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Analysis of blood pressure parameters and circadian variations in patients with transient global amnesia

Analiza parametrów ciśnienia tętniczego i jego dobowej zmienności u pacjentów z przejściową niepamięcią całkowitą

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Abstract

Introduction and objective: Transient global amnesia (TGA) remains one of the most enigmatic neurological diseases. The results of latest studies indicate a strong association between acute hypertensive peaks and TGA. Elevated blood pressure (BP) is the most frequently observed clinical feature accompanying TGA. Animal studies indicate that BP peaks may lead to oxidative stress affecting mainly the CA1 sector of the hippocampus (a crucial structure for memory processing). **Materials and methods:** Single-centre, retrospective, cross-sectional medical records analysis of 65 patients with TGA and 64 patients with transient ischaemic attack (TIA) (control group). Analysis included systolic and diastolic BP (SBP and DBP), mean arterial pressure (MAP), pulse pressure (PP) values at admission, as well as mean and maximal circadian values of these parameters from 24-hour ambulatory blood pressure monitoring. Circadian BP variations were also assessed. **Results:** Patients with TGA presented significantly higher SBP, DBP, MAP and PP values at hospital admission ($p < 0.05$). No significant differences between both groups were found in 24-hour ambulatory blood pressure monitoring for mean and maximal SBP, mean MAP, and maximal PP. Maximal MAP and DBP were significantly lower in the TGA group. Abnormal circadian BP rhythms predominated in both groups. Regardless of circadian BP variation, SBP and PP values at admission were significantly higher in patients with TGA. **Conclusions:** Extremely elevated BP is related to the occurrence of TGA. These elevated values are not sustained after the end of the acute phase of TGA.

Keywords: blood pressure, TGA, arterial hypertension, transient global amnesia

Streszczenie

Wstęp: Przejściowa niepamięć całkowita (*transient global amnesia*, TGA) pozostaje jedną z najbardziej zagadkowych chorób neurologicznych. Wyniki najnowszych badań wskazują na silny związek między nagłymi wysokimi skokami ciśnienia tętniczego a TGA. Podwyższone ciśnienie tętnicze (*blood pressure*, BP) jest najczęstszym stanem klinicznym towarzyszącym TGA w ostrej fazie. W badaniach na zwierzętach wykazano, że nagły wzrost BP może powodować stres oksydacyjny zlokalizowany głównie w neuronach sektora CA1 hipokampa (struktura kluczowa w procesie zapamiętywania). **Cele:** Celem pracy była analiza parametrów BP i jego dobowej zmienności u pacjentów z TGA wkrótce po wystąpieniu epizodu. **Materiał i metody:** Jednoośrodkowa, retrospektywna, przekrojowa analiza dokumentacji medycznej 65 pacjentów z TGA i 64 pacjentów z przemijającym niedokrwieniem mózgu (*transient ischaemic attack*, TIA) (grupa kontrolna). Analizie poddano wartości skurczowego (*systolic* BP, SBP), rozkurczowego (*diastolic* BP, DBP) i średniego BP (*mean arterial pressure*, MAP), a także ciśnienia tętna (*pulse pressure*, PP) przy przyjęciu do szpitala oraz średnie i maksymalne wartości dobowe tych parametrów w całodobowym ambulatoryjnym monitorowaniu ciśnienia krwi. Oceniono również dobową zmienność BP u tych chorych. **Wyniki:** Pacjenci z TGA w porównaniu z pacjentami z TIA przy przyjęciu do szpitala wykazywali istotnie wyższe wartości SBP, DBP, MAP i PP ($p < 0,05$). Nie stwierdzono istotnych różnic pomiędzy obiema grupami w 24-godzinnym ambulatoryjnym monitorowaniu ciśnienia krwi w zakresie średniego i maksymalnego SBP, średniego MAP i maksymalnego PP.

W obu grupach dominowały nieprawidłowe rytmy dobowe BP. Niezależnie od dobowej zmienności BP wartości SBP i PP przy przyjęciu do szpitala były istotnie wyższe u pacjentów z TGA. **Wnioski:** Ekstremalnie wysoki wzrost wartości BP ma związek z występowaniem TGA. Tak wysokie wartości nie występują po zakończeniu ostrej fazy TGA.

