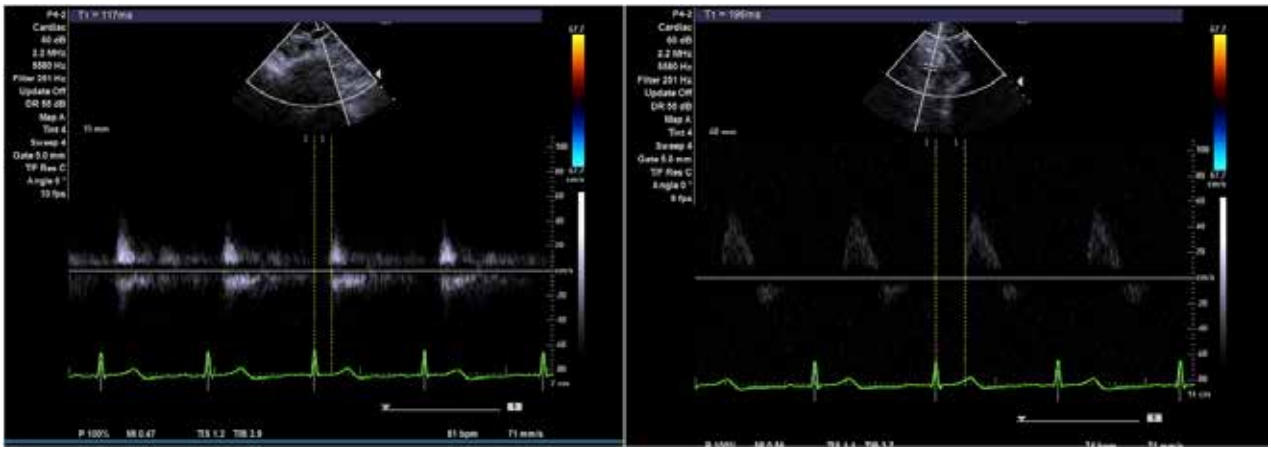

Fig. 1. Example of measurement of pulse wave velocity using ultrasound

Table 1

Baseline characteristics of the study participants

Variable Name	Group 1 (n=18)	Group 2 (n=25)	Group 3 (n=22)	p-value
Male	12 (66.7%)	10 (40.0%)	14 (63.6%)	0.14
Female	6 (33.3%)	15 (60.0%)	8 (36.4%)	
Age	55.50 [48.50;60.00]	53.00 [50.00;57.00]	55.50 [44.00;58.75]	0.713
Previous antihypertensive treatment – No	15 (83.3%)	20 (80.0%)	17 (77.3%)	0.893
Previous antihypertensive treatment – Yes	3 (16.7%)	5 (20.0%)	5 (22.7%)	
Body Mass Index (BMI) (kg/m^2)	28.43 [27.56;32.60]	28.40 [25.78;31.47]	28.35 [27.69;31.02]	0.728
Waist Circumference (cm)	98.64 [84.82;100.88]	95.47 [85.66;100.24]	93.27 [85.39;100.56]	0.829
Sleep Duration (hours)	8.44 [7.98;9.17]	8.23 [7.76;9.04]	8.29 [7.45;8.93]	0.743

Table 2

ABPM and PWV results of study population

Variable Name		Group 1 (n=18)	Group 2 (n=25)	Group 3 (n=22)
Day SBP, mmHg	Pre treatment	146.00 [134.00;151.25]	150.00 [143.00;153.00]	147.50 [139.25;154.50]
	Post treatment	126.50 [121.25;140.25]	120.00 [111.00;132.00]	123.00 [116.00;127.50]
	Δ%, p	-9.69%, p = 0.003	-18.14%, p < 0.001	-16.99%, p < 0.001
Night SBP, mmHg	Pre treatment	137.00 [126.50;142.00]	135.00 [127.00;143.00]	132.50 [124.50;139.25]
	Post treatment	120.50 [117.00;127.75]	113.00 [105.00;121.00]*	112.50 [100.50;116.50]*
	Δ%, p	-10.22%, p = 0.001	-14.69%, p < 0.001	-16.28%, p < 0.001
Mean SBP, mmHg	Pre treatment	140.50 [131.00;150.00]	143.00 [136.00;147.00]	133.00 [128.25;140.00]
	Post treatment	127.00 [121.00;133.00]	116.00 [107.00;120.00]*	114.00 [109.25;123.75]*
	Δ%, p	-10.82%, p = 0.002	-19.09%, p < 0.001	-14.65%, p < 0.001
Difference day/ night SBP, %	Pre treatment	4.00 [2.25;7.00]	6.00 [3.00;8.00]	6.00 [2.00;7.00]
	Post treatment	6.00 [5.00;8.00]	11.00 [10.00;12.00]*	16.50 [14.00;17.00]*#
	Δ%, p	55.56%, p = 0.023	91.78%, p < 0.001	212.73%, p < 0.001
Day DBP, mmHg	Pre treatment	88.00 [82.25;93.75]	92.00 [84.00;96.00]	86.00 [84.00;91.00]
	Post treatment	80.00 [76.50;85.00]	79.00 [75.00;83.00]	80.00 [75.00;84.75]
	Δ%, p	-8.14%, p = 0.022	-12.02%, p < 0.001	-8.35%, p < 0.001
Night DBP, mmHg	Pre treatment	77.00 [74.00;83.50]	82.00 [79.00;86.00]	81.00 [79.00;84.00]
	Post treatment	70.50 [64.50;74.50]	64.00 [61.00;68.00]*	66.00 [61.25;70.00]
	Δ%, p	-10.61%, p = 0.005	-21.19%, p < 0.001	-19.61%, p < 0.001
Mean DBP, mmHg	Pre treatment	85.00 [82.25;87.00]	84.00 [80.00;89.00]	86.50 [83.00;87.75]
	Post treatment	73.00 [70.25;76.25]	74.00 [70.00;78.00]	67.50 [63.25;71.00]*#
	Δ%, p	-13.34%, p < 0.001	-12.81%, p < 0.001	-20.12%, p < 0.001
Difference day/ night DBP, %	Pre treatment	4.00 [2.00;5.00]	6.00 [4.00;7.00]	6.00 [3.25;7.75]
	Post treatment	7.50 [6.00;9.75]	13.00 [11.00;15.00]*	16.50 [15.00;18.00]*#
	Δ%, p	88.16%, p = 0.001	128.08%, p < 0.001	198.33%, p < 0.001
Non-dipper	Pre treatment	18 (100,0%)	25 (100,0%)	22 (100,0%)
	Post treatment	16 (88,9%)	5 (20,0%)*	2 (9,1%)*#
Mean pulse pressure, mmHg	Pre treatment	62.00 [39.75;68.25]	57.00 [51.00;68.00]	60.00 [52.25;67.50]
	Post treatment	48.00 [36.25;59.00]	43.00 [31.00;54.00]	41.00 [35.50;47.75]
	Δ%, p	-12.17%, p = 0.257	-27.44%, p < 0.001	-29.52%, p < 0.001
PWV, m/s	Pre treatment	12.79 [11.64;14.74]	13.76 [12.39;15.04]	13.69 [12.31;14.55]
	Post treatment	12.29 [10.78;13.12]	9.36 [8.57;12.15]*	9.70 [8.57;12.47]*
	Δ%, p	-10.46%, p = 0.077	-24.56%, p < 0.001	-26.07%, p < 0.001

* – denotes a p value <0.05 between group 2 or 3 with group 1

\# – denotes a p value <0.05 between group 3 and 2

daytime SBP, evening administration might offer a slight advantage.

Initial nighttime SBP values were similar among the groups. After treatment, significant reductions in nighttime SBP were observed, especially in Groups 2 and 3, which received medication in the evening. This indicates that evening administration of antihypertensive drugs is more effective in controlling nighttime SBP, potentially providing better cardiovascular protection during sleep.

Mean SBP before treatment was consistent across groups. Following treatment, all groups experienced significant reductions, with the greatest reductions observed in the evening medication groups. This supports the hypothesis that evening administration of antihypertensive medication is more effective in achieving overall SBP control.

Before treatment, the day/night SBP differences were not significant between groups. Post-treatment, Groups 2 and 3 showed significantly greater improvements in day/night SBP differences, indicating that evening medication administration helps normalize the circadian blood pressure pattern more effectively.

Daytime diastolic blood (DBP) pressure values were similar across groups before treatment. Post-treatment reductions were observed in all groups, with no significant differences between them. This suggests that both morning and evening administration are effective in lowering daytime DBP.

Pre-treatment nighttime DBP was higher in Groups 2 and 3 compared to Group 1. Post-treatment, Groups 2 and 3 showed significant reductions, highlighting the effectiveness of evening administration in reducing nighttime DBP more effectively than morning administration.

Mean DBP before treatment was consistent across groups. Significant reductions were noted post-treatment in all groups, with the most pronounced reductions in Group 3, which included L-tryptophan and vitamins, suggesting an added benefit in overall DBP control.

Pre-treatment, day/night DBP differences were comparable across groups. Post-treatment, Groups 2 and

3 showed significantly greater improvements, indicating that evening medication administration more effectively normalizes circadian DBP patterns.