Słowa kluczowe: ciśnienie tętnicze, TGA, nadciśnienie tętnicze, przejściowa niepamięć całkowita

INTRODUCTION

Transient global amnesia (TGA) is an acute, temporary, and reversible short-memory disorder lasting up to 24 hours, without any accompanying focal neurological symptoms (Arena and Rabinstein, 2015; Mancia et al., 2023; Sparaco et al., 2022a, 2022b). The diagnosis is based on the criteria proposed by Hodges and Warlow (1990). The aetiology of TGA is not well understood. Several factors, including cerebral ischaemia, venous flow abnormalities, migraine, and epilepsy, have been discussed as possible causes. In 2020, Ding and Peng proposed a pathophysiological model based on cortical spreading depression (CSD). In 2022, Larner et al. introduced an extended version of this model, based on functional conduction disorders within the internal neuronal networks of the limbic system responsible for memory (especially in the CA3 sector) as a result of excessive positive feedback initiated probably by CSD (Larner et al., 2022).

Arterial hypertension (AH) is the most common vascular risk factor, and highly elevated blood pressure (BP) is the most frequently observed clinical feature accompanying TGA (Dziubek and Dziubek, 2024; Taheri et al., 2023). Circadian BP rhythm is characterised by a nocturnal fall and a diurnal rise. Ambulatory blood pressure monitoring (ABPM) enables the analysis of mean and maximal circadian BP values and variations. There are four types of circadian BP variability: "dipper" (physiological), with nocturnal BP falls by >10% and ≤20%; "non-dipper", with a reduced (≤10%) nocturnal BP fall; "extreme dipper", with an excessive BP fall (>20%); and "reverse dipper", characterised by a nocturnal BP rise (Mancia et al., 2023).

The aim of the study was to analyse BP parameters and circadian BP variations in patients with TGA during the acute phase and shortly after its resolution.

MATERIALS AND METHODS

Medical records of 78 patients diagnosed with TGA and hospitalised in the single-centre Stroke Unit from January 2016 to December 2023 were subjected to retrospective cross-sectional analysis. The following inclusion criteria were applied:

- admission to hospital within 24 hours of symptom onset;
- documented BP measurement at admission;
- ABPM performed after the acute phase of the disease;
- no symptoms of focal central nervous system damage in clinical and radiological examinations;
- exclusion of epilepsy.

Inclusion criteria were met in 65 cases, which were subsequently analysed.

Upon admission, each patient underwent a single automatic non-invasive BP measurement. Hypertension grade was then determined (Mancia et al., 2023). Mean arterial pressure (MAP) was estimated based on the following formula: MAP [mm Hg] = 2/3 × DBP (diastolic blood pressure) + 1/3 × SBP (systolic blood pressure). Pulse pressure (PP) was calculated by subtracting DBP from SBP. During hospitalisation (on the second or third day), each patient underwent ABPM using the Aspel HolCARD CR-07 device and software. Mean and maximal circadian BP values were determined, along with the circadian variability profile. The ABPM record was divided into two periods:

- "I"/diurnal, 6:00 a.m.–10:00 p.m.; BP measurements every 20 minutes;
- "II"/nocturnal, 10 p.m.–6 a.m.; BP measurements every 30 minutes.

The threshold value for the average BP for the "I" period was 135/85 mm Hg, for the "II" period – 120/70 mm Hg, and for 24-hour recordings – 130/80 mm Hg (Mancia et al., 2023). Records with >70% effective measurements were considered diagnostic. A similar retrospective analysis of medical records was performed in 64 patients with transient ischaemic attack (TIA), who met the inclusion criteria and sequentially added until a comparable cohort was obtained. The complete anonymity of the patients was maintained, the documentation was not made available to third parties, and only the data necessary for the study were viewed.

Statistical analysis

Statistical analysis was performed using MS Excel 2013 and Statistica 13.3 software. The Shapiro–Wilk test was applied to check the distribution of variables. If the data distribution was normal, the Student's *t*-test was used; otherwise, the Mann–Whitney test was employed. The results were presented as arithmetic means ± standard deviation. Also, *p*-values <0.05 were considered statistically significant.

RESULTS

Patients with TGA (n = 65) were statistically younger than those with TIA (n = 64) and had a higher proportion of women (Tab. 1). 72.3% (n = 47) of the patients with TGA had been diagnosed with AH before hospitalisation (vs. 89.1%; n = 57 in control group), and 98% of them at admission had BP values exceeding the normal range. A direct relationship was found between the number of patients with

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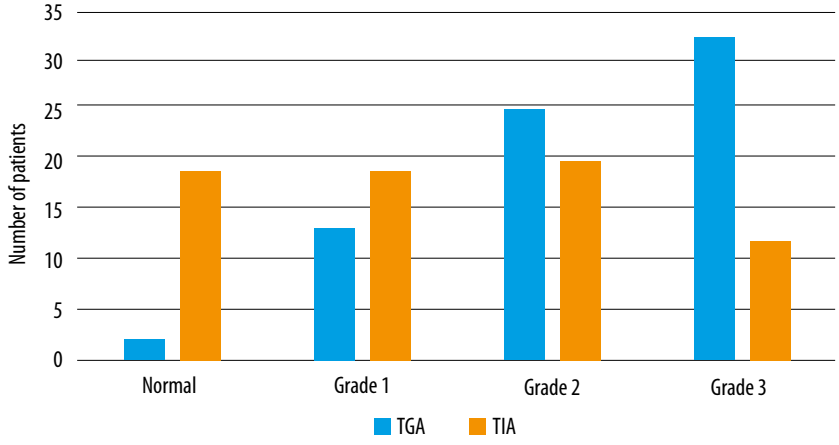
	TGA ($n = 65$)	TIA ($n = 64$)	Statistics
Sex ratio: female to male [%]	72 vs. 28	53 vs. 47	–
Average age [years] **Women** **Men**	66.9 ± 6.9 68.3 ± 7.4 63.5 ± 3.6	71.4 ± 10.3 71.9 ± 9.6 70.9 ± 11.1	$p < 0.05; t = -2.92$ $p < 0.05; t = 2.94$ $p < 0.05; t = -2.95$
History of hypertension [%]	72.3	89.1	–
History of diabetes [%]	16.9	39.1	–

TGA – transient global amnesia; **TIA** – transient ischaemic attack.

Tab. 1. Comparative characteristics of patients with TGA and TIA



TGA – transient global amnesia; **TIA** – transient ischaemic attack.

Fig. 1. Comparison of hypertension grades at admission according to the European Society of Cardiology/European Society of Hypertension 2023 guidelines

TGA and the AH grade; in the control group, the relationship was inversely proportional (Tab. 1, Fig. 1). During hospitalisation, AH was diagnosed *de novo* in 18% ($n = 12$) of patients with TGA and in 8% ($n = 4$) of patients with TIA. Patients with TGA presented significantly higher SBP, DBP, MAP, and PP values at admission compared to patients with TIA ($p < 0.05$) (Tab. 2). Pulse pressure values at admission exceeded the upper limit of normal in 90% ($n = 59$) of patients with TGA and 62.5% ($n = 40$) of patients with TIA. In 66% ($n = 43$) of patients with TGA and 25% ($n = 16$) of patients with TIA, systolic blood pressure values measured at admission were higher than the maximum SBP values recorded in the 24-hour ABPM study. A similar relationship was noted for PP (91%; $n = 59$ vs. 63%; $n = 40$).