Initially, all patients were classified as non-dippers. Post-treatment, a significant reduction in non-dipper status was observed in Groups 2 and 3, indicating that evening administration of antihypertensive medication is more effective in restoring normal dipping patterns, which is associated with better cardiovascular outcomes.

Before treatment, pulse pressure was similar across groups. Post-treatment, reductions were observed in all groups, with Groups 2 and 3 showing more pronounced improvements, suggesting that evening administration of medication might better reduce pulse pressure.

PWV was similar across groups before treatment. Post-treatment, significant reductions in PWV were observed in Groups 2 and 3, indicating that evening administration of antihypertensive drugs, especially when combined with L-tryptophan and vitamins, is more effective in improving arterial stiffness.

The results suggest that evening administration of antihypertensive medication, particularly when combined with L-tryptophan and vitamins, offers superior control of blood pressure, especially nighttime SBP and DBP. This approach not only improves overall blood pressure control but also normalizes circadian blood pressure patterns, reducing non-dipper status, which is beneficial for cardiovascular health. The significant improvements in arterial stiffness with evening administration further support this regimen as a preferred strategy for managing non-dipper hypertension. These findings highlight the potential benefits of timing antihypertensive medication to align with circadian rhythms to enhance treatment efficacy and cardiovascular protection.

The dynamics of PSQI scores is demonstrated in Table 3.

Table 3

Dynamics of PSQI scores of study population

Variable Name		Pre-treatment		Post-treatment	
		Group 1/2/3, %	p value	Group 1/2/3, %	p value
Subjec-tive sleep quality	Very good	9/12/10 (50.0%/48.0%/45.5%)	0.916	10/14/20 (55.6%/56.0%/90.9%)	0.011*
	Fairly good	5/8/7 (27.8%/32.0%/31.8%)		4/6/2 (22.2%/24.0%/9.1 %)	
	Fairly bad	4/4/5 (22.2%/16.0%/22.7%)		3/4/0 (16.7%/16.0%/0.0 %)	
	Very bad	0/1/0 (0.0%/4.0%/0.0%)		1/1/0 (5.6%/4.0%/0.0%)	
Sleep latency (score)	No diffi-culty	8/14/10 (44.4%/56.0%/45.5%)	0.708	10/15/16 (55.6%/60.0%/72.7%)	0.579
	Mild diffi-culty	6/7/9 (33.3%/28.0%/40.9%)		4/7/5 (22.2%/28.0%/22.7%)	
	Mode-rate diffi-culty	1/3/1 (5.6%/12.0%/4.5%)		3/3/1 (16.7%/12.0%/4.5%)	
	Severe diffi-culty	3/1/2 (16.7%/4.0%/9.1%)		1/0/0 (5.6%/0.0%/0.0%)	
Sleep duration (score)	>7 hours	6/10/7 (33.3%/40.0%/31.8%)	0.865	7/12/18 (38.9%/48.0%/81.8%)	0.024
	6~7 hours	6/11/9 (33.3%/44.0%/40.9%)		5/10/4 (27.8%/40.0%/18.2%)	
	5~6 hours	5/4/5 (27.8%/16.0%/22.7%)		5/3/0 (27.8%/12.0%/0.0%)	
	< 5 hours	1/0/1 (5.6%/0.0%/4.5%)		1/0/0 (5.6%/0.0%/0.0%)	
Habitual sleep efficien-cy	>85%	11/14/14 (61.1%/56.0%/63.6%)	0.862	10/15/19 (55.6%/60.0%/86.4%)	0.032
	75~84%	5/6/5 (27.8%/24.0%/22.7%)		7/8/3 (38.9%/32.0%/13.6%)	
	65~74%	1/3/3 (5.6%/12.0%/13.6%)		0/2/0 (0.0%/8.0%/0.0%)	
	< 65%	1/2/0 (5.6%/8.0%/0.0%)		1/0/0 (5.6%/0.0%/0.0%)	
Sleep distur-bances	Never	5/8/7 (27.8%/32.0%/31.8%)	0.912	6/11/17 (33.3%/44.0%/77.3%)	0.007*
	<1 p/w	9/11/12 (50.0%/44.0%/54.5%)		10/11/5 (55.6%/44.0%/22.7%)	
	1 or 2 p/w	3/4/3 (16.7%/16.0%/13.6%)		1/2/0 (5.6%/8.0%/0.0%)	
	>3 times p/w	1/2/0 (5.6%/8.0%/0.0%)		1/1/0 (5.6%/4.0%/0.0%)	
Use of sleeping medica-tion	Never	16/22/19 (88.9%/88.0%/86.4%)	0.944	16/23/21 (88.9%/92.0%/95.5%)	0.877
	<1 p/w	1/1/2 (5.6%/4.0%/9.1%)		1/1/1 (5.6%/4.0%/4.5%)	
	1 or 2 p/w	1/2/1 (5.6%/8.0%/4.5%)		1/1/0 (5.6%/4.0%/0.0%)	
	>3 times p/w	0/0/0 (0.0%/0.0%/0.0%)		0/0/0 (0.0%/0.0%/0.0%)	
Daytime dysfun-ction	Never	16/21/18 (88.9%/84.0%/81.8%)	0.870	15/19/21 (83.3%/76.0%/95.5%)	0.285
	<1 p/w	1/2/3 (5.6%/8.0%/13.6%)		2/4/1 (11.1%/16.0%/4.5%)	
	1 or 2 p/w	0/1/0 (0.0%/4.0%/0.0%)		1/1/0 (5.6%/4.0%/0.0%)	
	>3 times p/w	1/1/1 (5.6%/4.0%/4.5%)		0/1/0 (0.0%/4.0%/0.0%)	

* – denotes a p value <0.05 between group 2 and 3 by Bonferroni equation

p/w – per week

Before treatment, subjective sleep quality ratings were similar across all groups (p=0.916). Post-treatment, Group 3 showed a significant improvement, with 90.9% rating their sleep as "Very good," compared to 55.6% in Group 1 and 56.0% in Group 2 (p=0.011). Pre-treatment sleep latency was similar across groups (p=0.708). After treatment, improvements were noted, particularly in Group 3, but differences were not statistically significant (p=0.579). Sleep duration was comparable pre-treatment (p=0.865). Post-treatment, Group 3 saw a significant increase, with 81.8% sleeping more than 7 hours, compared to 38.9% in Group 1 and 48.0% in Group 2 (p=0.024). Pre-treatment sleep efficiency was similar across groups (p=0.862). Post-treatment, Group 3 significantly improved, with 86.4% achieving over 85% sleep efficiency, compared to 55.6% in Group 1 and 60.0% in Group 2 (p=0.032). Frequency of sleep disturbances was similar pre-treatment (p=0.912). Post-treatment, Group 3 had significantly fewer disturbances, with 77.3% reporting no disturbances, compared to 33.3% in Group 1 and 44.0% in Group 2 (p=0.007). The use of sleeping medication was low and similar across all groups before and after treatment (p>0.05). Pre-treatment daytime dysfunction was similar across groups (p=0.87). Post-treatment, there were improvements, but no significant differences were found (p=0.285).

The study demonstrated significant benefits of evening administration of antihypertensive medication, especially when combined with L-tryptophan and vitamins, in improving both blood pressure control and sleep quality in non-dipper hypertensive patients. The results clearly indicate that evening administration effectively reduces nighttime systolic and diastolic blood pressure, improves arterial stiffness, and enhances sleep quality.

A critical point requiring further discussion is the potential and expediency of taking diuretics in the evening. This practice can lead to increased nocturnal diuresis, potentially decreasing sleep quality due to frequent awakenings. Diuretics are generally prescribed in the morning to avoid this issue, as nocturnal diuresis can significantly impair sleep and thereby counteract the benefits of the improved circadian rhythm achieved through evening medication administration.

Our findings suggest a reconsideration of the timing for diuretic administration in conjunction with antihypertensive therapy. Future studies should focus on evaluating the optimal timing for diuretics to maximize both cardiovascular and sleep quality outcomes.

Overall, while the results support the hypothesis that evening administration of antihypertensive drugs is beneficial, the impact of diuretics on nocturnal diuresis and sleep quality warrants careful consideration. Balancing effective blood pressure control with minimal disruption to sleep remains a crucial goal in managing non-dipper hypertension.

Conclusions

1. Evening administration of antihypertensive drugs (Groups 2 and 3) significantly reduced nighttime systolic and diastolic blood pressure compared to morning administration (Group 1).

2. The combination therapy with L-tryptophan and vitamins administered in the evening (Group 3) significantly improved subjective sleep quality, sleep duration, and habitual sleep efficiency.

3. The proportion of non-dipper patients significantly decreased in Groups 2 and 3, demonstrating that bedtime administration of antihypertensive drugs helps restore normal circadian blood pressure patterns. Bedtime administration of antihypertensive drugs, particularly when combined with sleep-enhancing agents, effectively reduces arterial stiffness.

The authors declare no conflict of interest.

Further research will focus on long-term efficacy and safety of bedtime antihypertensive therapy combined with sleep-enhancing agents, along with understanding the underlying mechanisms. Additionally, studies should explore personalized treatment strategies and the impact on major cardiovascular events to optimize patient outcomes.

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