	TGA ($n = 65$)	TIA ($n = 64$)	Statistics
SBP [mm Hg]:			
• at admission	174.6 ± 19.6	154.0 ± 25.2	$p < 0.05; t = 5.2$
• averages in the ABPM recording	124 (117–134)	128.8 ± 16.5	$p = 0.06; Z = -1.55$
• maximal in the ABPM recording	161 (153–172)	167.8 ± 20.9	$p = 0.08; Z = -1.42$
DBP [mm Hg]:			
• at admission	90 (85–100)	84.5 ± 14.8	$p < 0.05; Z = 2.89$
• averages in the ABPM recording	76.1 ± 9.5	75.0 ± 10.7	$p = 0.34; t = 0.39$
• maximal in the ABPM recording	99.2 ± 12.8	106 (96.8–117.3)	$p < 0.05; Z = -3.09$
MAP [mm Hg]:			
• at admission	119.2 ± 13.7	107.7 ± 16.7	$p < 0.05; t = 4.29$
• averages in the ABPM recording	91.6 ± 10.7	93.0 ± 11.9	$p = 0.17; t = 0.96$
• maximal in the ABPM recording	120.3 ± 12.7	128.4 ± 16.4	$p < 0.05; t = -3.11$
PP [mm Hg]:			
• at admission	80 (70–90)	69.7 ± 18.7	$p < 0.05; Z = 4.26$
• averages in the ABPM recording	48 (43–56)	50 (45.8–59.3)	$p < 0.05; Z = -2.31$
• maximal in the ABPM recording	61 (50–73)	59.2 ± 13.7	$p = 0.09; Z = 1.31$

ABPM – ambulatory blood pressure monitoring; **DBP** – diastolic blood pressure; **MAP** – mean arterial pressure; **PP** – pulse pressure; **SBP** – systolic blood pressure; **TGA** – transient global amnesia; **TIA** – transient ischaemic attack.

Tab. 2. Comparison of blood pressure parameters in patients with TGA and TIA

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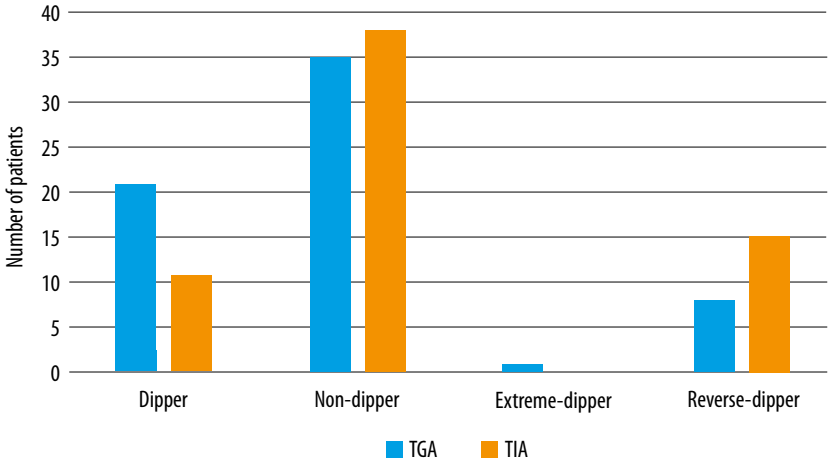

TGA – transient global amnesia; **TIA** – transient ischaemic attack.

Fig. 2. Number of patients with particular types of circadian BP variability

There were no significant differences in the mean circadian values of SBP ($p = 0.06$), DBP ($p = 0.34$), and MAP ($p = 0.17$) recorded with ABPM. However, mean circadian PP values were significantly higher in patients with TIA ($p < 0.05$). No significant differences were found between maximal circadian SBP ($p = 0.08$) and PP ($p = 0.09$) values. Maximal DBP ($p < 0.05$) and MAP ($p < 0.05$) values were higher, while maximal circadian PP values were insignificantly lower in the control group (Tab. 2). Abnormal circadian BP rhythm (non-dipper) predominated in both groups (53.8% vs. 60.9%) (Fig. 2). Physiological nocturnal BP fall (dipper) was found in 32.4% patients with TGA and 17.2% with TIA. Regardless of circadian BP profile (excluding extreme-dipper from the analysis due to the small number of cases), SBP and PP values at admission were significantly higher in patients with TGA ($p < 0.05$) (Tab. 3).

DISCUSSION

TGA remains one of the most enigmatic neurological disorders. The results of latest studies indicate a strong association between acute hypertensive peaks and TGA, as well as the crucial influence of BP fluctuations on the pathophysiology of cerebral ischaemia (Rogalewski et al., 2021). Referring to animal studies, acute, high BP peaks may lead to increased permeability of cerebral microvessels, local neuroinflammation, and oxidative stress primarily affecting the hippocampus and regions of the cerebral cortex controlling cognitive functions (Mohammadi and Dehghani, 2014; Poulet et al., 2006). The CA1 sector of the hippocampus plays a crucial role in the memorisation process and shows selective vulnerability to oxidative and metabolic stress, mediated by glutamate excitotoxicity and calcium influx (Bartsch and Deuschl, 2010). Considering all these reports, high BP elevation may be potentially related to metabolic stress in hippocampal cells and trigger the onset of TGA symptoms through the CSD mechanism.

The demographic data obtained in our study were consisted with previous findings (Rogalewski et al., 2021, 2022; Waliszewska-Prosol et al., 2020), but the prevalence of AH was more prominent (Taheri et al., 2023). In the studies conducted by Rogalewski et al. (2021, 2022), hypertensively dysregulated BP at hospital admission in TGA patients was significantly higher compared to TIA patients – an observation confirmed by our findings. It was suggested that TGA-patients are not well adapted to high BP episodes, although this conclusion was based solely on single BP measurements at hospital admission (Rogalewski et al., 2021). In our study, BP measurements at admission were compared to mean and maximum circadian BP values obtained

	TGA ($n = 65$)	TIA ($n = 64$)	Statistics
SBP at admission depending on the type of circadian BP variation [mm Hg]:			
• dipper	172.6 ± 23.7	141.8 ± 18.0	$p < 0.05; Z = 4.94$
• non-dipper	169.7 ± 16.1	155.9 ± 28.5	$p < 0.05; Z = -4.93$
• reverse-dipper	191.5 ± 16.3	149.6 ± 21.0	$p < 0.05; Z = -4.95$
PP at admission depending on the type of circadian BP variation:			
• dipper	83.1 ± 15.1	67.1 ± 15.1	$p < 0.05; Z = 4.05$
• non-dipper	89.7 ± 16.1	73.5 ± 28.5	$p < 0.05; Z = -4.21$
• reverse-dipper	96.8 ± 17.1	61.5 ± 21.0	$p < 0.05; Z = -4.05$

BP – blood pressure; **SBP** – systolic blood pressure; **PP** – pulse pressure; **TGA** – transient global amnesia; **TIA** – transient ischaemic attack.

Tab. 3. SBP and PP values at admission depending on the type of circadian variability of BP

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via ABPM. Average circadian SBP, DBP, MAP, as well as maximal circadian SBP and PP values, were similar in both groups. Therefore, after the acute phase, patients with TGA and TIA appear to be equally adapted to BP fluctuations. At admission (acute phase), sympathetic BP dysregulation is much more prominent in TGA patients – they reached record-high SBP and PP values, exceeding the maximal circadian values recorded in ABPM.

Latest studies showed no correlation between elevated BP and the recurrence of TGA (Kim et al., 2021; Mathews et al., 2021; Morris et al., 2020; Obara et al., 2020) because acute BP peaks were observed in patients with both single and recurrent episodes of TGA. Risk factors for TGA recurrence include coexisting migraine and depression.

Our study showed that disruptions in circadian BP variability predominated in both groups but in TGA patients they were less expressed. No comparable studies have been identified to assess or support this specific finding.

CONCLUSIONS

Patients with TGA, at the time of hospital admission (during the acute phase), exhibited significantly higher SBP and PP values than usual and more prominent compared to patients with TIA. These findings may suggest a relationship between TGA occurrence and dysregulation of autonomic blood pressure control, which could be responsible for BP peaks during the acute phase. After 24 hours, both groups showed a similar level of autonomic BP control disturbances. Patients with TGA are less prone to develop AH compared to those with TIA.

LIMITATIONS

Repetitive BP measurements during the acute phase are needed to better characterise BP variability during and after the acute phase of the disorder. It is necessary to conduct studies on larger cohorts to better understand the relationship between BP fluctuations and TGA. The limited reproducibility of circadian variations on 24-hour ABPM may be overcome by extending the recording period from 24 to 48 hours (Machado, 2018).

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Author contribution

Original concept of study; collection, recording and/or compilation of data; final approval of manuscript: DD. Analysis and interpretation of data; writing of manuscript; critical review of manuscript: DD, KD.

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